

APMF

ASIA PACIFIC MENOPAUSE FEDERATION
THE 8TH SCIENTIFIC MEETING
第八届亚太绝经联盟 (APMF) 学术大会



ASIA PACIFIC
MENOPAUSE
FEDERATION

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2021

THE 8TH SCIENTIFIC MEETING ABSTRACT BOOK



中国·杭州 | 2021年10月14-17日
HangZhou, China | October 14-17, 2021

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Effects of Psychosomatic Mutual Aid Treatment on anxiety and depression in Turner Syndrome

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Background

Turner syndrome (TS) affects approximately one out of 2500 females. Previous research indicates that girls with TS experience psychosocial impairment in addition to their physical health issues. However, there is no current data demonstrating whether reducing the clinical symptoms of girls or women with TS through hormone replacement therapy (HRT) combined with psychological interventions, referred to as psychosomatic mutual aid treatment (PMAT), improves physical and psychological self-identification, so that psychological problems such as anxiety, depression, low self-esteem, social loneliness and psychological resilience are improved. Therefore, the objective of this research was to assess the efficacy of PMAT on anxiety and depression in girls and women with TS.

Methods

Twenty-six girls and women with TS aged 11-29 years (17.5 ± 4.2 years) were recruited. Anxiety and depression were assessed using Hamilton Anxiety Rating Scale (HAMA) and Zung Self-Rating Depression Scale (SDS) questionnaires respectively. The 26 TS patients were surveyed for anxiety and depression before the beginning of PMAT and again in January 2020. In addition, 20 healthy volunteer women aged 16-39 years (23.1 ± 5.7 years) were selected as the control group and filled in the questionnaire.

Results

Pre-therapy (pre-HRT and Pre-PMAT) there were significant differences between the TS patients ($n=26$) and healthy controls ($n=20$). In particular, the TS patients had higher anxiety status ($P=0.04$) and severity ($P=0.03$) (HAMA score), as well as depression status ($P=0.002$) and severity ($P<0.001$) (SDS score). Post-therapy there was no longer any difference in depression scores, but TS patients still had higher levels of anxiety post-therapy compared with healthy control women (psychic symptoms score, $P=0.03$; anxiety status score, $P=0.04$; anxiety severity score, $P=0.04$). In the TS patients, there was an improvement in depression scores (SDS score $P<0.001$; depression severity score, $P=0.005$) after therapy but no change in levels of anxiety.

Conclusions

PMAT significantly improves depression status, but not anxiety, in girls and women with TS.

Key words Keywords Turner syndrome; Psychosomatic Mutual Aid Treatment (PMAT); Depression; Anxiety; Hormone replacement therapy (HRT)

A NOVEL COMBINED MODEL FOR PREDICTING THE RECURRENCE IN ENDOMETRIAL CANCER

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Background: The aim of this study was to establish a nomogram to predict the recurrence of endometrial cancer(EC) by adding immunohistochemical markers to the traditional clinical and pathological parameters.

Methods: The archived data of 537 patients with stage I-III endometrial cancer who received primary surgical treatment between October 2013 and May 2018 were retrieved and analyzed. Data of 473 included cases were randomly split into two sets: training and validation in a predefined ratio of 7:3. A univariate regression was performed to screen factors associated with recurrence in EC in the training cohort (n=332), and a Cox proportional hazards multivariate model of selected prognostic features was applied to develop a nomogram, which was further validated in the validation cohort (n=141). The prediction capabilities of different combinations of parameters were also compared to confirm the capacity of this proposed model in clinical utility.

Results: There were 47 recurrent cases in the training cohort and 20 cases in the validation cohort. Screened by univariate Cox regression, FIGO stage, histological type, histological grade, myometrial invasion, cervical stromal invasion, postoperative adjuvant treatment, adequate treatment, and four immunohistochemical makers were the most related factors for recurrence in EC, among which FIGO stage, histological type, ER and P53 were considered statistically and clinically correlated with recurrence in EC. Therefore, recurrence-free survival (RFS) was best predicted by the proposed nomogram with a C-index of 0.88 (95% confidence interval (CI), 0.84 - 0.92), and the validation set confirmed the findings with a c-index of 0.79 (95% CI, 0.66 - 0.92).

Conclusions: Immunohistochemical markers in addition to traditional clinicopathological parameters can best predict the recurrence in FIGO stage I-III EC. This nomogram model was demonstrated to be a robust tool for predicting recurrence free survival rate. Young women with early stage EC would also be benefited in consultation for fertility preservation.

Key words ENDOMETRIAL CANCER; RECURRENCE; PREDICTING MODEL

SIRT1-mediated oxidative phosphorylation in protection of ovarian reserve

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Objective

Oxidative stress inhibits follicular growth and development, and is an important cause of premature ovarian insufficiency (POI). However, the underlying mechanism remains unclear. Thus, we aimed to build an oxidative stress-induced POI model and explore the underlying mechanism.

Methods

3-nitropropionic acid (3-NPA) was used to induce a decrease in ovarian reserve. SIRT1 was knocked down in human granulosa cells (GCs) using lentiviral injections and its role in the function of human GCs was examined. Furthermore, the effects of a SIRT1 inhibitor and agonist on mitochondrial oxidative phosphorylation and apoptosis were studied *in vivo*.

Results

The knockdown of SIRT1 impaired the hormone synthesis capacity of human GCs and decreased receptor expression. SIRT1 affected ovarian function and induced apoptosis via oxidative phosphorylation.

Conclusion

Intraperitoneal injection of 3-NPA can effectively induce POI in mice via increased oxidative stress. SIRT1 affects ovarian function via mitochondrial oxidative phosphorylation and inhibits follicular apoptosis. This study is of great significance for disease prevention and exploration of clinical therapeutic targets for POI.

Key words Ovarian reserve , Premature ovarian insufficiency, SIRT1, oxidative phosphorylation

Study on the correlation between body mass index and breast lesions in perimenopausal and early menopausal women

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Abstract Objective: To investigate the correlation between body mass index (BMI) and breast density and breast lesions in perimenopausal and early menopausal women, and the influence of different types of breast density on the prevalence of breast calcification and breast masses. Methods: 82 healthy women in perimenopausal and early menopause were enrolled, and grouped according to the body mass index and breast density type of the subjects: ①Grouped according to body mass index: 57 cases of ideal body size ($18 \text{ kg/m}^2 \leq \text{BMI} < 24 \text{ kg/m}^2$), 25 cases of high body recombination ($24 \leq \text{BMI} \leq 30 \text{ kg/m}^2$); grouped according to breast density: 65 cases of fat type group ($0\% \leq \text{MD} < 25\%$), 17 cases of scattered fiber gland group type ($25 \leq \text{MD} < 50\%$). Research subjects received mammography examination, and used Quantra software to detect the breast density of both breasts, record the occurrence of breast calcification and breast lumps for analysis. Results: Comparison of ideal body remodeling and high body remodeling, breast density, There was no statistically significant difference in the incidence of breast calcification ($P > 0.05$); the incidence of breast fibrous tissue volume, breast volume, and breast mass in high-body reorganization was higher than that in ideal body reorganization, and the difference was statistically significant ($P < 0.05$); scattered fibers Comparing the glandular type group with the fat type group, there was no significant difference in the rate of breast calcification and the incidence of breast masses ($P > 0.05$). Conclusion: There is no significant difference in breast density in perimenopausal and early menopausal women with different BMI, but high body weight The incidence of breast fibrous tissue volume, breast volume, and breast masses is increased. There is no obvious correlation between the different types of breast density and the incidence of breast masses.

Key words Body Mass Index, Breast Density, Breast Calcification, Breast Mass, Breast Lesions

Optimized menopausal hormone treatment on breast lesions in Chinese perimenopausal women

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Objective: To investigate the effect of menopausal hormone therapy (MHT) on breast lesions in women of perimenopausal age in China, and to provide effective evidence for MHT intervention.

Methods: A total of 160 perimenopausal women aged 40 to 60 years were enrolled in the study. Of these, 80 women on hormone therapy were enrolled in the study group and 80 who had never taken hormone therapy were included in the control group. According to the different MHT regimens, the study group was divided into three subgroups: Group A received estrogen and progestogen sequential combined therapy; Group B received estrogen and progestogen continuous combined therapy; Group C received estrogen-only therapy for having hysterectomy before. All participants were voluntarily underwent mammography before MHT initiation and in the following two more years. Finally, we recorded and analyzed their information, primarily the changes of breast density, volume of breast fibrous tissue, the volume of breast, the detection rate of calcification and mass of all participants.

Results: A total of 80 perimenopausal women were enrolled in the MHT group, 49 in group A, 26 in group B, 5 in group C, and 80 were in control group. The follow-up survey showed that there was no statistical difference in breast density, breast fibrous tissue volume, breast volume before and after MHT intervention among different groups, the difference between groups and the time interaction were not statistically significant ($P>0.05$); The detection rate of breast calcification and breast mass between the study group and the control group were statistically significant before and after intervention ($P<0.05$), while there was no significant difference between the groups and the interaction between groups and time ($P>0.05$).

Conclusion: The risk of breast disease in perimenopausal women was not found to be related to MHT intervention.

Key words Perimenopause; Menopausal hormone therapy; Mammographic density; Breast fibrous tissue volume; Breast calcification

Correlation Analysis between Expression of E-Cadherin, N-Cadherin and Clinicopathological Characters in Endometrial Cancer with MMR Protein Deficiency

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Objective: To analyze the correlation between the clinicopathological features and the expression of E-cadherin and N-cadherin in patients with MMR protein-deficient endometrial carcinoma. **Methods:** 40 cases of postoperative pathological confirmed endometrial cancer patients with MMR (-) were selected in our hospital from January 2016 to June 2018, another control group include 40 cases of endometrial cancer with MMR (+) were recruited as peer. Immunohistochemical staining of paraffin-embedded specimens sections was performed with E-Cadherin and N-Cadherin monoclonal antibodies, The correlation between the differential expression of E-Cadherin, N-Cadherin and clinicopathological parameters were comparatively analyzed. **Results:** The positive rate, total staining intensity and number of positive cells in MMR(-) endometrial cancer tissue were lower than those in MMR(+) type, but the expression of N-cadherin showed opposite trend, shown the statistically difference ($P < 0.01$). The expression of E-cadherin and N-cadherin was negatively correlated in MMR (-) EC ($r = -0.729$, $P < 0.01$). The expression of E-cadherin was correlated with age, pathological type, FIGO stage, histological differentiation, lower site tumor infiltration in uterine cavity, vaginal and paracervical invasive, depth of infiltration of myometrium, LVSI and lymph node metastasis ($r > 0.5$, $P < 0.05$). The expression of N-cadherin was correlated with age, pathological type, FIGO stage, histological differentiation, depth of infiltration of myometrium, vaginal and paracervical invasive, and LVSI ($r > 0.5$, $P < 0.05$), but there was no significant correlation with lower site tumor infiltration in uterine cavity and lymph node metastasis ($P > 0.05$). **Conclusions:** The expression of E-cadherin/N-cadherin have different trend in MMR (-) EC from that of MMR (+) EC, shows differentiation of epithelial-mesenchymal transformation, which may lead to the differences of clinicopathological characteristics.

Key words MMR protein; Endometrial cancer; Lynch syndrome; E-cadherin; N-cadherin

Application of gynecological rong Capsule in menopausal syndrome

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[Abstract] Objective: To observe the effect of gynecological rong capsule in the treatment of menopausal syndrome.

Methods: 100 patients with menopausal syndrome in our menopause clinic from October 2019 to October 2020, 20 cases were randomly divided into treatment group and 50 control group according to the order of visits. The treatment group began oral gynecological rong capsules on the day ,and the 21d; control group took 21d gluvitamin on the day. Menopause- related symptoms were observed in 2 groups, and their efficacy was assessed.

Results: The insomnia, heat drying and irritability were significantly improved, the control group and the difference ($P < 0.05$). Conclusion :Gynecrong capsule can effectively improve menopausal syndrome and be the clinical promotion

Key words gynecological Yangrong capsule; perimenopausal syndrome;

The value of neutrophil/lymphocyte ratio (NLR) in predicting abnormal lipid metabolism in peri-menopausal women

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Objective To explore the value of neutrophil/lymphocyte ratio (NLR) in predicting abnormal lipid metabolism in peri-menopausal women.

Methods A total of 149 peri-menopausal women (age 40-60 y) who visited the gynecological clinic of the Third Affiliated Hospital of Soochow University from January 2020 to January 2021 were selected and divided into groups according to whether the patients had abnormal blood lipid metabolism, that is, the non-dyslipidemia group and the dyslipidemia group. Measure the patient's height and weight, and detect the patient's serum neutrophils, platelets, lymphocytes, fasting blood glucose, fasting insulin, C-reactive protein (CPR), triacylglycerol (TG), high-density lipoprotein (HDL), and low-density fat Protein (LDL), apolipoprotein A1 (ApoA1) and apolipoprotein B (ApoB) levels, calculate NLR, platelet/lymphocyte ratio (PLR), body mass index (BMI), and Compare the differences between the two groups.

Results The levels of NLR, BMI, TG, LDL, ApoB, and CRP in the abnormal lipid metabolism group were significantly higher than those in the non-lipid metabolism group, and the difference was statistically significant ($P < 0.05$). The level of ApoA1 in the abnormal lipid metabolism group was lower than that in the non-lipid metabolism group, and the difference was statistically significant ($P < 0.05$). Binary logistic regression analysis showed that NLR was an independent risk factor for abnormal lipid metabolism (95%CI was 1.268-4.249, $P < 0.05$), and the best cut-off point of NLR was 2.87 (AUC=0.781, 95%CI was 0.699-0.863, Youden index 54%, sensitivity = 63.8%, specificity = 90.2%).

Conclusion The ratio of neutrophils to lymphocytes reflects the inflammatory state and immune response level in the body, and is an economical inflammatory response index. This study shows that NLR changes are closely related to abnormal blood lipid metabolism in peri-menopausal women, and it is expected to become a predictor of blood lipid metabolism in peri-menopausal women.

Key words neutrophil/lymphocyte ratio; abnormal lipid metabolism; menopause

A combination of Bone marrow mesenchymal stem cells with estrogen improves rabbit endometrial injury repair by a mechanism involved in an activation of Wnt/ β -catenin signaling

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Although the effect of bone marrow mesenchymal stem cells (BMSCs) combined with estrogen therapy in the repair of endometrial injury has been confirmed, its underlying molecular mechanism in intrauterine adhesion (IUA) remains unclear. In this study, we aim to investigate the effect and involvement of a combination of BMSCs with estrogen in restoration of injured endometrium by applying a rabbit endometrial injury model. The results revealed by immunofluorescence showed that red fluorescent dye (PKH-26)-labelled BMSCs can differentiate into endometrial epithelial cells in vivo. At 3W after combined treatment of BMSCs and estrogen, the uterine cavity morphology basically recovered to normal, the number of glands increased significantly, and the area of fibrosis reduced evidently, accompanied by a downregulation of mesenchymal markers and upregulation of epithelial markers when compared with each single treatment group. In addition, the expression levels of core molecules in the Wnt/ β -catenin signaling pathway detected by western blot were higher in the BMSCs+E2 group than in the other treatment groups. Taken together, these results suggested that BMSCs combined with estrogen can improve endometrial injury by partially activating the Wnt/ β -catenin pathway to inhibit endometrial fibrosis and EMT.

Key words Intrauterine adhesion, bone marrow mesenchymal stem cells, Estrogen, Wnt/ β -catenin pathway

The Application of Perimenopausal Contraceptives

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Among the 1.9 billion women of reproductive living in the world; 1.1 billion need for family planning; 842 million use modern methods of contraception and 80 million use traditional methods; 190 million women have no need for family planning and do not use any contraceptive method; About 150 million of these women use oral contraceptives to prevent pregnancy. Do women over 40 still need contraception? Can I continue to take birth control pills after 40? What are the risks of health? This paper first summarizes the development history of the 50 years of the contraceptives, and then refers to some guidelines of oral contraceptives in China, the United States, the United Kingdom, WHO and the European Union. Conclusions: It is recommended that patients age 40 and older be provided with information on fertility, pregnancy risks, vascular, metabolic and cancer risks, combined with age-related risk factors, to establish a low-risk balance. No study has been able to formally ban contraception based on age alone.

The British Guide writes: Most contraceptive users are medically fit and can use any available contraceptive method safely. However, some medical conditions are associated with potential or theoretical increased health risks when certain contraceptive methods are used, either because the method adversely affects the condition or because the condition or its treatment affects the safety of the contraceptive. Since most trials of new contraceptive methods deliberately exclude subjects with chronic medical conditions, there is often little direct evidence on which to base accurate prescribing advice.

Always find a balance between contraception and risk.

Key words Perimenopausal; oral contraceptive; family planning;

Prediction model based on ultrasonic parameters of three-dimensional power doppler scanning for endometrial cancer in women with postmenopausal bleeding

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Objective: To analyze the ultrasonic imaging characteristics of different pathological types of endometrium, and to establish ultrasonic prediction model for differentiation between benign endometrial lesions and endometrial carcinoma (EC) in women with postmenopausal bleeding (PMB).

Methods: PMB women with $ET \geq 5 \text{ mm}$ ($n=412$) or $ET < 5 \text{ mm}$ presented recurrent vaginal bleeding ($n=57$) were enrolled in this prospective observational study. According to the pathological examination results of endometrium, women with PMB were divided into endometrial atrophy (EA) ($n=231$), endometrial polyp (EP) ($n=98$), endometrial hyperplasia (EH) ($n=58$) and EC ($n=82$). Ultrasonic parameters were compared among the four groups. The predictive value of different parameters for differentiation between benign endometrial lesions and EC in women with PMB was performed by ROC curves. The best cut-off of ultrasonic parameters analyzed by ROC curves were used to establish prediction model.

Results: Women with EC had significantly thicker endometrial thickness (ET) and higher endometrial volume (EV), vascularization index (VI), flow index (FI) and vascularization-flow index (VFI) than women with other pathological types of endometrium ($P < 0.05$). The endometrial VI, FI and VFI of women with EH were significantly higher than that of women with EA and EP ($P < 0.05$). For patients with $ET \geq 5 \text{ mm}$, the best parameter for distinguishing between benign and EC was FI, with area under curve (AUC) of 0.86, sensitivity 86.7% and specificity 81.4%. In addition, for patients with $ET < 5 \text{ mm}$, the best parameter for distinguishing between benign and EC was VI, with AUC of 0.92, sensitivity 92.1% and specificity 72.9%. The ultrasonic prediction model based on FI and VI had better prediction value for EC both in patients with $ET \geq 5 \text{ mm}$ and patients with $ET < 5 \text{ mm}$.

Conclusions: The ultrasonic parameters were different among different pathological types of endometrium in women with PMB. Ultrasonic prediction model based on endometrial FI and VI was clinically useful for differentiation between benign endometrial lesions and EC, especially in women with PMB presenting ET less than 5mm.

Key words postmenopausal bleeding, benign endometrial lesions, endometrial cancer, three-dimensional power Doppler ultrasound, ultrasonic prediction model

Research progress of laser treatment of vaginal laxity

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Vaginal laxity is mainly caused by childbirth and other causes of vaginal relaxation, Affects women's quality of life. In recent years, a variety of non-surgical treatment techniques and equipment have been widely used in the treatment and research of improving vaginal laxity. Among them, physical rehabilitation, energy instruments (including laser radiofrequency) are gradually becoming one of the most promising and widely supplied therapeutic measures in clinical practice, its objective and reliable therapeutic effect and potential adverse reactions still need to be supported by more high-quality evidence-based medicine. This article will analyze and review the treatment of vaginal laxity by laser, as well as some problems that need to be paid attention to.

Key words Vaginal laxity; Laser; Pelvic floor rehabilitation

An in vivo investigation of pelvic organ prolapse relative parameters in the vaginal wall

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Aim of this study: To investigate the pelvic organ prolapse relative parameters in the vaginal wall and explore the connective tissue layer, muscular, and basement membrane about the pathogenesis of pelvic organ prolapse (POP).

Materials and methods: In this research prolific SD rats simulation of birth trauma, designed model creation free-test and post-tests for 7 days then carried out for 7 days interfered by TGF- β or Fibulin-5 and measured the height of the perineal body, length of perineal body, and vaginal diameter. Haematoxylin and eosin, and modified Masson's trichrome staining methods were observed to histopathological change of vaginal tissue. PCR and WB methods measured to MMP-9, MMP-2, Elastin, Fibulin-5, smad2/3, p-smad2/3, TGF- β , and Lox gene expression and protein expression.

Results: Model creation caused the height of the perineal body and vaginal diameter to markedly increase and the length of the perineal body markedly decreased and histopathological change of vaginal tissue. Model creation also caused to increase in MMP-9 and MMP-2 gene expression and a decrease of Elastin, Fibulin-5, smad2/3, p-smad2/3, TGF- β , and Lox gene expression and protein expression. But, 7 days interfered by recombine TGF- β or Fibulin-5 caused to decrease of the height of the perineal body and vaginal diameter and increase of the length of the perineal body and significantly decrease of MMP-9, and MMP-2 gene expression and increase of Elastin, Fibulin-5, smad2/3, p-smad2/3, TGF- β , and Lox gene expression.

Interfered the TGF- β significantly reversed up-regulation of MMP-9 and MMP-2 proteins expression, and down-regulation of Elastin, Fibulin-5, p-smad2/3, TGF- β , and Lox proteins expression, interfered the Fibulin-5 significantly reversed up-regulation of MMP-9 proteins expression and downregulation of Elastin, Fibulin-5, smad2/3, p-smad2/3, TGF- β , and Lox proteins expression. Interfered by TGF- β can't be effected to smad2/3 proteins expression and interfered by Fibulin-5 can't be effected to MMP-2 proteins

Conclusions: 7 days interfered by TGF- β or Fibulin-5 caused to decrease of the height of the perineal body and vaginal diameter and increase of the length of the perineal body, significantly decrease of MMP-9, and MMP-2 gene expression and increase of Elastin, Fibulin-5, smad2/3, p-smad2/3, TGF- β , and Lox gene expression and reversed up-regulation of MMP-9 and MMP-2 proteins expression, and down-regulation of Elastin, Fibulin-5, p-smad2/3, TGF- β , and Lox proteins expression.

Key words Pelvic organ prolapse; Rat model: Transforming growth factor- β ; Fibulin-5; Vaginal wall;

Understanding of the Etiology, Symptomatology, and Treatment Options in Premature Ovarian Insufficiency (POI)

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POI is associated, in the long term, with an increased risk of cardiovascular disorders and osteoporosis and with some degree of cognitive deterioration. In addition, POI is reported to be associated with earlier mortality (1).

Most of the genetic factors related to the etiology of POI are unknown. The etiological factors known to cause familial POI are chromosomal abnormalities and some gene mutations. Most of the genetic studies in POI were conducted on genes already known to play a role in folliculogenesis (NR5A1, NOBOX, FIGLA, and FOXL2), as folliculogenesis growth factors (inhibin A, GDF9, and BMP15), or in ovarian steroidogenesis (FSHR, FSH, LHR, and LH) (2-4). The disease course of POI differs significantly among the causative genes, the types of mutations, or possibly combinations of mutated genes that are mostly unknown at present. Besides, POI is frequently associated with autoimmune disorders, more than in the general population, and autoimmune disorders are more frequently seen in POI patients than in the general population. It has been reported that autoantibodies directed to different targets, including the luteinizing hormone (LH) receptor, FSH receptor, and zona pellucida are detectable in POI (5-7). It has been shown in case reports that viral infections can be followed by ovarian failure. However, only mumps oophoritis has been considered to be a cause of POI, accounting for 3-7% of POI cases. However, there have been only case reports, and no established data that clearly show infectious disease as a cause of POI have been reported.

Patients with POI have been reported to have shortened life expectancy (8). The main reason for this is considered to be cardiovascular disease. Women with POI have been reported to have several risk factors for the development of cardiovascular disease: endothelial dysfunction, autonomic dysfunction, abnormal lipid profile, insulin action disturbances, and metabolic syndrome (9). Many women experience depression and/or reduced libido due to the sense of loss of reproductive function and physical changes, such as vaginal dryness. Declining short-term memory and cognitive function and an increased incidence of Alzheimer's disease have been reported in patients with POI, but these phenomena have not been observed before or after the age-appropriate menopause. Estrogen deficiency leads to urogenital atrophy, causing common urogenital symptoms such as vaginal dryness, vaginal irritation, and itching.

The primary treatment modality is HRT, and, for POI patients, HRT is generally safe and beneficial for alleviating vasomotor and urogenital symptoms and preventing cardiovascular diseases and osteoporosis, thus improving patients' quality of life. However, the optimal dosage, hormone preparations used, and duration of HRT for POI patients have not been fully investigated. Due to the tendency for late childbearing,

infertility caused by POI along with the age-related decrease in ovarian reserve is a serious problem in all developed countries. A trial of a new approach to fertility treatment for POI patients was recently reported (10).

Key words Etiology, Symptomatology, Treatment Options, Premature Ovarian Insufficiency (POI)

Study of glutamatergic and GABAergic neurons in preoptic area of hypothalamus triggering menopausal hot flashes

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Objective: The purpose of this study is to explore the mechanism that low estrogen regulates the transcription and expression of glutamate decarboxylase (GAD1 or GAD2) through its nuclear receptor ER α or ER β , and then affects the number and function of glutamatergic and GABAergic neurons in preoptic area, which leads to the dysfunction of thermoregulation center in regulating heat dissipation and heat production, and finally causes hot flashes during menopause.

Methods: Adult female Sprague Dawley rats were randomly divided into sham-operated (SHAM) group, ovariectomized (OVX) group and ovariectomized with estrogen treatment group (OVX+E). (1) The changes of body skin temperature of rats were monitored in real time by infrared thermography under the stimulation of different cold and hot environment temperatures. (2) The hypothalamic differential proteins were screened by TMT labeled quantitative proteomics and analyzed by bioinformatics, and the key differential proteins were verified by Western Blot and qRT-PCR. (3) The expression of glutamatergic neuron specific marker (vesicular glutamate transporter 2, Vglut2) and GABA neuron specific marker (vesicular GABA transporter, Vgat) in preoptic area were detected by qRT-PCR and Western Blot. And the numbers of glutamatergic and GABAergic neurons were observed by RNAscope and immunofluorescence staining. (4) Chemogenetics was used to specifically activate or inhibit glutamatergic or GABAergic neurons, and the changes of body temperature were observed. (5) QRT-PCR, Western Blot and immunofluorescence staining were used to detect the expression of GAD1, GAD2, ER α , ER β and GPR30 in preoptic area.

Results: Under the condition of low estrogen: (1) The changes of body skin temperature were faster and larger under the stimulation of cold and hot environment. (2) The bioinformatics analysis of hypothalamic proteomic showed that the differential proteins were enriched in the functional pathways related to glutamatergic and GABAergic synapses. (3) The expression of Vglut2 and the number of glutamatergic neurons decreased, while the expression of Vgat and the number of GABAergic neurons increased. (4) The function of glutamatergic neurons initiating heat dissipation was decreased, while the function of GABAergic neurons initiating heat production was enhanced. (5) The expression of GAD1 increased, while the expression of GAD2 decreased, the expression of ER α and ER β and the numbers of their positive neurons decreased, and there was co-expression of ER α or ER β with GAD1 or GAD2 in the same neuron. Estrogen supplementation can effectively correct the changes in the state of low estrogen.

Conclusion: Low estrogen during menopause may regulate the transcription and expression of GAD1 and GAD2 through its reduced nuclear receptors ER α and ER β , resulting in increased expression of GAD1 and decreased expression of GAD2, leading to a decrease in the number and function of glutamatergic neurons, as well as an increase in the number and function of GABAergic neurons in preoptic area. The functional abnormalities of the two may be the key factors leading to the imbalance

of preoptic area in regulating heat dissipation and heat production, which leads to hot flashes.

Key words Glutamatergic neuron, GABAergic neuron, Preoptic area, Hot flashes, Menopause

Ovarian tissue transplantation to rescue ovarian function after rectal carcinoma treatment: case report

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Objective: To observe the recovery of ovarian function after ovarian tissue transplantation for a POF patient after rectal carcinoma treatment.

Procedure: A 26-year-old woman was diagnosed rectal carcinoma in 2017, requiring ovarian preservation before radical treatment for malignancy. The patient was unmarried and has no child at that time. Before her anorectal surgical, the patient underwent left ovarian resection and freezing and right ovarian transposition. The ovarian tissue was trimmed into 25 pieces, sized 0.5×0.4 cm to 0.8×0.6 cm, 0.1mm thickness. All the ovarian slices were frozen following slow freezing protocol. Surgery for rectal cancer, radiotherapy and chemotherapy were performed after the operation. After the treatment, the menstruation stopped. The FSH reached 70.26IU/L. She maintained her period by cyclical hormone replacement. She was followed up in Oncological department without relapse. Four years after rectal cancer surgery, she got married and was about to have children, so she went to the Gynecologic department again for autologous ovarian tissue transplantation. During the operation, 8 pieces thawed ovarian tissue was transplanted and fixed in the peritoneum of the posterior lobe of the left broad ligament. The hormone level, menstruation, follicle development and menopause symptom were observed intensively.

Outcome: 50 days after the transplantation, her hot flash faded. B-ultrasound showed that there were blood flow signals and follicular growing at left pelvis, the endometrium thickness was 7.6mm. Blood FSH was 16.93IU/L, LH 14.63IU/L. Her menstruation recovered 60 days after ovarian tissue transplantation.

Conclusion: Ovarian tissue freezing is an effective method to preserve the ovarian reserve before radical treatment for malignancy.

Key words Ovarian tissue transplantation, fertility preservation, rectal carcinoma

Recognition of menopause among health professionals in Hebei, China

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ABSTRACT

Objective: This study aims to understand the recognition of menopause and menopausal hormone therapy (MHT) among health professionals aged 40–60 in Hebei, which provides a basis for health services.

Methods: From June 1st to September 30th in 2020, an anonymous questionnaire recruited 1125 female health professionals in Hebei through online surveys and on-site interviews at professional meetings. The questionnaire content includes general situation, menstrual conditions, reproductive history, the recognition of menopause and MHT. The results were statistically analyzed using SPSS 25.0 software.

Results: A total of 1125 questionnaires were distributed and 961 valid questionnaires were collected. the mean age at natural menopause was 49.85 years. 62.85% female health professionals were fully aware of early menopausal symptoms, and 42.87% were fully aware of long-term menopausal impacts. 69.72% participants have felt that menopausal symptoms should be treated. 43.39% participants were aware of MHT, and 58.48% were fully aware of the benefits of MHT. 58.27% of them were willing to accept MHT, but only 11.97% had used MHT. 65.7% health professionals would recommend MHT to other people and 85.95% intent to know about menopause and MHT.

Conclusions: The mean age at natural menopause of female health professionals in Hebei was 49.85 years, which was consistent with the natural menopause age of Chinese women and earlier than that of women in Western countries. In Hebei, the lack of awareness of early menopausal symptoms and long-term menopausal hazards caused the negative attitudes of health professionals toward menopause management. Furthermore, they were less aware of MHT, which caused their low usage, low acceptance and low recommendation rate of MHT. There was a great demand for knowledge about menopause and MHT in Hebei. In order to help menopausal women, we should strengthen the promotion and popularization of menopause-related knowledge.

Key words Hebei, Health professionals, Menopause, Menopausal syndromes, MHT, Recognition

Investigation on Menopausal Cognition and Related Factors of Female Non-medical Workers in Hebei Province

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Objective: With the extension of human life span, the number of postmenopausal women in China has increased dramatically. It is estimated that by 2030, the total postmenopausal population in China will reach 380 million. At the same time, the life span of women in perimenopausal and postmenopausal period can reach one third. Menopause is the embryonic stage of many chronic diseases. The health management of postmenopausal women is of great significance to improve the quality of life of postmenopausal women. This study investigated the incidence of menopause-related symptoms and menopausal syndrome among female non-medical workers in Hebei Province, and found out their cognition of menopause-related symptoms and other knowledge, and finally discussed the related influencing factors, so as to provide the basis for scientific and reasonable formulation of perimenopausal health care strategies in the later period, thus improving the quality of life of women in perimenopausal and postmenopausal period.

Methods: The subjects of the study were female non-medical workers who had a physical examination in the Second Hospital of Hebei Medical University from August 2020 to December 2020 and who had lived in Hebei Province for a long time. The questionnaire is designed and released by "Questionnaire Star", and the survey method is self-filled questionnaire.

Results: 1. A total of 2215 subjects were included in this study, including 1222 young women (< 40 years old) (55.17%) and 993 older women (≥ 40 years old) (44.83%). Older women know better than younger women in terms of early symptoms and long-term hazards of menopause, and younger women have a stronger sense of seeking medical treatment than older women. In the occupational composition, public officials account for the vast majority (42.344%); The main place of residence is the city (73.59%). There are a large number of universities (including college education) (74.04%), and their income is mainly below 5,000 (50.11%). The number of births of young women is lower than that of older women, and the difference is statistically significant. Older women, higher education level and urban residents know more about climacteric symptoms than younger, lower education level and rural women, and the difference is statistically significant ($P < 0.05$). 2. 49.12% of the surveyed people have menopausal symptoms. If there are menopausal symptoms, 59.37 people are willing to receive treatment. The top five highest incidence rates are fatigue, emotional excitement, insomnia, osteoarthritis, dizziness, dizziness, dizziness, etc. The average score of the improved Kupperman score was 10.65 ± 7.44 . Menopausal symptoms are positively correlated with age and negatively correlated with educational background and monthly income. 47.27% of women choose to consult gynecologists after menopause. The awareness rate of HRT was 59.37%, and age, education background and monthly income were significantly correlated with HRT use.

Key words Menopausal related symptoms, Cognitive conditions, Menopausal hormone therapy, Menopausal syndrome

Inverse association between bone mineral density and fibrinogen in peri and postmenopausal women

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Objective: Inflammatory is a risk factor for osteoporosis. We aimed to explore whether fibrinogen is associated with bone mineral density (BMD) with chronic inflammation in peri and postmenopausal women.

Methods: This cross-sectional study analysed 339 peri and postmenopausal women in Zhejiang Province from January 2016 to October 2019. Linear regression analysis was performed to assess the relationship between fibrinogen and BMD.

Results: Serum fibrinogen had a significant inverse association with BMD in peri and postmenopausal women. Mean BMD among women in quartiles 1-4 of fibrinogen were 0.901g/cm², 0.897g/cm², 0.892 g/cm², and 0.855 g/cm², respectively (P for trend<0.01). After adjustment for age, body mass index, estradiol, metabolic profiles, blood inflammatory factors, calcium, and phosphorus, and alkaline phosphatase, fibrinogen levels remained significantly associated with BMD (regression coefficients for quartiles 1-3 vs quartiles 4 were 0.046, 0.027, and 0.036, respectively; P for trend<0.05)

Conclusions: Overall, higher peri and postmenopausal women fibrinogen levels were associated with lower BMD, independent of age, body mass index, estradiol, and other factors. Our findings provide new ideas for the prevention of osteoporosis.

Key words Fibrinogen; Bone mineral density; Osteoporosis.

Follicle stimulating hormone, its association with glucose and lipid metabolism during the menopausal transition

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Aim: Accumulative evidence shows that follicle stimulating hormone (FSH) is associated with metabolic disorders. We aimed to ascertain the relationship between FSH, blood glucose and lipid metabolism in general perimenopausal women.

Methods: This cross-sectional study analyzed 2121 perimenopausal women aged 40–54 years in Zhejiang Province from January 2016 to December 2018. Regression analysis was performed to assess the relationship between FSH and metabolic parameters.

Results: Serum FSH had a significant inverse association with fasting plasma glucose ($P < 0.05$) and triglycerides (TG) ($P < 0.01$) in perimenopausal women. However, after adjusting for body mass index, there was no significant association between FSH and fasting plasma glucose. In a model fully adjusted for demographic variables, estradiol, body mass index, high-density lipoprotein, low-density lipoprotein, homocysteine, systolic blood pressure and blood viscosity, a significant association still existed between FSH and TG (standardized $\beta = -0.095$; $R^2 = 0.155$; $P = 0.002$).

Conclusion: Overall, FSH is negatively associated with metabolic parameters, especially TG, in perimenopausal women. These results indicated that FSH might be a biomarker for the primary prevention of disorders with lipid metabolism during the menopausal period.

Key words follicle stimulating hormone, glucose, metabolism, perimenopause, triglycerides.

A nomogram for decision-making in menopause patients with atypical endometrial hyperplasia: reduce misdiagnosis of endometrial carcinoma.

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Abstract:Our objective was to explore risk factors for misdiagnosis of endometrial carcinoma (ECa) in patients with atypical endometrial hyperplasia(AEH) by analyzing the clinicopathological datas, and predict individual risk forecast nomogram model to reduce the misdiagnosis rate which may provide guidance for clinical diagnosis and treatment decisions.

Methods:This retrospective study included menopause women(N = 226) who underwent hysterectomy for a diagnosis of atypical endometrial hyperplasia between January 2012 and April 2021 at a tertiary gynaecologic centre.Data regarding clinical and pathological risk factors were recorded,including age,weight,menstruation, fertility,ADC value in the MRI diffusion weighted imaging (DWI) sequence, serum CA125, CA199 and other clinical risk factors.A nomogram based on the multivariate results was constructed for personalized prediction of missed diagnosis of ECa in patients with AEH.

Results:The misdiagnosis rate of endometrial carcinoma was 37.61% (n=85) with most being stage 1A endometrioid.Univariate analysis showed that age, menopausal status, infertility history, abnormal uterine bleeding, hypertension and ADC value were statistically significant. Multivariate logistic regression analysis showed that age , infertility history and ADC value were statistically significant. According to the results of logistic regression analysis, a model was constructed to predict the missed diagnosis of ECa in patients with AEH, and a nomogram was drawn. The consistency coefficient (c-index) obtained by bootstrap self sampling method was 0.741, suggesting that the nomogram has a certain clinical predictive value.

Conclusions: 1.The incidence of missed diagnosis of ECA in patients with AEH after hysterectomy was 36.87%. Most of the missed ECA were early endometrioid adenocarcinoma with high differentiation.2.Age ≥ 49.5 years, history of infertility and ADC value $\leq 110 \times 10^{-5} \text{mm}^2 / \text{s}$ were the risk factors for missed diagnosis of ECA in patients with AEH. The combined prediction value of the three factors was significantly higher than that of the independent factors.3.The nomogram model based on the prediction of missed diagnosis of ECA in patients with AEH has certain prediction accuracy, which can be used to evaluate the risk of ECA in patients with AEH individually.

Key words atypical endometrial hyperplasia, endometrial cancer, high risk factors;ADC values

Research progress of bone marrow mesenchymal stem cells in the treatment of premature ovarian failure

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Premature ovarian failure (POI), also known as primary ovarian insufficiency, refers to the decline of ovarian function in women from puberty to 40 years old, which is mainly characterized by high serum gonadotropin and low estrogen, oligomenorrhea, amenorrhea, and fertility decline [1]. The specific pathogenesis of premature ovarian failure is still unclear, and there are no effective recovery measures for the impaired ovarian tissue structure and reserve function. In recent years, it is considered that the recovery of ovarian function and improvement of the reproductive capacity of patients with POI are the key links in the treatment of premature ovarian failure. Mesenchymal stem cells (MSc) with multi differentiation potential and self-renewal ability and their secretion of a variety of cytokines and exosomes have been confirmed to play an active role in the treatment of various degenerative diseases [2]. Bone marrow-derived mesenchymal stem cells (BM MSCs) are the most common source of stem cells in tissue and organ repair engineering and regenerative medicine. BM-MSC has a great potential to promote organ repair. Many studies have proved that bone marrow-derived mesenchymal stem cells may have a recovery effect on the structure and fertility of injured ovarian tissue, which is a potential method for the treatment of patients with premature ovarian failure [3]. This review mainly summarizes the characteristics and functions of BM MSCs, and expounds on the possible mechanism, problems and corresponding solutions of BM MSCs in the treatment of premature ovarian failure.

Key words Premature ovarian insufficiency, bone marrow-derived mesenchymal stem cells, ovarian function, reproductive outcome

Clinical analysis of highly effective progesterone combined with LNG-IUS in fertility-preserving therapy for endometrial carcinoma

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Objective : explore the clinical effect of high-efficiency progesterone combined with levonorgestrel releasing intrauterine system (LNG-IUS) in the treatment of endometrial cancer with fertility preservation. **Method:** the clinical data of 33 patients with endometrial cancer who wish to preserve fertility were retrospectively analyzed. According to the different treatment methods, 18 patients who were treated with LNG-IUS were included in the study group, while the other 15 patients who were treated with conventional high-efficiency progesterone acetate were included in the control group. The clinical effects of the two groups were compared and observed. **Result :** the total effective rate of the study group (78.74%) was higher than that of the control group (67.68%) ($P > 0.05$), but the CR rate was higher than that of the control group ($P < 0.05$); There was no significant difference in pregnancy rate and recurrence rate between the two groups ($P > 0.05$); The operation rate in the study group (52.94%) was lower than that in the control group (84.21%), and the incidence of adverse reactions in the study group (41.18%) was lower than that in the control group (73.68%) ($P < 0.05$). **Conclusion :** high efficiency progesterone combined with LNG-IUS in the treatment of endometrial cancer with fertility preservation has a good effect, and it has a certain application value for patients with fertility preservation.

Key words endometrial carcinoma; Keep fertility function; LNG-IUS; Medroxyprogesterone acetate

The relationship between regular moderate-intensity exercise and menopausal symptoms in peri-postmenopausal female—— a single-institution study

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Objective • To understand the relationship between regular exercise and menopausal symptoms in peri-postmenopausal females. **Method** • Participants were investigated by trained researchers about demographic information, menstrual state, exercise state and menopausal symptoms. Menopausal symptoms and severity were assessed by Kupperman scale. Data analysis was done by SPSS25.0. **Result** • There were 285 women recruited in this research whose average age was 52.01 ± 4.59 , including 152(53.33%) with no regular exercise, 27(9.47%) with exercise less than 150min, 106(37.19%) with exercise more than 150min. There were 26(9.12%) participants with no menopausal symptoms, 63(22.11%) with mild symptoms, 154(54.04%) with moderate symptoms, 42(14.74%) with severe symptoms. It showed that Women without regular exercise were more likely to have severe menopausal symptoms ($p < 0.05$). And regular exercise could improve sleep quality ($p < 0.05$). Menstrual state had nothing to do with exercise state ($P > 0.05$). **Conclusion** • Peri-postmenopausal females may improve their living quality by regular exercise as it reduced the severity of menopausal symptoms.

Key words peri-postmenopause; menopausal symptoms; regular exercise

Study on the relationship between menopausal symptoms and everyday cognition in (peri) menopausal women

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Objective To evaluate the relationship between menopausal symptoms and everyday cognition in (peri) menopausal women. **Methods** 314 Women who first visited the menopausal clinic of Shanghai Sixth People's Hospital were enrolled. The modified Kupperman Menopausal Index scale was used to assess the prevalence and severity of climacteric symptoms, and a short version of everyday cognition scale was used to evaluate everyday cognition. **Results** Women with severe menopausal symptoms had higher scores on their everyday cognition. After adjusting for demographic confounding factors such as age, body mass index, personal monthly income, education level, menopausal status, parity, regular exercise, and history of hypertension and diabetes, regression analysis showed that a positive correlation between hot flashes/sweating, depression and fatigue symptoms and ECog scores; insomnia and irritability symptoms were no longer associated with ECog scores. **Conclusion** Overall menopausal symptoms severity, hot flashes/sweating, depression and fatigue symptoms are the predictors of everyday cognition in (peri) postmenopausal women.

Key words menopause; hot flashes/sweating; insomnia; depression; fatigue; everyday cognition

Study on the relationship between menopausal hormone replacement therapy and cardiovascular disease

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Objective: To investigate the clinical epidemiology of cardiovascular diseases and the risk of thrombosis in different menopausal states in Shanghai, to discuss the factors affecting cardiovascular diseases and coagulation function in women and the influence of tibolone on the risk of thrombosis.

Methods: From December 2017 to December 2019, women aged 40–65 years from menopause transition to post-menopause and treated in the menopause clinic of Shanghai Jiao Tong University Affiliated Sixth People's Hospital were enrolled, to investigate the basic demographic characteristics, and the incidence of subclinical atherosclerosis by carotid ultrasound and to assess blood coagulation function by TEG.

Results: The incidence of subclinical atherosclerosis was 33.5%, carotid plaque 21.4%, Age ($P = 0.021$; $OR=1.074$) and HDL-C ($P=0.028$; $OR=0.412$) are risk factor for subclinical atherosclerosis; HDL - C ($P = 0.005$; $OR=0.257$) and menopausal status ($P=0.016$; $OR=0.374$) are risk factor for plaque. Linear regression analysis showed that age ($P=0.001$; $\beta=0.203$) and Body mass index ($P=0.016$; $\beta=0.153$) are risk factor for the thickness of the medial media in the right common carotid artery; FSH is related factors of R in both the menopausal transition period and the postmenopausal period, ($\beta=0.208$; $P=0.019$); ($\beta=0.178$; $P=0.027$); KMI is related with K in the menopausal transition period ($\beta=-0.245$; $P=0.019$); E2 is related with K in the postmenopausal period ($\beta=0.175$; $P=0.046$); KMI is related with α in the menopausal transition period ($\beta=0.288$; $P=0.002$), TG is related with α in the postmenopausal period ($\beta=0.171$; $P=0.047$); TG is related with CI in the postmenopausal period ($\beta=0.186$; $P=0.034$). In women treated with tibolone for 3 months and 1 year, the clotting status of the body stabilized and the risk of thrombus decreased from 3 months to 1 year.

Conclusion: The incidence of subclinical atherosclerosis in postmenopausal women is higher than that in menopausal transitional women.

Menopausal hormone replacement therapy may improve menopausal symptoms, but it also raises the risk of blood clots.

Key words Menopause; Cardiovascular disease; Thrombelastogram; Subclinical atherosclerosis; Menopause hormone therapy; Carotid ultrasound

Network pharmacology was employed to explore the mechanism of Wuzi Yanzong Pills in treatment of women with premature ovarian failure

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Background: The onset of premature ovarian failure is getting younger. While, wuzi Yanzong Pills, as a traditional Chinese herbal medicine mixture in China, is indeed effective in the treatment of premature ovarian failure, but its mechanism is still unclear.

Purpose: To clarify the mechanism of Wuzi Yanzong pill in the treatment of premature ovarian failure through network pharmacology.

Method: In the TCMSP database, according to oral availability (OB) and drug-like properties (DL), the effective ingredients and target genes of Wuzi Yanzong pill were searched. Then, Search for target genes related to premature ovarian failure in four databases: GeneCards, OMIM, PharmGKB, and TTD. The drug-active ingredient-therapeutic target gene network diagram showed the intersection of the two part target genes. Protein interaction network (PPI) analysis, GO function and KEGG pathway enrichment analysis on the target gene were performed. Finally, cytoNca in Cytoscape was employed to construct core genes of the intersection target genes.

Results: A total of 1045 active ingredients and target genes in Wuzi Yanzong Pills were obtained from the TCMSP database, and 508 target genes related to the treatment of premature ovarian failure were obtained from 4 databases. The drug-active ingredient-therapeutic target gene network diagram shows that all four traditional Chinese medicines contain quercetin (mol000098), and the active ingredient is the most related to the target gene, as the most prominently expressed effective ingredient, and NCOA2 and PGR are the most significant therapeutic targets. The biological process of GO analysis (BP biological process) mainly focuses on the process of reactive oxygen metabolism and reactive oxygen biosynthesis. KEGG pathway enrichment results in 30 significant signaling pathways, including PI3K-Akt signaling pathway, Estrogen signaling pathway, and AGE-RAGE signaling pathway in diabetic complications.

Conclusion: Wuzi Yanzong Pill, as the traditional Chinese medicine, was employed to treat premature ovarian failure through multiple effective ingredients, multiple targets, and multiple ways. Exploring its mechanism may lay the foundation for the study of the treatment mechanism of premature ovarian failure.

Key words network pharmacology; Wuzi Yanzong; premature ovarian failure.

Neglected Van Wyk-Grumbach Syndrome-Reports from Twins

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Objective: To analyze the clinical data of twins with Van Wyk-Grumbach syndrome, and the pathogenesis, clinical manifestations, diagnosis, treatment of Van Wyk-Grumbach syndrome (VWGS) were discussed combined with relevant literature.

Method: The medical history, physical examination, auxiliary examination and treatment of twins with VWGS were analyzed.

Results: Patient A, female, 15 years old, was admitted to the emergency department in October 2019 due to abdominal pain for 8 hours without obvious cause. She was small and obese with pale facial coloration, facial swelling, coarse dry skin. Her height was 131 cm, weight was 40 kg. Menstruation commenced at the age of 13. By the age of 9, the child's linear growth had almost ceased. Her breasts began to develop at the age of 11. Breast development was Tanner stage 3, without galactorrhea. She had no axillary or pubic hairs. She presented paroxysmal pain without fever, nausea, vomit or diarrhea. Transanal ultrasonography showed a uterine size of $4.52 \times 4.23 \times 3.90$ cm with enlarged multicystic ovaries (right ovary measuring $12.79 \times 9.11 \times 6.35$ cm and left ovary $5.6 \times 5.05 \times 3.87$ cm), ovarian blood supply were normal. There was insufficient evidence to diagnose ovarian tumor, so surgery was not performed immediately. Phloroglucinol was administered intravenously to relieve pain. Laboratory examination showed hypothyroidism. X-ray of the wrist revealed epiphysis was not closed. Her bone age was 11 years. MRI-pituitary showed a pituitary adenoma. The gonadotropin-releasing hormone (GnRH) stimulation test was negative, patient A was pseudo precocious puberty. VWGS was diagnosed based on hypothyroidism, cystic ovarian enlargement, pseudo puberty and delayed bone age. So thyroxine replacement therapy was started. Unfortunately, the patient returned to the hospital one months later with abdominal pain. Color Doppler flow imaging (CDFI) revealed a thimbleful bilateral ovarian blood supply signals. Laparoscopic operative exploration showed the right ovary was approximately 13 cm in diameter, with blue-purple color, twisted by 720 degrees. Therefore, patient A underwent reduction of ovarian torsion. Patient B, the identical twin sister of A. Her height was 143 cm. Patient B received left ovary torsion reduction surgery at the age of 13 due to ovarian torsion. We found that Patient B had short stature and had the same history of ovarian enlargement with polycystic changes as Patient A. Laboratory tests indicate that patient B also suffers from hypothyroidism. MRI-pituitary revealed pituitary adenomas. So patient B was also diagnosed with VWGS. Thyroid replacement therapy was started. During one year follow-up, it was found that the patient's condition was improved and the Imaging examination showed that both ovaries and pituitary gland were smaller than before.

Conclusion: VWGS is easily misdiagnosed as simple primary hypothyroidism, ovarian cyst or pituitary tumor. Before proceeding with surgical evaluation, we should exclusion of hypothyroidism to rule out this rare but treatable disease. Although there has little consensus regarding the precise etiopathogenesis of VWGS, the treatment approach is clear and thyroid hormone replacement therapy is the first choice. Timely supplement of thyroid hormone therapy is the key factor to promote patients to get the expected height. The only indication require immediate surgical

intervention in VWGS is ovarian torsion. In identical twins, if one of the twins has VWGS, we should examine whether the other twin siblings has it.

Key words Hypothyroidism;Ovarian enlargement;Delayed bone age;Pituitary hyperplasia;Twins

Research Progress on the Correlation between LAMA4 and Cancer

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Laminin subunit alpha 4 (LAMA4) is a member of the Laminin family, which is widely found in the intercellular stroma of adult tissues and a major component of basement membrane. In recent years, many studies have investigated the molecular structure and biological function of LAMA4, and it has been found that LAMA4 plays an important role in the growth, proliferation and migration of cells. LAMA4 is involved in cell fixation and can recognize corresponding integrin receptors for signal transduction. A number of studies have shown that LAMA4 has an important relationship with the occurrence and development of tumors, and the expression of LAMA4 can be used as a marker of tumor diagnosis and prognosis. In this paper, the relationship between LAMA4 and tumor genesis would be discussed, which is expected to provide new ideas for future research.

Key words Laminins; Laminin subunit alpha 4; LAMA4; cancer

Relationship Between Blood Levels of Estradiol and hs-CRP, Homocysteine, Fibrinogen in Postmenopausal Women With Hypertension

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Objective:To explore the relationship between the decline in estrogen levels and the development of hypertension in postmenopausal women. **Methods:** Selected a total of 110 female patients who had menopause for more than 1 year were selected (age 55-75 years old), including 70 hypertensive patients and 60 non-hypertensive patients. Investigate their age and menopausal age, and test and count their fasting blood glucose, triglycerides, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, high-sensitivity C-reactive protein, blood homocysteine, fibrinogen, estrogen, progesterone, and testosterone, etc. Sort out the obtained data and analyze them with statistical methods. **Results:**High-sensitivity C-reactive protein, blood homocysteine, and fibrinogen are the influencing factors of estradiol levels in postmenopausal women with hypertension ($P < 0.05$). **Conclusion:**Decreased estradiol levels, elevated levels of high-sensitivity C-reactive protein, blood homocysteine, fibrinogen, and glucose and lipid metabolism disorders may be risk factors for hypertension in postmenopausal women.

Key words estradiol, hypertension, postmenopause

Association between bile acids and osteopenia in postmenopausal women

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Abstract

Objective: In the present study, the risk coefficients of serum total bile acids(TBA), C-reactive protein(CRP), and lipid levels in postmenopausal osteopenic women were determined.

Design: The retrospective research design was applied.

Methods: We enrolled 228 patients with postmenopausal women from Hangzhou Women' s Hospital gynecological clinic, who aged 45 to 60 years old, and never received menopause hormone therapy. According to the bone mineral density determination results, subjects were divided into the normal group (n=118), osteopenia group (n=110). Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (DXA). Serum bile acids, CRP, and lipid indexes were determined by enzyme chemiluminescence immunoassay.

Results: The odds ratios and 95% confidence intervals of those variables (menopausal age, duration of menopause, LDL, CRP, and TBA) were found significant ($p < 0.05$).

Menopausal age, duration of menopause, LDL, CRP, and TBA variables were found statistically significant in the analysis of receiver operating characteristics (ROCs).

Limitations: Observational study; small sample size.

Conclusion: The present study shows that menopause age, duration of menopause, serum LDL, CRP levels are risk factors for postmenopausal osteopenic women, serum TBA level is a protective factor for postmenopausal osteopenic women, which may be used as the indicators of bone loss in postmenopausal women.

Key words Postmenopausal, osteopenia, total bile acids

Application of neutrophils to lymphocytes ratio in ovarian diseases

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Neutrophil-lymphocyte ratio (NLR) is one of the markers of systemic inflammatory response that has been studied extensively in recent years. The occurrence and development of common ovarian diseases (such as ovarian tumor, ovarian intratotypic dysplasia, ovarian cyst torsion and rupture, early ovarian insufficiency, polycystic ovary syndrome, etc.) are often accompanied by the occurrence of inflammatory reaction. NLR can be used for prediction and diagnosis, and it is also of great significance to evaluate the prognosis of patients. Easy to measure, accessible and inexpensive, they are widely used. However, reports on the specificity and sensitivity of NLR value for diseases vary, and the acquisition of the optimal truncation value needs further study. In the future, NLR is expected to be used as a predictive model to improve the diagnostic rate and prognosis evaluation of ovarian diseases.

Key words ratio of neutrophils to lymphocytes; Ovarian disease; Application; diagnosis

The effect of autoimmune thyroid disease on premature ovarian insufficiency

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Premature ovarian insufficiency (POI) refers to a clinical syndrome in which women experience ovarian dysfunction before the age of 40. It is characterized by high gonadotropins, low estrogen, and menstrual disorders. Further development may cause cardiovascular disease, abnormal glucose and lipid metabolism and osteoporosis. Recent studies have shown that autoimmune dysfunction may be involved in the pathogenesis of POI, and as a precursor state of POI, causing ovarian dysfunction. Epidemiology and numerous clinical studies suggest that autoimmune thyroid disease (AITD) has a higher incidence in POI patients than the general population, and it is significantly related to the clinical manifestations of POI such as menstrual abnormalities and low fertility, which suggests that there may be a close relationship between POI and AITD in pathogenesis, disease progression, and outcome. Therefore, the article reviews the impact of AITD on POI.

Key words POI AITD

A single-center study of Screening sarcopenia through SARC-F-calf score in middle-aged and elderly women

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Objective: The aim of this study was to assess the prevalence of middle-aged and older women at high risk of sarcopenia and to analyze the correlation between time of menopause and high risk of sarcopenia using the SARC-F-calf score to compare their quality of life (QOL) with those at low risk.

Materials and methods: We conducted a cross-sectional study of all middle-aged and elderly women attending outpatient clinics at the Cardiovascular and Cerebrovascular Disease Hospital of Ningxia Medical University from December 2020 to March 2021.

Eligible patients aged >41 years were included, excluding those with previous surgery or radiotherapy for malignant or aggressive tumors, those with previous cardiac surgery or joint replacement, those with severe underlying metabolic diseases, genetic disorders or psychiatric disorders who were unable to cooperate, and those with incomplete information or who refused to participate in the study. The risk of sarcopenia was determined by the SARC-F-calf score: the SARC-Calf score correlates the SARC-F score with the calf circumference (CC) measurement, and the CC was scored on the basis of the SARC-F score, with a score of 10 for women with $CC \leq 33$ cm and 0 for $CC > 33$ cm; a total score of 0 – 20, A score of ≥ 11 was considered suspicious for sarcopenia, while a score of < 11 was considered normal. The general data of the patients were collected, including age, height, weight, calf circumference, age at menopause, history of hormone replacement therapy drugs, previous history, and surgical history, and the menopause rating scale (MRS scale) and physical activity scale were completed, and the quality of life of middle-aged and elderly women was measured according to the menopause rating scale.

Results: A total of 220 middle-aged and elderly women with a mean age of 56.1 ± 11.2 years were included in this study, and no non-menopausal patients with suspected sarcopenia were found. The prevalence of suspected sarcopenia in postmenopausal women was 12.5% (28 cases), and a higher proportion of women in the suspected sarcopenia group had severe symptoms in three domains compared with the normal group (somatic 8% versus 25%, psychological 20% versus 46%, and urological reproductive 30% versus 58%; $p < 0.05$), and the quality of life was worse in the suspected sarcopenia group compared to the normal group. The prevalence of sarcopenia in the suspected sarcopenic group was positively correlated with the duration of menopause, and the older the age at menopause, the higher the prevalence of suspected sarcopenia.

Key words SARC-F-calf; sarcopenia; menopause

PLODs are overexpressed in ovarian cancer and are associated with gap junctions via connexin 43

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Aim: Procollagen-lysine, 2-oxoglutarate 5-dioxygenases (PLODs) play important roles in cancer progression, but their role in ovarian cancer remains elusive.

Method: In silico analysis of expression of PLODs in ovarian cancer was performed with reproduction of The Cancer Genome Atlas dataset. PLOD-enriched pathways and related gene(s) were validated by immunohistochemistry (IHC) in 80 ovarian cancer tissue blocks and in vivo xenograft murine models.

Result: PLODs (PLOD-1, -2, and -3) were overexpressed in ovarian cancer tissue. Overexpression of individual PLODs showed mutual exclusivity. Each of the three PLODs was differentially expressed between normal and cancer tissue of the ovary. PLOD1 was not prognostic, whereas lower PLOD2 and higher PLOD3 expression were associated with worsened prognosis, respectively. Cases with PLOD overexpression showed enrichment in gap junctions. GJA1 (connexin 43) was significantly overexpressed in cases with PLOD overexpression. IHC in tissue showed the strongest positive correlation between PLOD3 and connexin 43 expression, followed by PLOD2. As per Harmonizome, we selected SKOV3 and CAOV3 cell lines based on constitutive high PLOD1 and PLOD2/PLOD3 expression, respectively for in vitro and in vivo modeling. Only knockdown of PLOD3 was significantly associated with decreased GJA1 expression level in both cell lines. IHC in murine xenograft tumors also showed significantly lower connexin 43 in PLOD3-KD SKOV3 tumors.

Conclusion: We conclude that PLODs are generally overexpressed in ovarian cancer and each PLOD may be functionally non-redundant. Association between PLOD3 and gap junctions warrants further investigation.

Key words ovarian cancer, PLODs, connexin 43

Clinical and surgical factors associated with effectiveness of surgical repair of cesarean scar diverticulum

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(AIM) Cesarean scar diverticulum (CSD) is a refractory post-cesarean complication. We aim to evaluate clinical and surgical parameters associated CSD.

(METHOD) One hundred and four CSD patients who underwent diverticulum repair at Obstetrics and Gynecology Hospital of Fudan University between Aug 2010 and Aug 2014 were followed. Clinical and surgical parameters were reviewed and analyzed retrospectively for potential association with surgical effectiveness.

(RESULTS) Demographic data of etiology showed 35 cases (33.7%) of scarred uterus, 33 cases (31.7%) of sociodemographic reason, 14 cases (13.5%) of abnormal labor, 5 cases (4.8%) of breech position, 5 cases (13.5%) of fetal distress, 4 cases (3.8%) of macrosomia, 4 cases (3.8%) of cephalopelvic disproportion, 3 cases (2.9%) of twins and 1 case (1.0%) of placenta previa. Univariate analysis showed pre-operative menstruation duration, suture type and depth of diverticulum were associated with surgical effectiveness, respectively and was validated in multivariate analysis, which showed time between CSD onset and cesarean section being a significant factor.

(CONCLUSION) Patients with preoperative menstruation duration less than 14 days, diverticulum depth less than 7mm, and time between CSD symptoms onset and cesarean section less than 1 year can benefit better from surgical repair. The use of delayed absorption thread during the operation can obtain better surgical results.

Key words Cesarean scar diverticulum; Surgical repair; Risk factors

Clinical significance of MDT in the diagnosis and treatment of climacteric syndrome

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Objective To explore the clinical significance of multidisciplinary combined therapy in the diagnosis and treatment of climacteric syndrome. **Materials and methods** Collect the data of 77 patients with climacteric syndrome related symptoms who treated in the General Hospital of Ningxia Medical University from October 2020 to October 2022 , and 1 case was excluded. According to their clinical symptoms, they were divided into 57 cases in the control group and 19 cases in the observation group. The control group was given routine treatment of climacteric syndrome (including hormone supplementary treatment, Healthy lifestyle guidance and menopause knowledge education) for 6 months; According to their clinical symptoms, the observation group received MDT from multiple disciplines including cardiovascular medicine, neurology, Gastroenterology, psychology, rheumatology and immunology, orthopedics and other relevant departments mainly organized by Gynecology, and according to their clinical symptoms, further improved the relevant tests and examinations (including ECG, breast B-ultrasound, thyroid B-ultrasound, bone mineral density, rheumatism related factors, 25 hydroxyvitamin D Neck vascular ultrasound, etc.), and fill in the improved Kupperman score scale, self rating Anxiety Scale (SAS) and self rating Depression Scale (SDS), measure the level of serum sex hormone. Based on the patients' s clinical symptoms and examinations results, provide multidisciplinary combined treatment: First, those with non gynecological diseases shall be transferred to another department for treatment in time; Second, those with gynecological related organic diseases shall be given corresponding treatment, and hormone supplement treatment was given when there no contraindications after evaluation, and corresponding guidance shall be given for the prevention, treatment and rehabilitation of cardiovascular diseases; Give medication guidance and psychological counseling for psychological and mental problems; Third, regularly carry out lectures on menopausal health knowledge, popularize health knowledge about menopause syndrome and answer their questions about self-examination and treatment of menopause syndrome. **Results** After 6 months of treatment, the decline of scores, the increase of E2, the decrease of FSH and LH in menopausal women combined with multidisciplinary management on the basis of hormone supplementary treatment were significantly better than those in the control group. **Conclusion** MDT can clarify the overall disease situation of patients, significantly alleviate the clinical symptoms of climacteric women, prevent the occurrence of long-term complications and improve the quality of life of patients with climacteric syndrome.

Key words MDT , diagnosis and treatment , climacteric syndrome , clinical significance

Study on perimenopausal syndrome and bone mineral density of middle-aged and elderly women in huama Town, Yanchi County, Ningxia Province

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Objective: To investigate the incidence of perimenopausal syndrome and the prevalence of osteoporosis (OP) among middle-aged and elderly women in huama Town, Yanchi County, Ningxia, and to analyze the relevant factors affecting OP, so as to provide reasonable suggestions for improving the quality of life of middle-aged and elderly women and the prevention of osteoporosis. **Methods:** 302 women, aged 40–60, who participated in the climacteric health education activities in huama Town, Yanchi County in June 2021, were selected as the research objects. Part I: the questionnaire of awareness rate of perimenopause and osteoporosis and menopausal quantitative assessment (MRS) were completed by face-to-face survey. Part II: osteo kj2000 ultrasonic bone densitometer produced by Nanjing Kejin company was used to detect the bone mineral density of the subjects's heel, and register the subjects's bone mineral density, height, weight, number of births, menopausal age, smoking, drinking, etc. **Results:** the first part: (1) the natural menopause age of women in Yacai town is 53.03 ± 4.54 years old, and the incidence rate of perimenopausal syndrome is 84.8%. 2) The awareness rate of perimenopausal symptoms was 27.3%, and that of osteoporosis was 34.1% (3) the top five incidence rate of perimenopausal syndrome is sleep disorders, hot flashes, sweating, heart beating, depression, physical and mental exhaustion. The second part: (1) the decline rate of bone mineral density of middle-aged and elderly women in huama Town, Yanchi County was 35.1%, and the rate of osteoporosis was 4.6% (2) The decline rates of bone mineral density in premenopausal group, perimenopausal group and postmenopausal group were 11.8%, 33.3% and 50.5% respectively, and the prevalence rates of OP were 2.8%, 3.9% and 4.2% respectively (3) Age, menopause and body mass index were the risk factors of bone mineral density decline and osteoporosis. There was no significant difference between fertility, smoking, drinking and bone mineral density. **Conclusion:** the awareness rate and treatment rate of middle-aged and elderly women in huama Town, Yanchi County are far lower than those in developed areas, which has seriously affected the quality of life of middle-aged and elderly women. Health education, advocating healthy lifestyle and improving the treatment rate of perimenopausal syndrome and osteoporosis are the top priorities of health care for middle-aged and elderly women in underdeveloped areas.

Key words Perimenopausal syndrome 、osteoporosis 、bone density、menopause

Differentiation of granulosa like cell from iPSc: A new light to improve ovarian function of POI

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Objectives: Induced pluripotent stem cells (iPSc) have multiple differentiation potential and can be induced to differentiate into ovarian granulosa cells in vivo, which may improve the hypoestrogenic symptoms of premature ovarian insufficiency (POI). However, the exact mechanism remains unclear. The purpose of this study was to induce iPSc to differentiate into granulosa like cells in vitro, explore the mechanism of induced differentiation process, and study the effect of differentiated granulosa like cells on ovarian function in vivo.

Materials and Methods: Co-culture the mouse iPSc with ovarian granulosa cells for 7 days to induce iPSc into ovarian granulosa like cells. Rt-PCR and Immunofluorescence were used to identify follicle-stimulating hormone receptor in granulosa like cells. The effect of granulosa like cell orthotopic transplantation on decreased ovarian function in mice was investigated. Moreover, LC-MS was used to analyze the protein expression profiling in co-culture supernatant in D1, D3, D5 and D7. Differentially expressed proteins were further adopted to protein-protein interaction network analysis, Gene Ontology analysis (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis.

Results: Ovarian granulosa like cells could express follicle-stimulating hormone receptor and luteinizing hormone receptor. Primordial follicles and growth follicles were significantly increased after orthotopic transplantation. Proteomics analysis showed that 109 proteins were highly expressed in granulosa like cells and 367 proteins were significantly decreased in the differentiation of D7. By GO and KEGG analysis, these differentially expressed proteins were found to be enriched in metabolic process, cellular process and several other pathways.

Conclusion: iPSc can be induced into ovarian granulosa like cells in vitro and can improve ovarian function of POI mouse. The Proteomics analysis may provide novel insights in optimizing the differentiation of granulosa cells in vitro, leading a new way to alleviate the symptoms of POI with low estrogen and improve fertility.

Key words Induced pluripotent stem cells (iPSc) , premature ovarian insufficiency (POI) , ovarian granulosa cell

Association of HCY, CRP, lipid level, and sleep quality in perimenopausal and postmenopausal women

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Abstract:

Objective: This work is to investigate the correlation between homocysteine (HCY), C-reactive protein (CRP), lipid levels, and sleep quality in perimenopausal and postmenopausal women.

Methods: We collected data from 217 patients (perimenopause and postmenopausal) who visited the gynecological endocrine outpatient department in our hospital from January 2017 to January 2019. The quality and patterns of sleep were measured by Pittsburgh Sleep Quality Index(PSQI), and the relationship between HCY, CRP, lipid levels, and sleep quality was analyzed according to $PSQI \geq 8$.

Results: There were significant differences in age, education level, and occupation among patients with different sleep quality ($P < 0.05$). HCY, CRP, TC, TG, and LDL levels of the patients in poor sleep quality were higher than those in the group with good sleep quality ($P < 0.05$). Age, education level, occupation, HCY, CRP, lipid levels (TC, TG, LDL, HDL) were the main influencing factors for sleep quality in perimenopause and postmenopausal women (all $P < 0.05$). After adjusting for age, education level, occupation, and other factors, HCY and CRP were independent risk factors for sleep quality in perimenopause and postmenopausal women (all $P < 0.05$).

Conclusion: HCY, CRP, and lipid levels were significantly correlated with sleep quality in perimenopausal and postmenopausal women. HCY and CPR were independent risk factors for sleep quality in perimenopause and postmenopausal women, which provides theoretical support for clinical improvement of sleep quality.

Key words Menopause; Sleep Quality; Homocysteine; C-reactive protein; Lipid level

The Cognitive Effect of Perimenopausal One-day outpatient Multidisciplinary Model on Menopause Hormone Therapy for Perimenopausal Women

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【Abstract】 Objective: To evaluate the impact of Perimenopausal one-day outpatient on MHT cognition in perimenopausal women. Method: Data were from the perimenopausal women who took part in the Perimenopausal one-day outpatient , In 2020. Questionnaires were completed voluntarily, Including questions about perimenopausal syndrome symptoms, awareness rate of MHT, acceptance rate and concerns. Useing Excel and SPSS 26.0 software for statistical analysis. Results: A total of 295 perimenopausal women completed the questionnaire survey. The cognition rate has improved, including perimenopausal age (96.61% VS 99.32%, $P = 0.037$), the importance of perimenopausal health care knowledge (91.19% VS 96.95%, $P=0.000$), and whether the perimenopausal syndrome needs treatment (88.47% VS 99.32%, $P=0.000$), willingness to use MHT (70.59% VS 94.48%, $P=0.000$), MHT treatment timing (64.50% VS 95.17%, $P=0.000$), MHT indications (51.26% VS 93.79%, $P=0.000$), reduce the risk of cardiovascular disease (51.68% VS 96.55%, $P=0.000$), delay aging (69.75% VS 97.58%, $P=0.000$), prevent osteoporosis (65.13% VS 97.58%), $P=0.000$, Medical staff is higher than non-medical staff, and it's statistically significant. 90% of perimenopausal women who participated in the one-day outpatient to gain health knowledge, Include the prevention and treatment of chronic diseases, healthy diet, mental health, knowledge of hormone therapy, and exercise methods. The time to accept MHT for 1-10 years (31.09% VS 47.93%) of perimenopausal women is significantly increased. These concerns about the risk of thrombosis (60.24% VS 36.81%), weight gain (59.64% VS 14.84%), and life-long dependence (52.41% VS 18.13%) are significantly reduced, but Concerns about cancer risk have not diminished. From 2017 to 2020, the rate of MHT has increased from 2.22% to 62.16% in perimenopausal women who participated in perimenopausal one-day outpatient program. Conclusion: The perimenopausal one-day outpatient can improve the awareness of MHT among perimenopausal women, eliminate misunderstandings, and increase the use rate of MHT. This model of preventive care is worth pursuing.

Key words Perimenopausal period; Perimenopausal one-day outpatient; menopause hormone therapy; MHT

Study on the feasibility of improving menopausal syndrome based on multidisciplinary integrated management model

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OBJECTIVES: To explore the multidisciplinary integrated management model based “one-day outpatient” and continuous management, and examine its feasibility and preliminary effects for improving menopausal syndrome and emotion among menopausal women. **METHODS:** Clinical intervention study was conducted in Obstetrics and Gynecology Center of the Third Affiliated Hospital of Chongqing Medical University from May 2020 to May 2021. The continuous management mode of “one-day outpatient service” for menopause was constructed in terms of multidisciplinary resources, including offline “one-day outpatient” health education, online 7-week group continuous intervention on “healthy lifestyle” and offline half-day focus group interview. Pre- and post- scores of the modified Kupperman scale and the positive/negative emotional scale (PANAS) were measured to compare the status of menopausal syndrome and emotional experience of eighty-two female participants (40~60 years old), meanwhile, before and after comparison of the blood lipid and body composition indexes of participants were also performed. In addition, according to the information saturation principle, 22 patients were interviewed after the multidisciplinary integrated management model based “one-day outpatient” and continuous management to summarize their experience. **RESULTS:** Paired t test or Wilcoxon signed rank test were used. Results showed that the pre-and post- Kupperman scores were 14.37 ± 8.40 vs 10.06 ± 5.79 ($t = -5.72$, $P < 0.01$), and the post-positive emotional score was higher than the pre-one (pre- 28.56 ± 5.86 vs post- 30.07 ± 6.22 , $t = 2.54$, $P = 0.013$) and the post-negative emotional score was lower than the pre-one [pre- $20.0(9)$ vs post- $17.0(7)$, $Z = -4.96$, $P < 0.01$]. The triglyceride level of participants declined from 1.27 ± 0.54 mmol/L to 1.09 ± 0.38 mmol/L ($t = -2.45$, $P < 0.05$). Meanwhile, the body mass index (pre- 22.52 ± 2.34 vs post- 22.06 ± 2.22), percentage of body fat (pre- 31.72 ± 6.22 vs post- 30.91 ± 6.52) and Visceral fat area (pre- 83.96 ± 30.26 vs post- 79.66 ± 29.71) were all improved ($t = -3.58/t = -2.57/t = -2.59$, $P < 0.05$). Furthermore, the interview showed that the symptoms and negative emotions of the patients were effectively improved, positive emotions were strengthened after the intervention. Meanwhile, it also showed that the participants developed a healthy lifestyle, better understanding of scientific knowledge of menopause and greater confidence in coping with menopause. **CONCLUSIONS:** the multidisciplinary integrated management model based “one-day outpatient” and continuous management can effectively improve menopausal syndrome and adverse mood, reduce patients’ blood lipid, improve the body composition, and maybe contribute to the prevention of long-term chronic diseases, which is worthy of further clinical application and deep exploration.

Key words Menopause; Menopausal syndrome; Emotions; multidisciplinary management

Assessment menopausal symptoms and quality of life in women with premature ovarian failure after hematopoietic stem-cell transplantation for hematologic diseases

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Objective: This study aimed to evaluate and compare the menopausal symptoms and quality of life between women with premature ovarian failure (POF) who underwent hematopoietic stem-cell transplantation (HSCT) for hematologic diseases and natural menopausal women.

Methods: This observational study enrolled women who had POF following HSCT for hematologic diseases between June 2017 and November 2019 in the menopause clinic of Peking University People's Hospital. Most HSCT women were from Peking University Institute of Hematology, People's Hospital, or Hebei Yanda LuDaoPei Hospital (95% women were from Peking University Institute of Hematology, People's Hospital, 4% women were from Hebei Yanda LuDaoPei Hospital, 1% women were from other hospitals). This observational study enrolled 415 women (215 HSCT women and 200 natural menopausal women as control group) from June 2017 and November 2019 in the menopause clinic of Peking University People's Hospital. The menopausal symptoms and quality of life were evaluated using the modified Kupperman index (KI), menopause rating scale (MRS), and menopause quality of life questionnaire (MENQOL). Numerical data were analyzed with descriptive methods and were expressed as mean and standard deviation as well as 25%, median, and 75%. Differences between the modified KI and MRS were compared based on categorical variables. The unpaired Student's t-test was used for normally distributed data, and the Mann-Whitney U test was used for skewed data. The risk factors for menopausal syndrome were identified by multivariable logistic regression analysis. The results were presented as an odds ratio (OR) with 95% confidence interval (CI). $P < 0.05$ was defined as statistically significant. SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for the analysis.

Results: The total KI and MRS scores were 12.53 ± 8.27 and 7.69 ± 6.50 in the HSCT group and 21.57 ± 9.23 and 12.05 ± 6.70 in the control group, respectively ($p < 0.05$). The scores on sexual problems and dryness of the vagina were 1.20 ± 1.24 and 1.07 ± 1.24 in the HSCT group and 1.15 ± 1.01 and 1.01 ± 1.01 in the control group, respectively ($p > 0.05$). Age was a risk factor for menopausal symptoms (odds ratio 1.70, 95% confidence interval 1.01–1.12). The main reasons for visit of the HSCT group were amenorrhea and infertility (76.74%).

Conclusion: Compared with natural menopausal women with the same number of years since menopause, the MRS and KI scores of POF women who underwent HSCT showed milder symptoms. The MRS may be a better alternative to reflect the severity of menopausal symptoms. Age was a risk factor for menopausal symptoms. Oncofertility counseling should be initiated as early as possible before the start of treatment.

Key words premature ovarian failure, hematopoietic stem cell transplantation, menopausal symptoms, menopausal rating scales

Glanzmann Thrombasthenia (GT) due to ITGA2B mutation: report of a China family

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Background:

Mutations of chromosome 17q21, specifically the ITGA2B or ITGB3 genes cause autosomal recessive Glanzmann thrombasthenia and more than hundreds of mutations have been reported[1, 2]. GT results when a patient is homozygous for the same mutation or is a compound heterozygote for different mutations[3].

Objective:

We describe physical and histological features, and the molecular impact of mutation ITGA2B in a China family.

Methods:

We report two female patients, daughters of non-consanguineous parents, with onset of symptoms within the first three years of life, developing severe functional impairment, including mucocutaneous bleedings, heavy menstrual bleeding (HMB) and shock. The platelet aggregation rate showed a low pattern. Trio whole exome sequencing was requested and the study identified two genetic variants on chr17:42457372 and chr17:42457057. This result confirms the diagnosis of Glanzmann thrombasthenia. This article introduces the incidence, genetic characteristics, clinical manifestations, diagnostic methods and genetic counseling of GT. Carrier testing and genetic counselling have become an important component of comprehensive care in GT patients. Common testing methods include direct gene analysis, flow cytometry, Western blot, cord blood, chorionic villus sampling.

Results

The patients were referred to the gynecology department of Peking University People's Hospital, in order to be evaluated for ambulation assistance. They received the LNG-IUS as treatment for management of HMB. Genetic counseling was offered. The study of the genealogy of the patient, phenotypic features, and genetic test must be included as valuable tools in the clinical approach of the patient with Glanzmann thrombasthenia, in order to define treatment protocols, genetic counselling and the procreation guidance.

Conclusion

We should do genetic testing for patients with GT and their families, offer genetic counseling as well as prenatal and preimplantation genetic testing, in order to discuss reproductive options, mate selection and risks of the offspring.

Key words genetic counseling, trio whole exome sequencing, Levonorgestrel-releasing intrauterine system, Glanzmann thrombasthenia

Dynamic effects of bone marrow transplantation and preconditioning on ovarian function in prepubertal children with blood diseases

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Objective: To evaluate the dynamic effects of bone marrow transplantation and pre-transplantation pretreatment on ovarian function in prepubertal children with blood diseases.

Methods: Collected from The Fourth Department of Hematology, Beijing Children's Hospital, Capital Medical University from October 2018 to August 2019, Blood samples from 37 female children with hematologic diseases (acute lymphoblastic leukemia, acute myeloid leukemia, hemophagocytic syndrome, myelodysplastic syndrome, aplastic anemia, lithomyelia, thalassaemia, hyperigemia, and non-Hodgkin's lymphoma), with an average age of 8 years (1-15 years). Six levels of sex hormones were recorded before transplantation, 3 months, 6 months, 12 months and 24 months after transplantation, and the pre-treatment programs before bone marrow transplantation (cyclophosphamide, malilane, cytarabine, simustine, fludarabine, ATG, buxylan, etc.) were recorded. To explore the dynamic effects of bone marrow transplantation and preconditioning on ovarian function in prepubertal children with blood diseases.

Results: The follicle estrogen (FSH) increased significantly after transplantation. The mean FSH before transplantation was 5.20IU/ml (0.38-26.4IU/ml), (FSH > 25IU/ml in 2 girls, 25.IU/ml6 and 26.4IU/ml, respectively). The mean AMH before transplantation was $2.11 \pm 3.045.20$ ng/ml (0.04-5.71ng/ml). After follow-up, 13 patients had FSH > 25IU/ml (90.IU/ml, 38IU/ml, 38.7IU/ml, > 170IU/ml, 36.8IU/ml, 39.3IU/ml, 115IU/ml, 40.7IU/ml, 107IU/ml, respectively). 76.4IU/ml, 109IU/ml, 155IU/ml, 132IU/ml, 134IU/ml). FSH was greater than 40IU/ml in 9 patients. The AMH after transplantation was < 1.0ng/ml.

Conclusions: At present, there are few foreign studies on the effects of bone marrow transplantation for children with blood diseases on ovarian function, and most of them are retrospective studies with small sample size. At present, there is no relevant report in China, let alone prospective studies. This study shows that bone marrow transplantation and pre-transplantation pretreatment affect the ovarian function of children, but the related drug influencing factors, the dynamic recovery of ovarian function, ovulation and reproductive function still need to be studied with a large sample and long-term follow-up observation.

Key words Hematopoietic Stem Cell Transplantation, primary ovarian insufficiency

Long-term outcomes of fertility-sparing surgery for stage II and III serous borderline ovarian tumors

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Objective: This study was performed to assess the feasibility of conservative treatment for stage II or III serous borderline ovarian tumors (SBOT). **Methods:** Thirty-five patients were treated conservatively for advanced SBOTs from January 2006 to July 2019. Six patients were lost to follow-up. The patients' clinical status, surgical results, fertility results, and oncological outcomes were collected. **Results:** The patients' median age at surgery was 27 years (range, 16–35 years). The median follow-up interval was 67 months (range, 17–231 months). Among the 35 patients, 3 had stage IIA tumors, 10 had stage IIB tumors and 22 had stage IIIC tumors. A total of 18 patients (51.4%) relapsed after surgery, of which 2 patients had two times recurrences, 1 got three times recurrences. 15 patients underwent secondary conservation surgery, while 3 patients chose secondary tumor reduction surgery. No patients died of their disease. 24 (82.8%) patients were nulliparous. Ten cases had fertility desire after operation, 6 live births were obtained, with one spontaneous abortion and one unsuccessful IVF-ET. **Conclusions:** Despite the high recurrence rate of the fertility-preservation surgery, due to favorable pregnancy outcome, this study supports the conservative surgery for patients with stage II-III ovarian serous borderline tumors. The final survival rate had not been changed by the preservation of fertility.

Key words fertility preservation, serous borderline ovarian tumors, oncological result, fertility outcome

Effects and mechanisms of amino acid metabolism on premature ovarian insufficiency

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Ovarian dysfunction could seriously affect women's fertility and quality of life. Firstly, Amino acids could participate in the process of folliculogenesis through the transport system of oocytes : The b0, +, L and ASC amino acid transport systems are active throughout the growth and maturation of oocytes while XAG-, B0, +, A and CAT / γ + amino acid transport systems do not participate in the growth of oocytes or the process of meiosis. In contrast, the GLY, β and Xc-amino acid transport system is activated during the process of oocyte meiosis. It has been confirmed that glutamine can be used as an energy matrix to support follicular development which can restart the meiosis of oocytes in the cumulus-oocyte complex of mice and horses. Glycine can participate in the regulation of oocyte volume. GLYT1, the transporter of glycine in the follicle, regulates the cell volume of the oocyte by transporting glycine. Studies have shown that during the process of preantral follicles transforming into antral follicles, an increase in leucine intake in the follicles can be observed and an increase in serine intake can be observed during the process of meiosis and maturation of oocytes, But the specific mechanism of action of leucine and serine in follicular development is still unclear. Secondly, the metabolic disorder of amino acids could lead to female premature ovarian disease and other related diseases. An increase in the proportion of branched-chain amino acids in the follicular fluid may induce local insulin resistance in the ovary. It has been found that the levels of leucine, valine and glutamate in patients with PCOS increased, and is positively correlated with the level of insulin resistance. Metabolic profile analysis indicated that the PCOS group had less alanine, glycine, citrulline and proline content in the follicular fluid, and the arginine concentration was significantly increased while the concentration of arginine and the number of eggs and embryos were all present negative correlation. Thirdly, amino acid metabolism could affect ovarian function by regulating the level of ovarian oxidative stress and activating the mTOR signaling pathway. Studies have shown that amino acids can regulate Rheb (Ras homologue enriched in brain) and Rag GTPases by stimulating the TSC1-TSC2 complex, through regulating and activating mTORC1 and its downstream pathways. Amino acid metabolism can participate in the activation of the mTOR signaling pathway in various organs in the body: leucine can increase protein synthesis in the body's muscles through the mTOR pathway, and arginine can regulate the mTOR signaling pathway and regulate branched chains in Pompe disease models. Amino acids can mediate the mTOR signaling pathway to regulate the activation of follicles, for example, leucine, glutamine, and arginine can increase the activation level of primordial follicles by participating in the mTOR signaling pathway. Therefore, further and deeper research on the influence of amino acid metabolism on ovarian function and its mechanism will help to improve the comprehensive understanding of the developmental mechanism of follicles, and provide new clinical ideas for improving women's follicular development, ovarian function and reproductive health.

Key words amino acids; folliculogenesis; premature ovarian failure; mechanisms

Efficacy of different current therapies for genitourinary syndrome of menopause: A Bayesian network analysis

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Objectives: To compare efficiency of different treatment for genitourinary syndrome of menopause and give some useful suggestions for clinical medication.

Materials and Methods: PubMed, EmBase and Cochrane Library were searched for randomized controlled trials of various measures to treat genitourinary syndrome of menopause. The time limit was from the databases creation through June 2021, no language restrictions. Analysis was made to Assess efficiencies of different treatment from vaginal health index (VHI), Female Sexual Function Index (FSFI) and changes of GSM symptoms. The quality of literatures was assessed by Jadad scale and data were analyzed using the statistical analysis tool R 4.0.5.

Results: In 11 randomized clinical trials of 1114 women, Radiofrequency (RF), estrogen vaginal cream, laser, vaginal gel, vitamin E vaginal suppository, oxytocin vaginal gel, pueraria mirifica gel, promestriene, pelvic floor muscle training (PFMT) were used as treatment strategies. Among the postmenopausal patients, 259 (23.2%) were treated with laser, 149 (13.4%) were treated with Radiofrequency (RF), 210 (18.9%) were treated with estrogen vaginal cream, 150 (13.5%) were treated with vaginal gel. The network meta-analysis showed that all the

interventions were better than the control group. The VHI/FSFI score was highest in the Radiofrequency (RF) group. RF therapy had excellent effect on VHI vaginal dryness and dyspareunia, laser and vaginal estrogen also had significant efficiency on these aspects. The laser group showed worsening of pain domain in FSFI, While there was no significant difference in satisfaction among these groups.

Conclusion: The efficacy is similar in RF, laser and vaginal estrogen to treat women with GSM, vaginal gel is also a good choice for dryness.

Key words Genitourinary syndrome of menopause; Therapy; Radiofrequency; vaginal laser treatment; Female sexual function

The application value of medical narrative ability in the health education of menopausal patients

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[Abstract] Objective To analyze the specific mode, method and application value of medical narrative ability in the field of health education for menopausal patients, and to provide reference for practical medical narrative ability. Methods To review the significance and practice, the application of medical narrative ability, the theoretical basis of health education, the steps, executors and their qualifications, the methods and evaluation indicators. Discover the key points of its health education and then implement the method of health education intervention for the menopausal patients, its core is empathy and reflection to explore the key points of health education, and practice in diversified medical narrative methods such as dictation, text writing and music. Results Medical narrative practitioners through menopause patients to listen, absorb, interpretation, response, and menopausal disease stories and problems, using problem externalization and deconstruction, find troubled patients, patients feel powerless, pain, and find a breakthrough, to help patients recognize the problem, while looking for positive power in the story from the patient story, reconstruct a positive story, to help it find the life and menopause disease story significance and value, overcome the pain and suffering, to overcome the disease confidence. Conclusion The medical narrative ability of menopausal health education practitioners has long-term impact on menopausal health education, directly affects the psychological state, quality of sleep and quality of life, and important experience in the whole process, more affects the diagnosis and treatment ability of menopausal patients, worth application. Pay attention to the medical narrative ability of the executor of health education of menopausal patients, and give targeted training to improve the medical narrative ability level of the executor. And how to better expand the medical narrative mode, it still needs to be more practice and summarized.

Key words Medical narrative ability; menopause; health education

Association Between Menopausal Hormone Therapy and Health Outcomes A Systematic Review and Meta-analysis

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Background

Menopausal Hormone therapy (MHT) has been suggested for protection against age-related symptoms in women. However, data on the effect of MHT on Health outcomes are heterogeneous and conflicting, need to be systematically reviewed.

Objective

To determine whether MHT was associated with beneficial effects on age-related symptoms and whether the effects vary with the timing of therapy initiation(the hormone-timing hypothesis) by meta-analysis.

Methods

English databases Medline, the Cochrane Library, Embase and Chinese databases Wang Fang, CNKI and CQVIP were searched (from inception until February 28, 2021). For this systematic review and meta-analysis, randomized controlled studies including women undergoing MHT and control groups of women not receiving MHT were selected and extracted by 2 reviewers. Potential controversies were resolved by a third reviewer. Quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were used to abstract data and assess data quality. Data were pooled using a fixed-effects model.

Results

Total 33 eligible studies met the selection criteria. MHT caused a significant improvement in the following aspects compared with placebo or no treatment. High density lipoprotein increased (SMD=0.36, $P=0.001$), Low density lipoprotein(SMD=-0.48, $P<0.0001$) and total cholesterol(SMD=-0.36, $P=0.004$) decreased. The BMD of all measured sites increased significantly (neck of femur, $P=0.0002$; trochanter of trochanter, $P=0.002$; total hip, $P<0.00001$; lumbar vertebrae $P<0.00001$), the increase of total hip(SMD=1.02%) and lumbar vertebrae (SMD=1.36%) was slightly higher than femoral neck(SMD=0.74%) and trochanter (SMD=0.78%), but the differences were not significant ($P>0.05$). Also the increased maturation of the vaginal epithelium(SMD=0.99) and the decreased vaginal PH(SMD=-0.97) were observed after MHT($P<0.00001$). Kupperman score decreased (SMD=-2.05, $P<0.00001$) as well.

When stratified based on treatment type, the data shows oral estrogen caused a greater reduction in low density lipoprotein ($P<0.00001$) and total cholesterol ($P=0.0002$), a significant increase of high density lipoprotein ($P=0.0005$) than transdermal and vaginal estrogen. When stratified according to the timing of MHT initiation, the diastolic blood pressure of early menopausal women decreased slightly

(SMD=-0.42, P=0.009), and the systolic blood of late menopausal women increased slightly (SMD=0.06, P=0.0003). MHT was associated with less progression of subclinical atherosclerosis than was placebo when therapy was initiated within 6 years after menopause but not when it was initiated 10 or more years after menopause (P=0.007).

Women's body mass index decreased slightly (SMD=-0.01), muscle retention increased (SMD=0.39) and abdominal fat decreased (SMD=-0.29), but the difference was not statistically significant (P>0.05).

Conclusions

This systematic review and meta-analysis showed a significant beneficial association of MHT with vaginal atrophy, BMD, cardiovascular disease risk, and quality of life. MHT may have positive effect on body mass index, abdominal fat and muscle mass, but our analysis suggested little statistically significant change. The effects of hormone therapy on health outcomes may depend on the timing of therapy initiation relative to menopause(so-called the hormone-timing hypothesis).

Key words Menopause, Menopausal hormone therapy(MHT), the Quality of life, Randomized controlled study, Meta-analysis,

Endometrial Thickness Assessment and Clinical Significance of Thickened Endometrium In Asymptomatic Postmenopausal Women

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Background:

The uterine endometrium is the most sensitive tissue to sex hormones. The thickness of the endometrium changes regularly with the ovarian cycle. After menopause, the decline in ovarian function is accompanied by a significant decrease in estrogen concentrations in the blood, and the endometrium shrinks and thins to an average thickness of 2~3mm. The risk of endometrial cancer was 4.6% among women experiencing postmenopausal bleeding and an endometrial thickness greater than or equal to 5 mm. However, the risk of endometrial cancer was only 0.2% for postmenopausal asymptomatic women with thickened endometrium. If an endometrial thickness of 5 mm was used as the intervention threshold, it was likely to lead to over-consultation. There is still a great deal of international and national controversy and no unified conclusion as to what thickness of endometrium should be used for clinical intervention in postmenopausal asymptomatic women.

Objective:

The aim of this study was to analyse the endometrial thickness, histopathological features and general clinical data of postmenopausal asymptomatic women with endometrial thickening, to find pathological endometrial thickness cut-off values, to clarify the clinicopathological features of postmenopausal asymptomatic endometrial thickening and to assess the risk factors for endometrial cancer in this population.

Methods:

Women with natural menopause ≥ 1 year, endometrial thickness ≥ 5 mm, no clear symptoms (including vaginal bleeding and bellyache etc.) and willingness to undergo fractional curettage, who attended the Department of Obstetrics and Gynecology of the First Affiliated Hospital of Xi' an Jiao tong University, from October 2018 to January 2021, were enrolled for the study after participants signed an informed consent form.

Results:

1. The age of 139 asymptomatic postmenopausal women with endometrial thickening was 60.5 ± 7.2 years, and the endometrial thickness was 9.3 ± 4.5 mm. The histopathological results included 68 (48.9%) cases with atrophic endometrium, 41 (29.5%) with endometrial polyps, 18 (12.9%) with endometrial hyperplasia without atypical hyperplasia, 3 (2.2%) with submucosal myomas. In addition, 9 (6.5%) cases had endometrial carcinomas.

2. Univariate analysis showed that endometrial cancer in postmenopausal women with asymptomatic endometrial thickening was associated with diabetes and endometrial thickness. Multivariate logistic analysis showed that endometrial thickness was an independent risk factor for the development of endometrial cancer in this population ($p=0.011$).

3. The area under the ROC curve for the diagnosis of endometrial thickness in patients with endometrial cancer was 0.77 (95% CI 0.63–0.91, $P < 0.05$). The Youden index is maximised when the endometrial thickness is ≥ 8 mm, at which point the sensitivity, specificity, PPV and NPV are 100%, 43.9%, 11.0% and 100% respectively.

Conclusions:

1. Endometrial thickness of 8 mm in postmenopausal asymptomatic women with endometrial thickening is the best threshold for predicting malignant endometrial lesions. Endometrial thickness has moderate diagnostic value for endometrial cancer.
2. The most common pathological type of postmenopausal asymptomatic endometrial thickening is atrophic endometrium, followed by endometrial polyps and, less frequently, malignant endometrial lesions.
3. The thickness of the endometrium in postmenopausal asymptomatic women with endometrial thickening is a high risk factor for the development of endometrial cancer.

Key words Postmenopausal; Asymptomatic; Endometrial thickening; Pathological endometrial thickness threshold; Histopathology

Different effect of low dose and ultra-low dose hormone therapy on glycolipid metabolism in perimenopausal women

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Objective: This study aimed to compare the influence of different doses of menopausal hormone therapy (MHT) on glycolipid metabolism in perimenopausal women and to evaluate the efficacy and safety of ultra-low dose MHT. **Methods:** A retrospective study of females aged 40–60 years with perimenopausal syndrome receiving at least 12 months MHT was conducted. According to the dose of estrogen, all participants were divided into two groups, the low dose MHT (LD-MHT) group and the ultra-low dose MHT (ULD-MHT) group. Age, height, weight, body mass index, and the past medical history were recorded before the treatment. The serum level of sex hormone, fasting insulin (FINS), fasting blood glucose, total cholesterol, triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol were tested as well as menopausal symptoms were assessed by Kupperman Index at baseline and after 12 months MHT. **Results:** Among a total of 85 patients enrolled, there was no significant difference between LD-MHT group (N=50) and ultra-low dose MHT (ULD-MHT) group (N=35) at baseline. By the end of 12 months of treatment, the serum follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol between the two groups were showed a statistic difference ($p < 0.05$). FSH and LH decreased and estradiol increased in the LD-MHT group, while in the ULD-MHT group, LH and estradiol had no significant difference ($p > 0.05$). The Kupperman Index score decreased significantly in both groups ($p < 0.05$) and no difference at the 12th month between the two groups ($p > 0.05$) were noted. As compared to baseline values, the concentration of serum FINS decreased and HDL-C increased in LD-MHT group ($p < 0.05$), HDL-C and LDL-C decreased in ULD-MHT group ($p < 0.05$) after treatment. The level of TG and HDL-C were considerably lower after ULD-MHT than LD-MHT ($P < 0.05$). Both groups have negligible differences in incidence of adverse effects. **Conclusions:** Ultra-low dose MHT can maintain the minimum serum hormone level that is effective to menopausal syndrome and safe. Ultra-low dose of treatment may have more advantage in maintaining the homeostasis of glucolipid metabolism in perimenopausal women.

Key words menopause; hormone therapy; glycolipid metabolism

Estrogen therapy before hysteroscopic alters the cell proliferation by promoting the PPP metabolism

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Objectives: The fallopian tubes and uterine abnormalities are the major causes of female infertility, while hysteroscopy can diagnose the pathological factors and treat such disorders effectively. Unfortunately, it can also lead to complications such as the formation of intrauterine adhesions post-operatively. Oestrogen therapy has been widely used as a supplementary treatment after hysteroscopy since it could improve the endometrial regeneration and menstruation, inhibit recurrent adhesions and improve the conception rate. But whether high dose estrogen could improve prognosis before hysteroscopic is few and the mechanism of estrogen improving endometrial metabolism is also unclear. The safety needs to be further evaluated. We hope to know, in infertility patient, whether E2 treatment before hysteroscopic surgery will really cause serious adverse consequences, and meantime study effects of high doses of E2 on endometrial metabolism in proliferative phase.

Materials and Methods: Twelve infertility patients who had been diagnosed before processed with hysteroscopy combined with laparoscopy were recruited. Six patients were treated with estrogen (Estrogen Group) and the others were not (Control Group) before they all took the hysteroscopy combined with laparoscopy. Endometrial tissue of both estrogen treated and control groups were collected during the surgery. After fasting for 24 hours, the Ishikawa cells were treated with 100 nM estrogen or DMSO (vehicle control) for 48 hours. Metabolites were extracted from endometrium tissue samples and Ishikawa cell samples, and analyzed by UHPLC-MS (AB Sciex). The metabolomics data were analyzed using MetaboAnalyst 5.0 (Heatmap, PCA score plot, and VIP score) and GraphPad Prism 8 (Statistical analysis). The metabolic pathway analysis was referring to the KEGG metabolic pathway map. The cell Proliferation was measured using a CCK8 kit after the Ishikawa cells treated with 10 μ M/5 μ M pentose phosphate pathway metabolism inhibitor, 6-aminonicotinamide (6-AN), 100 nM estrogen, or 100 nM estrogen along with 10 μ M/5 μ M 6-AN.

Results: The metabolomic results indicate that estrogen could indeed cause the metabolic changes in patient's endometrial tissues. Both the glycolysis metabolites and pentose phosphate pathway (PPP) intermediates are upregulated after estrogen treated. The in vitro cell metabolomics result indicates that estrogen can extensively altered the metabolites of endometrial epithelium cells. Since 12 metabolic pathways were significantly changed, and the top one is pentose phosphate pathway. The 5-phosphoribosyl-1-pyrophosphate (PRPP) is also upregulated by the estrogen, which imply the de novo nucleotide biosynthesis is stimulated. While the cells treated only estrogen gain an accelerated growth as we expected, 6-AN both (5 μ M and 10 μ M 6-AN) treated cells did not observe any significant cell proliferation changes, both estrogen and 6-AN spotted a decelerated growth even slower than the vehicle treated cells. it was suggested when the G6PD activity being inhibited with 6-AN, the E2-ESR can promote the expression of G6PD without stimulating the de novo biosynthesis of nucleotides.

Conclusion: we observed the pentose phosphate pathway is perturbed by estrogen and the estrogen alters the cell proliferation by promoting the pentose phosphate pathway metabolism.

Key words Estrogen treatment, Hysteroscopy, 6-Aminonicotinamide, Pentose phosphate pathway, Metabolomics

The Reproductive and Ovarian Function of Survivors after Hematopoietic Stem Cell Transplantation

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Objectives:

1. To investigate the effect of Hematopoietic stem cell transplantation (HSCT) treatment on reproductive and ovarian function in female survivors with hematological diseases.
2. To obtain data about reproductive and ovarian function of female survivors after HSCT in China and establish a database to follow up the patients for a long time.

Materials and Methods:

All female survivors under 40 years old who had HSCT at Hebei Yanda Lu Daopei Hospital during 2017 were included. According to the screening criteria, a total of 55 research subjects were included finally.

Results:

1. Information about blood diseases: the age of the patients at the time of HSCT was between 8–37 years old. The main types of diseases were acute lymphocytic leukemia (ALL) and acute myeloid leukemia (AML) (44/55 participants). The main type of HSCT was haploid transplantation (38/55 participants). Human leukocyte antigen (HLA) was mostly 5/10 matched (23/55 participants). 89.1% (49/55) of the patients had received chemotherapy before HSCT. Except for AA patients, all the other patients (5/55 participants) have adopted MAC, mainly including modified total body irradiation/cyclophosphamide (TBI/Cy) (25/55 participants) and modified busulfan/cyclophosphamide (Bu/Cy) (23/55 participants). 50.9% (28/55) of the patients had chronic graft-versus-host disease (cGVHD).

2. Menstruation and pregnancy of patients after HSCT: ① Before HSCT, 23.6% participants had no menarche (13/55). 76.9% (10/13) of them still had no spontaneous menarche and 23.1% (3/13) had spontaneous menarche after HSCT. ② Among females (42/55) who had menstrual cycles before HSCT, 16.67% (7/42) had menstrual relapse after HSCT, and 83.3% (35/42) had amenorrhea. ③ All participants had no pregnancy after HSCT.

3. Analysis of factors related to POI: 81.8% (45/55) of the enrolled females can be diagnosed with POI. And the incidence of POI in the participants aged 21–40 years was 100% (25/25), in 11–20-year-old females was 79.2% (19/24), and in the ≤ 10 -year-old group was 16.7% (1/6). The probability of POI in survivors ≤ 10 years old and between 11–20 years old was significantly lower than that in patients between 21–40 years old. The probability of POI in participants had TBI/Cy regimen (64%) was significantly lower than that of patients had chemotherapy regimen alone (95.2%). The probability of POI in females receiving Bu/Cy regimen (96.0%) was significantly higher than that of other regimens (70.0%). In addition, patients with cGVHD were more likely to develop POI (95.3%).

4. Stratified analysis of factors related to POI in patients at HSCT-age ≤ 20 years: The incidence of POI in females who received TBI/Cy regimen (40%) was significantly decreased ($p=0.02$). Participants who received Bu/Cy regimen had a significant increase in the incidence of POI (92.3%) ($p=0.027$).

5. Menopausal symptoms: The Kupperman score suggests that 29.1% (16/55) of the female survivors had mild symptoms, 25.5% (14/55) had moderate symptoms, and 1.8% (1/55) had

severe symptoms. The participants who had received HRT accounted for 40.0% (22/55). Menopausal symptoms were significantly correlated with HSCT age. Patients with HSCT age ≤ 10 years old (0%) and 11-20 years (16.7%) were less likely to have moderate to severe menopausal symptoms than patients aged 21-40 years on HSCT (44.0%).

Key words hematopoietic stem cell transplantation; radiotherapy and chemotherapy; premature ovarian failure; reproductive function; hormone replacement therapy

Effect of long non-coding RNA IGF2AS on cognitive decline in ovariectomized rats

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Purpose To explore the IGF2AS function and related mechanism in cognitive impairment after menopause. **Methods** The 12 weeks Sprague-Dawley (SD) rats were divided into three groups as sham control group, ovariectomized (OVX) group and replacement treatment (ERT) group. The OVX group was established by ovariectomy. The sham control group was subjected to the same steps of operation without ovariectomy. The ERT group was orally administrated the pure peanut butter with 17 β -estradiol (0.1 μ g 17 β -estradiol /gram body weight per day) lasting for nearly 20 weeks. Then, cognitive function alteration was estimated by Morris water maze (MWM) test between baseline and endpoint of experiment. IGF2AS and related pathway molecular such as IGF2, BDNF, AKT and TrkB at both gene and protein expressions were assessed in hippocampus tissues. In addition, the serum estrogen and BDNF were also assessed. **Results** At baseline, there was no significant difference on the body weight and cognitive function of three groups. At the endpoint, the OVX rats were obviously heavier than sham rats ($P=0.006$) and ERT rats ($P=0.001$), while there was no significant difference between sham rats and ERT rats. At the endpoint, the OVX group showed less travelling distance ($P=0.035$) in the target quadrant, less crossing times at the location of the target quadrant ($P=0.002$) and platform ($P=0.015$) in comparison to the sham group, while the ERT group showed more travelling distance ($P<0.001$) in the target quadrant, more crossing times at the location of the target quadrant ($P<0.001$) and platform ($P=0.001$), less latency to first entry of target quadrant ($P=0.027$) and platform ($P=0.010$) in comparison to the OVX group. There was no significant difference between ERT group and sham group. The serum BDNF concentrations of OVX group were lower than that of sham group ($P=0.018$) and ERT group ($P=0.040$), while there was no significant difference between sham group and ERT group. Gene expression of TrkB, AKT, BDNF and IGF2 were significantly reduced, the IGF2AS expression was significantly increased in hippocampus of OVX group in comparison to sham group and ERT group, while there was no significant difference between sham group and ERT group. Protein products of TrkB, BDNF and IGF2 were significantly reduced in hippocampus of OVX group in comparison to sham group and ERT group, whereas AKT protein was unaffected. There was no significant difference in TrkB, BDNF and AKT protein expression between sham group and ERT group. **Conclusion** The rat cognitive function decreased after ovariectomy, and ERT was beneficial to improve the cognitive function of ovariectomized rats. IGF2AS may act as functional modulator in cognitive impairment of ovariectomized rats, possibly through the regulation of IGF2 via BDNF / TrkB / Akt signaling pathway. This work was supported by the National Natural Science Foundation of China [grant number 81801415].

Key words IGF2AS; long non-coding RNA; cognitive decline; estrogen

Advances in the mechanisms of exosomes and miRNA on ovaria-related diseases

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Ovarian diseases have serious harm to women's physical and mental health. Many ovaria-related diseases are hidden, difficult to find, and difficult to treat. The prognosis is easy to repeat. Therefore, early detection, early diagnosis and early treatment are particularly important. In recent years, many studies have shown that exosomes and miRNA are actively involved in the occurrence, development, metastasis, invasion and immunity of ovarie-related diseases. Exosomes and miRNA provide a new research direction for the early diagnosis, treatment and prognosis of various diseases. In this review, the mechanisms of exosomes and miRNA in the screening and treatment of ovaria-related diseases were reviewed.

Key words Exosome; miRNA; Ovarian disease

Activation of non-classic estrogen receptor GPR30 promotes Schwann cell proliferation, differentiation and myelination in Vitro

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Objective: To explore the role of G protein-coupled estrogen receptor (GPR30/GPER1), a non-classical estrogen receptor (ER), in the formation and regeneration of peripheral nerve myelin, via regulating the proliferation, differentiation and myelination of Schwann cells in vitro.

Materials and methods: We used the primary Schwann cells from neo-natal rats' sciatic nerves to monitor their proliferation and differentiation, as well as the explant co-culture of dorsal root ganglion (DRG) cells from mice to monitor the myelination of Schwann cells. The primary rat Schwann cells and the mice DRG cells were randomly categorized into four groups treated with 100 nM G1 (a GPR30 specific agonist), 100 nM 17 β -estradiol (E2), 100 nM E2+100 nM G15 (a GPR30 specific antagonist), and equal-volume of DMSO (the solvent), respectively. The proliferation of Schwann cells was examined by the BrdU Incorporation Assay combined with immunofluorescence assay; the expression of Schwann cell differential markers (Mag, Mpz, Krox20) were detected by the Western blot and immunofluorescence assay; the expression of myelin marker MBP in mice DRG explant co-culture was detected by immunofluorescence assay and the formation of peripheral nerve myelin sheaths in four groups were calculated and compared.

Results: The primary Schwann cells cultured in proliferation medium and treated with G1 or E2 for 24 hrs showed a higher BrdU positive percentage than the other two groups, especially the E2 treated group. Notably, the promoting effect of E2 on proliferation was inhibited by simultaneous addition of G15 (E2+G15 group) (see Fig 1 in the attachments). Shown by both Western blot and immunofluorescence assay, G1 or E2 administration for 48 hrs increased the expression of Mag, Mpz and Krox20 in primary Schwann cells cultured in differentiation medium, especially the E2 group; whereas the addition of G15 could downregulate the overexpression of the differentiation markers above in E2+G15 group. We also found consistent result in the immunofluorescence assay of MBP expression for the formation of peripheral nerve myelin in the DRG explant culture : G1 or E2 increased the number of MBP positive myelin fragments compared with other two groups after myelination induction for 5 days, and this effects of E2 could also be inhibited by addition of G15 (see Fig 2 in the attachments).

Conclusions: Both the G1 and E2 could promote the proliferation, differentiation, and the myelination of Schwann cells in vitro. The GPR30 may be the receptor which mediated the effects of E2 on Schwann cells.

Funding: This work was financially supported by the National Natural Science Foundation of China (No: 31900743)

Key words Estrogen, G protein-coupled estrogen receptor, Schwann cells, myelin, dorsal root ganglion

Study on the ovarian protection of GnRHa in female patients of childbearing age underwent hematopoietic cell transplantation

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The purpose of this study was to investigate the application efficacy of GnRHa before hematopoietic stem cell transplantation in patients with hematological diseases.

Methods: A total of 311 women of childbearing age under 40 years old after myeloablative chemotherapy and hematopoietic stem cell transplantation in the gynecology clinic of Peking University people's Hospital from December 2011 to December 2018 were analyzed retrospectively. 107 patients were treated with GnRHa before myeloablative chemotherapy were defined as treatment group, and 204 patients without treatment of GnRHa were taken as control group. The levels of sex hormone, gonadotropin, menopause-related symptoms and menstrual recovery were compared between the two groups. **Results:** Compared with the control group, the menopause-related symptoms in the treatment group were significantly lower (62.62% vs. 74.51% $P=0.029$). Six months after transplantation, in the treatment group, the level of FSH was lower (101.72 mIU/ml (68.97–151.40 mIU/ml) vs. 123.29 mIU/ml (92.46–160.70 mIU/ml), $P=0.001$) and the level of E2 was lower (5.05 pg/ml (0.23–12.12 pg/ml) vs. 9.00 pg/ml (1.80–19.64 pg/ml), $P=0.020$), but there was no significant difference in LH level ($P=0.083$). There was no significant difference in the incidence of spontaneous menstruation recovery and iatrogenic premature ovarian failure between the two groups ($P=0.477$). Furthermore, there was no significant difference after stratified analysis with confounding factors controlled, such as the type of disease ($P=0.469$) and regular chemotherapy before myeloablative chemotherapy ($P=0.365$). **Conclusion:** For female patients of childbearing age after myeloablative hematopoietic stem cell transplantation, GnRHa treatment may not reduce the incidence of premature ovarian failure. However, GnRHa treatment may significantly reduce the level of gonadotropin after myeloablative chemotherapy and reduce the menopause-related symptoms, which may have a certain ovarian protective effect. Further clinical trials are needed to verify our results.

Key words myeloablative chemotherapy, hematological diseases, premature ovarian failure, fertility

Menopause-specific quality of life during ovarian aging among Chinese women: A prospective cohort study

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Objective: To describe the menopause-specific quality of life in Chinese urban women at midlife in a prospective cohort.

Study design: Prospective cohort study

Main outcome measures: This study included 920 natural menopausal midlife Chinese women who were followed up for 10 years. The Menopause-Specific Quality of Life (MenQoL) questionnaire, which includes four domains (vasomotor, psychosocial, physical, and sexual functioning symptoms), and other physical and behavioral factors was administered. Generalized estimating equations were used to assess associations.

Results: The mean MenQoL scores of the above-mentioned domains were 1.75 ± 1.32 , 2.13 ± 1.16 , 2.33 ± 1.11 , and 2.20 ± 1.83 , respectively. The occurrence of vasomotor symptoms (VMS) persisted in >50% of women in the perimenopausal and early postmenopausal stages. However, the prevalence of moderate/severe bothersome VMS was relatively low. Most women presented mild physical and psychological symptoms, whereas few of them had moderate/severe symptoms. Sexual problems are highly frequent and bothersome, and the occurrence increased with advancing menopausal stage and age. Bothersome sexual symptoms and moderate/severe sexual symptoms ranged from 31.89% and 1.58% in premenopausal women to 78.09% and 39.35% in late postmenopausal women. Menopausal status and poor health status were significantly associated with the four symptom domains.

Conclusion: VMS are among the most frequent menopausal symptoms rated as severe. Sexual problems become more prevalent with advancing menopausal status. Clinicians should have a wide understanding of changes that occur during the transition to maximize women's health.

Key words Menopausal symptom; Menopause-Specific Quality of Life questionnaire; Vasomotor symptom; Sexual symptom

Prebiotics intervention to improve intestinal barrier function and reduce blood lead in patients with recurrent abortion:a randomized controlled trial

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Background: Intestinal barrier is important for the human health, and its damage resulting in leaky gut can induce chronic inflammation, with increased toxins (including bacterial components, some heavy metals etc.) absorption. The objective of this study is to test if consumption of a mixed prebiotics (Holofood, containing polyglucose, galactose, inulin, microcrystalline, b-glucan, guar gum, erythritol, stevioside etc.) could improve the intestinal barrier function in patients with recurrent spontaneous abortion and repeated plantation failure, and then analyse the potentially underlying mechanisms.

Methods: We recruited 70 women with recurrent spontaneous abortion and repeated plantation failure in early pregnancy, aged 22-42 years, then they were randomized to experimental group (48) and control group (22). All the patients were examined conventionally to exclude some physical disorders. Except for testing conventional biochemical items in blood we also determine the blood lead, bacterial lipopolysaccharide (LPS) and some cytokines for evaluating gut integrity. In addition to conventional treatment, the experimental group was intervened with a mixed prebiotics (Holofood) for 8 weeks , with 10g (1 sachet) 30 minutes before each meal. Statistical analysis was performed to compare the blood lead value, intestinal barrier function and biochemical index between the two groups and for the intervened group.

Results: Compared with pre-intervention, the blood lead value ($P=0.000$), D-lactic acid ($P=0.000$), diamine oxidase ($P=0.000$) and IL-6 ($P=0.039$) in the post-intervention of experiment group decreased significantly, and there was no significant difference in endotoxin and biochemical indexes. In the control group, except that diamine oxidase ($P=0.040$) increased significantly, there was no significant difference in other indexes before and after the intervention.

Conclusion: Intervention of balanced ratio dietary fiber (Holofood) can reduce blood lead and pro-inflammatory factor in recurrent spontaneous abortion patients, improving intestinal permeability.

Key words Recurrent spontaneous abortion; Prebiotics intervention; Intestinal barrier; Blood lead; Pro-inflammatory factors

Application of freehand exercise in Menopausal myenia in women

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[Abstract] Objective To explore the effectiveness and feasibility of freehand exercise in female menopausal myenia. Methods 300 patients were randomly divided into 150 patients, with routine diet and exercise guidance, routine exercise, including opening, upright arm swing, side bow step, SARC-F score and satisfaction before and after intervention. Results After 12 months, the SARC-F score was significantly higher than the control group ($P < 0.05$) and the satisfaction was improved. Conclusion freehand exercise can promote muscle strength and strength in female patients.

Key words Application of freehand exercise

Therapeutic effects of human umbilical cord mesenchymal stem cell-derived exosomes on chemotherapy-associated ovarian damage in mice

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Purpose

To investigate the effect of HucMSC-exos on the restoration of ovarian function in a chemotherapy-associated ovarian damage mouse model and provides novel insights for rejuvenation therapy for the protection of female reproductive function in clinical practice.

Materials and methods

Exosomes were obtained from the supernatant of cultured HucMSCs. A total of 100 female C57BL/6 mice (aged 7-8w old) were selected. The mice were fed until 12w of age, and cisplatin was administered by intraperitoneal injection for 10 consecutive days to induce chemotherapy-associated ovarian damage in mice. Seventy-five mice with estrous cycle disorder were screened and randomly divided into 3 groups according to their body weight: model group, positive control group, and HucMSC-exos group. Another 25 mice were used as negative controls. On day 12, the mice in the HucMSC-exos group were injected with PKH26-labeled HucMSC-exos in the tail vein, and the mice in the positive control group were given an oestradiol valerate solution and a medroxyprogesterone acetate solution in the tail vein. An injection of PBS served as the negative control.

Results

The estrous cycles of the model group mice were disrupted throughout the experiment. Mice in the HucMSC-exos group and the positive control group resumed normal estrous cycles. PKH26-labeled HucMSC-exos were detectable within the ovaries. The ovarian weight of the model group mice continued to decline. The ovarian weight of the HucMSC-exos group mice and the positive control group mice decreased first and then gradually increased. The pathological examination revealed the number of follicles at all stages was significantly reduced, the number of atretic follicles increased, the number of primordial follicles and corpus luteum significantly decreased, and the corpus luteum had an irregular shape. Compared with those of the model group, the lesions of the HucMSC-exos and positive control groups significantly improved, as well as the ovarian angiogenesis. The expression levels of total AKT, p-AKT, and angiogenic cytokines in the ovaries of mice damaged by chemotherapy were markedly upregulated after HucMSC-exos transplantation, suggesting that HucMSC-exos transplantation might recover ovarian function via the PI3K/AKT signaling pathway. Compared with the negative control group, the model group experienced a decrease in E2 and an increase in FSH. Compared with the model group, the HucMSC-exos and positive control groups experienced a slight increase in E2 and a decrease in FSH; the difference was statistically significant ($P < 0.05$).

Discussion

HucMSC-exos restored structure and function in the ovaries of mice damaged by chemotherapy. Our study provides new insights into the great clinical potential of HucMSC-exos in treating chemotherapy-associated ovarian damage.

Key words HucMSC-exos; chemotherapy-associated ovarian damage;rejuvenation therapy

Study on the mechanism of hypothalamic preoptic area dysfunction induced by low estrogen leading to menopausal hot flashes

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Objective: In the low estrogen state of menopause, the dysfunction of hypothalamic preoptic area (POA), the center of thermoregulation, causes hot flashes, including internal abnormalities and external regulatory changes of POA. Based on high-throughput screening, this study aims to explore the mechanism of low estrogen leading to the imbalance of POA regulation of heat dissipation and heat production and trigger hot flashes from both internal and external aspects.

Methods: Adult female rats were randomly divided into sham-operated (SHAM) group, ovariectomized (OVX) group and ovariectomized with estrogen treatment group (OVX+E).

(1) Transcriptomics and proteomics were used to screen differential RNA and proteins of POA and to analyze their functional pathways.

(2) Explore the changes within POA: ① The expression of ER α , ER β , GAD1 and GAD2 were detected by qRT-PCR, Western Blot and Immunofluorescence, and the co-expression of ER α or ER β and GAD1 or GAD2 were observed by double-labelling Immunofluorescence; ② The number of glutamatergic and GABAergic neurons was detected at RNA and protein levels by RNAscope and Immunofluorescence; ③ Vglut2-Cre and Vgat-Cre mice combined with chemogenetics were used to specifically activate or inhibit glutamatergic or GABAergic neurons to observe the changes of indexes related to hot flashes.

(3) Explore the changes of external regulation of POA: ① The expression of ER α and ER β in dorsal raphe nucleus (DR) and locus ceruleus (LC) were detected by qRT-PCR, Western Blot and Immunofluorescence; ② The number of serotonergic neurons in DR and noradrenergic neurons in LC were detected by Immunofluorescence; ③ Anterograde tracer AAV was injected into DR and LC respectively to observe the distribution of serotonergic and noradrenergic nerve fibers in POA, and retrograde tracer CTB was injected into POA to observe the infection of serotonergic neurons in DR and noradrenergic neurons in LC with CTB; ④ The distribution of receptors of serotonin and norepinephrine in POA was observed by Immunofluorescence.

Results: Levels of serum 17 β -estradiol decreased in ovariectomized rats and no estrous cycles occurred, along with symptoms similar to hot flashes. In the low estrogen state:

(1) The differential RNA and protein of POA were enriched in the functional pathways of glutamate, GABA, serotonin and norepinephrine.

(2) Changes within POA: ① The expression of ER α and ER β decreased, the expression of GAD1 increased while GAD2 decreased, and there was a co-expression of ER α or ER β with GAD1 or GAD2 in the same neuron; ② The number of glutamatergic neurons decreased and the function of initiating heat dissipation weakened, while the number

of GABAergic neurons increased and the function of initiating heat production enhanced.

(3) Changes of external regulation of POA: ① The expression of ER α and ER β decreased in DR and LC; ② The number of serotonergic neurons in DR and noradrenergic neurons in LC decreased; ③ The distribution of serotonergic and noradrenergic nerve fibers in POA decreased, and the distribution of serotonergic neurons in DR and noradrenergic neurons in LC projecting to POA decreased; ④ The distribution of receptors of serotonin and norepinephrine in POA decreased.

Conclusion: On the one hand, menopausal low estrogen may regulate the increased expression of GAD1 and the decreased expression of GAD2 in POA through its decreased nuclear receptors ER α and ER β , resulting in a decrease in the number of glutamatergic neurons and the weakened function of initiating heat dissipation while an increase in the number of GABAergic neurons and the enhanced function of initiating heat production. On the other hand, low estrogen may regulate the synthesis of serotonin in DR and norepinephrine in LC through its reduced nuclear receptors ER α and ER β , leading to the reduction of both serotonergic neurons and noradrenergic neurons and their nerve fibers projecting to POA, and regulating the dysfunction of glutamatergic and GABAergic neurons. Under the condition of low estrogen, the internal and external changes of POA regulate the abnormal number and function of glutamatergic and GABAergic neurons, which may be the key factor leading to the imbalance of its function of regulating heat dissipation and heat production and thus causing menopausal hot flashes.

[This study is supported by National Natural Science Foundation of China (grant number: 81873818); Beijing Natural Science Foundation (grant number: 7202075) ; Beijing Hospitals Authority' Ascent Plan (code: DFL20190701); Beijing Hospitals Authority Clinical Medicine Development of Special Funding Support (code: ZYLX202112).]

Key words

Vasomotor symptoms and osteoporosis in perimenopausal and early postmenopausal women

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Objective:

To investigate the correlation between vasomotor symptoms (VMS) and osteoporosis (OP) in perimenopausal and early postmenopausal women.

Methods:

A total of 100 perimenopausal and early postmenopausal women aged 40–55 years who visited the climacteric clinic of The Second Xiangya Hospital from January 1, 2018 to March 1, 2019 were studied. The vasomotor symptoms were assessed by modified Kupperman scale. Bone mineral density (BMD) was measured by dual energy X-ray absorptiometry. Bone T value was calculated, and then the BMD was stratified. Serum estradiol (E2), follicle stimulating hormone (FSH), fasting blood glucose (FBG), triglyceride (TG), total cholesterol (CHOL), high density lipoprotein cholesterol (HDL-CH), low density lipoprotein cholesterol (LDL-CH), serum insulin (INS), total serum procollagen type I amino terminal propeptide (T-PINP), 25-hydroxyvitamin D3 (25-OHD3) and β -collagen specific were also measured. Special sequence (β -CTX) level. The correlation between vasomotor symptoms and osteoporosis of lumbar spine and femur was analyzed by regression analysis.

Results:

The average age of all the researchers was 48.95 ± 3.85 years. According to the severity of vasomotor symptoms, 24 (24%) were asymptomatic, 35 (35%) were mild symptoms and 41 (41%) were moderate to severe symptoms. There were significant differences in age, FSH, E2, CHOL, LDL-CH, INS and beta-CTX levels among the three groups ($P < 0.05$). VMS was positively correlated with age, FSH, CHOL, LDL-CH, INS and beta-CTX levels ($P < 0.05$), and negatively correlated with E2 levels ($P < 0.05$). According to the BMD T value, the patients were divided into 20 cases of normal bone mass (20%), 54 cases of low bone mass (54%) and 26 cases of osteoporosis (26%). There were significant differences in age and beta-CTX levels among groups ($P < 0.05$). BMD T was positively correlated with E2 level and body weight ($P < 0.05$), negatively correlated with age and beta-CTX ($P < 0.05$). There was significant difference in BMD T between different degrees of vasomotor symptoms ($P < 0.05$). After adjusting factors such as age, weight, current menstrual status, follicle stimulating hormone, estrogen and special collagen sequence, etc. Moderate to severe vasomotor symptoms were still significantly associated with the risk of osteoporosis (OR = 86.94, 95% CI = 5.94–1272.93) ($P < 0.05$).

Conclusion:

Vasoconstriction symptoms in perimenopausal and early postmenopausal women are associated with osteoporosis. Vasomotor symptoms may be one of the risk predictors for screening high-risk population of osteoporosis.

Key words

Clinical Analysis of 200 Cases of Amenorrhea Patients Bing Late Menopause Transition Period with Progesterone Withdrawal Bleeding

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Objective: To evaluate the value of endometrial thickness and estrogen level in predicting progesterone withdrawal bleeding of amenorrhea patients in late menopause transition period.

Methods: Endometrium thickness and serum E2 level were measured through TVS and CLIA before progesterone withdrawal test in 200 patients who are in Late menopause transition period or have secondary amenorrhea syndrome. Then analyzing their chance of illness of intramuscular progesterone withdrawal bleeding by means of ROC.

Results: (1) the area under ROC curve AUC1 and AUC2 of prediction of progesterone withdrawal bleeding with EM and E2 were 0.89 and 0.98 respectively. Both were higher than the area under opportunity reference line ($P < 0.001$). ROC results showed that AUC2 was higher than AUC1, and also there was obvious statistically significant difference ($P = 0.001$) between AUC1 and AUC2. (2) According to the ROC curve calculation, the optimal cutoff value of EM is 0.45mm, the sensitivity of predictive progesterone withdrawal bleeding was 86.3%, the specificity was 84.3%, the positive predictive value was 75.9% and the negative predictive value was 91.5%. While the optimal cutoff value of E2 is 40.08pg/dl (146.4pmol/L), the sensitivity of predictive progesterone withdrawal bleeding was 86.3%, the specificity was 100%, the positive predictive value was 100% and the negative predictive value was 92.7%. (3) In patients with an endometrium thickness of 4.5mm and below, withdrawal bleeding was occurred in 10 cases, which was accounted for 8.55%, while in patients with an E2 level of 40pg/dl and below, withdrawal bleeding was occurred in 10 cases, which was accounted for 7.30%. Taking account of both E2 and EM, the sensitivity of prediction progesterone withdrawal bleeding was 89% and the specificity was 99.2%, the positive predictive value was 98.5% and the negative predictive value was 94%.

Conclusion: EM and E2 of amenorrhea patients being in late menopause transition period have clinical values in predicting the progesterone withdrawal bleeding.

Consideration both EM and E2 can improve the prediction sensitivity and specificity. For the amenorrhea patients being in late menopause transition period especially the patients with menopause symptom, it is practicable to predict progesterone withdrawal bleeding as per their EM and E2 in clinical practice. If the predictive result is negative, menstrual period adjustment treatment can be applied directly that can avoid the patient's waiting for progesterone withdrawal experiment and alleviate their clinical symptoms.

Key Words: Late menopause transition period; Amenorrhea; Endometrium thickness; Estrogen level; Progesterone withdrawal bleeding

Key words Late menopause transition period; Amenorrhea; Endometrium thickness; Estrogen level; Progesterone withdrawal bleeding

The Efficacy of Four Different Therapies in Postmenopausal Urogenital tract syndrome

Linuer Di

The First Affiliated Hospital of Xinjiang Medical University

Objective: To compare the therapeutic efficacy and safety of four different options for postmenopausal

Urogenital tract syndrome (GSM), to guide clinical diagnosis and treatment. **Methods:** 120 cases of Urogenital tract syndrome in our department of gynecology from November 2016 to August 2018 were voluntarily enrolled according to the inclusion and exclusion criteria and randomly divided into four groups, which were group A (vaginal moisturiser without hormone: Weirun collagen vaginal gel), group B (Honglilai estrogens cream), group C (Honglilai estrogens cream + herbal anti-inflammatory agent: Baofukang froth) and group D (Weirun collagen vaginal gel + Baofukang froth). After the treatment, we made comparison of efficacy and safety among the four groups.

Results: After the treatment, signs and symptoms scores of our groups are group A (7.59 ± 1.28), group B (6.76 ± 1.33), group C (4.48 ± 1.02), group D (5.34 ± 1.01), efficacy: group C > group D > group B > group A, and the difference was statistically significant ($P < 0.05$). Vaginal pH results of four groups are group A (5.10 ± 0.15), group B (4.38 ± 0.17), group C (4.04 ± 0.18), group D (4.24 ± 0.13), efficacy: group C > group D > group B > group A, and the difference was statistically significant ($P < 0.05$). MV results are group A (31.94 ± 3.16), group B (65.68 ± 2.44), group C (72.19 ± 2.86), group D (54.40 ± 2.56). MV of group A shows no statistical difference after the treatment ($P > 0.05$), but the other three groups were significantly higher, efficacy: group C > group B > group D, and the difference was statistically significant ($P < 0.05$). In terms of safety, plasma level of E2, FSH, LH and endometrial stripe show no significant difference ($P > 0.05$). **Conclusions:** All four treatment schemes have obvious efficacy for GSM, of which plan C has the best efficacy, followed by Plan B. For those who have contraindications and refuse hormone therapy, the use of non-estrogens combined with local anti-inflammatory drugs (Plan A and Plan D) can be an effective alternative.

【Keywords】 Urogenital tract syndrome; Therapy; Hormones; Estrogens; Administration, intravaginal

Key words Urogenital tract syndrome; Therapy; Hormones; Estrogens; Administration, intravaginal

The Significance of different administration routes of estrogen in MHT

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The menopausal population in China is huge and is expected to continue to grow rapidly in the last 10 years. Most of them will face short-term symptoms and long-term harm related to menopause.

Years of clinical practice has proved that menopausal hormone therapy (MHT) can effectively relieve related symptoms, improve the quality of life of menopausal women, and prevent the occurrence of chronic diseases in the elderly to a certain extent. The key to the safety of MHT lies in the different routes of administration of estrogen, the use of appropriate estrogen, and the appropriate route of administration can minimize potential risks and achieve the best individualized treatment.

Commonly used routes of administration of MHT are mainly divided into oral estrogen, non-oral includes transdermal administration and vaginal administration, subcutaneous implantation and intramuscular injection are less used. Oral estrogen may cause ischemic stroke, induce thrombosis, and increase the risk of VTE. It is rare in patients under 60 years of age. Transdermal estrogen does not increase the risk. Evidence-based medical evidence supports a lower risk of transdermal estrogen thrombosis. The cautious use of MHT mainly includes thrombosis, gallbladder disease, systemic lupus erythematosus, asthma, and transdermal estrogen all have higher safety. The principle of MHT medication is safe, effective, and individualized. In addition to using natural estrogen as much as possible, appropriate administration routes have become more and more important. Oral estrogen, transdermal estrogen, and vaginal estrogen have become the three main routes of administration, each with its own advantages. Among them, transdermal estrogen has the widest response range and the highest safety. Refer to the guidelines and choose the appropriate route of administration according to the patient's condition.

Key words Menopausal hormone therapy (MHT), Routes of administration

Early diagnosis and early treatment of premature ovarian insufficiency

Shulan Lv

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POI (premature ovarian insufficiency) is a clinical syndrome of decreased ovarian activity in women before the age of 40, characterized by menstrual disorders (such as amenorrhea or oligomenorrhea) accompanied by high gonadotropin and low estrogen. Menopause or menstrual cycle length was >4 months, and two consecutive FSH > 25 U/L for more than a 4-week interval.

POI is proposed on the basis of premature ovarian failure (POF), with the purpose of advancing the diagnostic threshold and protecting the reproductive and endocrine functions of patients to a greater extent. However, some young patients still need further early detection to maximize reproductive function. This article reviews how to detect, diagnose and manage POI early in adolescents.

Key words POI early diagnosis early treatment

Features of National Menopause Guidelines in China

Rong Chen

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Background:

China has a vast territory. There are huge differences between urban and rural areas with uneven development. China has entered an aging society and the public's demand for menopause management is urgent. Menopause management started late in China. Chinese Menopause Society was founded in 2000 in Beijing. Traditional Chinese medicine is used to treat climacteric symptoms, which is highly accepted by the public.

Structure of Guidelines for menopause management and menopausal hormone therapy in China (2018)

- Diagnosis of menopause and STRAW+10
- Health management strategy of menopausal women
- General Principles for Menopausal Hormone Therapy (MHT) Indications, Contraindications and situations with caution of MHT
- Commonly-used medicine, Standardized process of the diagnosis and treatment (flowchart)
- Long-term benefits and risks profiles of MHT Treatment strategies for menopausal-related symptoms/problems
- Premature ovarian insufficiency

Strengths of Chinese menopause guideline

- Comprehensive: it includes the overall strategy of menopause management, and details of MHT and non-MHT.
- Taking into account the uneven level of medical care throughout the country, basic knowledge and academic progress are both included.
- Distinct viewpoints: indications, contraindications, the use of caution, the benefits and risks of MHT were all clearly listed.
- Practicability: Flowcharts + detailed MHT regimen to facilitate ease of use for clinicians to apply in practice.
- unfinished agenda: the next edition of Chinese Menopause Guideline is now being rewritten.

Key words Menopause, Guidelines

Perimenopausal/Postmenopausal Endometriosis and Malignant Transformation

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Endometriosis has a high prevalence, with an incidence of about 10% among women of childbearing age. Endometriosis in perimenopausal and postmenopausal women is mostly the persistence or recurrence of premenopausal disease. A German study showed that 19.64% of patients with endometriosis were perimenopausal and postmenopausal women. Menopausal hormone therapy (MHT) should be used cautiously in patients with endometriosis, and the main concerns about its use are whether it will cause recurrence of endometriosis and whether it will increase the possibility of malignant transformation of endometriosis. Most guidelines and consensus suggest that patients with endometriosis who require MHT after natural menopause should be treated with a continuous combination of estrogen and progestogen regimen or tibolone, and estrogen should be used at the lowest effective dose. Even after hysterectomy with bilateral salpingo-oophorectomy, MHT is recommended as an estrogen-progestogen combination regimen or tibolone therapy for at least 2 years before changing to estrogen alone. A cohort study and case-control study that included endometriosis associated with malignancy risk found that endometriosis was positively correlated with clear cell carcinoma, endometrioid carcinoma, and low-grade serous carcinoma. There was a positive correlation between endometriotic cysts and ovarian cancer (RR 2.56, 95% CI 1.98 - 3.27), while there was no association between superficial and deep infiltrating endometriosis of the peritoneum and ovarian cancer.

Menopause is an independent risk factor for malignant transformation of endometriosis. Attention should be paid to identify the presence of malignant transformation of endometriosis in the following situations: changes in pain rhythm in patients with endometriosis in perimenopausal period, ovarian cysts grow rapidly and the diameter of cysts is greater than 10 cm, imaging examination revealed solid or papillary structures in the cysts with abundant blood flow in the lesions, serum CA125 level > 200 kU/L (except infection or adenomyosis).

Key words

Challenges to manage mental disorders during the menopausal transition and beyond

Wen Di

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Mental disorders are the main contributors to global disability. Women are at significant higher risk than men of developing mental disorders. The perimenopausal period is a “Window of vulnerability” for the development of mental disorders. Lack of understanding of menopause related mental disorders in Chinese women and lack of standardized management, leading to aggravation of the disease, a decline in the quality of life and a large economic burden.

Perimenopausal mental disorders present variable clinical manifestations, several common symptoms of the perimenopause cooccur and overlap with the presentation of mental disorders during this stage, leading to delays in diagnosis. The diagnosis of perimenopausal mental disorders needs to be confirmed through the identification of the menopause stage, the diagnosis of mental disorders, and the differential diagnosis. The standard management for perimenopausal mental disorders is still controversial. Currently, the recommended therapies include: antipsychotic agents, hormone therapy, cognitive behavioral therapy, etc. The therapy should be determined tailored to the individual patient, but must take into account the benefits and risks.

The stigmatization of menopause and psychosis in our society, insufficient mental health care manpower and unevenly distributed across regions, the knowledge gap between the frontier of new medical technology and the local practice standards are major challenges for the management of menopausal mental disorders. There is an urgent need to strengthen the understanding of physicians, especially ob-gyns, about perimenopausal mental disorders, and to establish a new mental health management model, including on-site screening, patient engagement, education, multidisciplinary management, tracking and psychiatric consultation, to promote the physical and mental health of perimenopausal women.

Key words Perimenopausal period, mental disorder

Diagnosis and intervention of female Sarcopenia

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Summary:

With the acceleration of the aging process in China, gynecologic clinicians and maternal health care workers should pay more attention to screening and diagnosis of perimenopausal and postmenopausal women with Sarcopenia, providing effective preventive measures. It is of great significance to realize "healthy China" . Sarcopenia an age-related disease that often coexists with osteoporosis. It has become a public health problem that endangers the health and quality of life of the elderly.

The pathogenesis is related to many factors such as environment and heredity. Many studies have proved that the disease is related to aging, Sex hormone changes , insulin resistance, inflammatory cytokines, nutrition, exercise and other lifestyle factors and diseases.

At present, there is no specific drug treatment for Sarcopenia, potential patients might be identified through standard screening of targeted population, and the potential patients with Sarcopenia can be promptly diagnosed and assessed, through perimenopausal hormone replacement therapy (MHT) , exercise intervention and nutritional treatment, can effectively reduce and delay the occurrence and development of disease.

All levels of medical and health care institutions and medical personnel should pay attention to the prevention and treatment of female Sarcopenia.To increase the use of hormone therapy (MHT) in perimenopausal period.To standardize the clinical work of "screening-diagnosis-evaluation-intervention" for Sarcopenia.For each Chinese woman life cycle health management to make due contribution

Key words Sarcopenia, MHT, exercise intervention, nutritional therapy

Sharing of perimenopausal MDT continuous management mode based on “one-day outpatient”

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With the increasing population of menopausal and postmenopausal women in the country and abroad, more and more women are facing the interference of menopausal-related short-term, medium-term and long-term symptoms, which seriously affect their quality of life.

Menopause has become a topic of much concern for modern women. For obstetricians and gynecologists, it is also a hot issue worthy of exploration that how to diagnose, treat and manage the special group of menopausal women. In the aspect of diverse menopausal-related symptoms, doctors also face many difficulties and tests in the diagnosis and treatment process. For example, many patients do not understand “menopause” and “disorderly” seek medical treatment, “afraid of” hormones, long-winded irritability and forgetfulness, which lead to long-time medical treatment, incidental medical disputes, etc.

Therefore, it is imperative to improve traditional methods of diagnosis and treatment and explore new mode of diagnosis and treatment. In addition to the traditional menopausal “specialized disease outpatient departments”, our hospital also carried out offline “one-day clinic” multidisciplinary health education, online 7-week group “healthy lifestyle” continuous intervention and offline half-day focus group interview. Thus, based on “one-day outpatient clinic”, the perimenopausal Multidisciplinary sustainable management mode is innovatively constructed. This mode adds collective education for common problems, which can effectively eliminate misunderstandings and update concepts, and then use online team-style continuous management to consolidate and strengthen health care knowledge and promote the four cornerstones of health, effectively decrease the side effects of menopausal hormone therapy, reduce chronic aging the occurrence of diseases and improve the quality of life.

The management mode is based on the core concept of “prevention is better than cure”, the keys of the confidence of doctors and the power of role models, the support of hospital leaders, department leaders, multidisciplinary clinical and scientific research team members. Under the love, responsibility and dedication of the attending doctors, we continuously optimize, update the concepts of medical staff and update professional menopausal knowledge, so that more and more menopausal patients benefit from the mode, reaching our goal that “Menopause is wiser and more elegant, and old age is healthier and more beautiful”.

Key words Menopause, one-day outpatient clinic, multidisciplinary, diagnosis and treatment model

How to use MHT in cautious conditions

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With extension of life expectancy, the peri- and post-menopausal period has become the longest stage in the whole life cycle of women, and suitable health care management should be taken at this stage. Use of MHT has been proved to alleviate related symptoms efficiently and could prevent some chronic diseases occurred in aged population if initiated at beginning of menopause.

The key point of initiating MHT lies in discriminating its indications and contraindications. It should be used only after indications are included and contraindications excluded, as well as the patient intended to improve the quality of life. In some clinical situations that MHT can be used as appropriate measure but need to be followed up closely, however, it should be used prudently, which we called cautious use. Compared with those with clear indications or contraindications, the evidence for cautious use is relatively insufficient, and the borderline between usable and non-use is blurred, much less the specific protocol is controversial. Here we are going to discuss the following issues: what conditions or diseases in peri- and post-menopausal women need to be treated with MHT in caution? How to assess efficacy in a specific disease or situation? What are information in evidence-based medicine? How to use MHT in cautious condition? With further understanding of the disease and the development of new therapeutics, these cautious situation turned to be indications or contraindications.

Key words MHT, cautious use, management

Diagnosis and treatment of abnormal uterine bleeding (AUB-O)

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Abnormal uterine bleeding (AUB) is one of the most common symptoms and signs in gynecology. AUB refers to abnormal bleeding from the uterine cavity that is inconsistent with the normal menstrual cycle frequency, regularity, duration, or the volume of flow. The International Federation of Gynecology and Obstetrics (FIGO) divides AUB into nine categories based on etiology (PALM-COEIN). This article mainly introduces AUB-O (ovulation disorder).

AUB-O can be seen in adolescence, menopausal transition and reproductive periods. AUB-O can be divided into anovulatory and ovulatory types. Anovulatory AUB is more common in the two stages of ovarian instability, adolescence and menopausal transition. Ovulatory AUB is seen in the reproductive period, manifested as abnormal luteal function or periovulation spotting. The diagnosis of AUB-O must exclude uterine bleeding due to organic disease. The treatment principle of AUB-O is to stop bleeding and rectify anemia during bleeding period, to adjust the cycle after hemostasis to prevent endometrial hyperplasia and AUB recurrence, and to induce ovulation therapy for those who have fertility requirements. Methods of hemostasis include drug hemostasis, commonly used progestin to exfoliate the endometria, high-dose estrogen to repair the endometria, short-acting oral contraceptives or high-efficiency synthetic progesterone endometrium atrophy, and diagnostic curettage. The main method to adjust the cycle is progesterone therapy in the second half of the cycle, sequential therapy of estrogen and progesterone cycles. Adolescent and reproductive age patients should choose natural or nearly natural progesterone, which is conducive to the establishment or recovery of ovarian axis function. For those who have completed childbirth or menopausal transition period, LNG-IUS can be placed to prevent endometrial hyperplasia.

Key words abnormal uterine bleeding, diagnosis, treatment

Etiology and Diagnosis of Premature Ovarian Insufficiency

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Premature ovarian insufficiency (POI) is a clinical syndrome of ovarian function decline and infertility in women before age 40. POI is associated with multiple health risks, including change in menstrual cycle characteristics, menopausal symptoms, decreased bone density and increased risk of fractures, early progression of cardiovascular disease, urogenital atrophy, psychologic impact, and dry eye syndrome. The etiology of POI has been found to be chromosomal, genetic and autoimmune, infectious disease, along with patients who have undergone ovarian surgery, and history of chemoradiotherapy. According to the Chinese Expert Consensus on the clinical diagnosis and treatment of POI in 2017, the etiology and diagnostic methods of POI are explained in detail. If a diagnosis is issued before POI onset, counseling on currently available fertility preservation techniques is advisable.

Key words POI

The development of national climacteric healthcare specialty

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Objective: To demonstrate the development and achievements of national climacteric healthcare specialty in Fujian Maternity and Child Health Hospital.

Materials and methods: To summarize and analyze the process of how to carry out people-oriented work in the process of characteristic specialty construction in order to satisfy the requirements of menopausal women's health care. The hospital attaches great importance to the construction of specialized talent echelon, forms a reasonably structured medical team with high overall strength at different levels and is equipped with all the devices required to carry out the work. A multi-disciplinary comprehensive management model with the characteristics of OBGYN hospital was established, and various forms of health education activities were developed to provide climacteric women with one-stop, continuous, multi-directional and individualized high-quality services. A longitudinal comparison was conducted based on data collected from questionnaire surveys including menopausal healthcare and hormone therapy, among patients aged 40-60 who visited the general gynecological clinic in 2015 and 2021.

Result: ①The overall awareness of menopausal health care was 60.2% in 2021, which was significantly higher than 37.1% in 2015. ②The number of outpatients and hormone treatment rates were increasing yearly. The number of outpatients increased from 1523 in 2015 to 3674 in the first half of 2021, and the hormone treatment rate rose from 61% in 2015 to 92.5% in 2021. ③The specialized work has been recognized as the number of grass-roots doctors who were receiving advanced studies increased yearly.

Conclusion: With the enrichment of climacteric healthcare services, the improvement of service processes and the innovation of service model, the service capacity has been significantly improved and played a demonstrative role in Fujian.

Key words national climacteric healthcare

The Diagnosis and Management of Endometrial Thickness in Postmenopausal Women

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There is no consensus in cut-off value of endometrial thickness in asymptomatic patients or patients with postmenopausal bleeding (PMB). According to guidelines and advances : Endometrial sampling in a postmenopausal woman without bleeding should not be routinely performed; PMB of first occurrence with homogeneous endometrial echogenicity and thickness ≤ 8 mm on ultrasonography does not require curettage and close observation is recommended; Endometrial cancer screening is recommended for endometrial thickness >5 mm with increased vascularity, endometrial heterogeneity, and poorly transmissible fluid on ultrasonography; Patients with persistent bleeding or recurrent PMB need to be managed with caution, especially in those with high risk factors for endometrial lesions; Considering the possibility of a small probability of endometrial lesions, especially type II endometrial cancer, endometrial sampling for pathological examination is recommended in recurrent PMB, even if the endometrial thickness is <3 mm; If the endometrial biopsy tissue is too little to diagnose, it only means no malignancy for the time being or EIN, and endometrial lesions cannot be completely excluded. Close follow-up is recommended for this group of patients. The selection of endometrial histological sampling methods is crucial for sensitive and specific detection of lesions. Segmental diagnostic curettage, hysteroscope, sampler sampling and endometrial cytology test (ECT) are currently well studied. More and more physicians recommend hysteroscopy combined with sampling under direct visualization as the preferred sampling approach for PMB patients. ECT is an absolutely reliable method for cancer detection, but it is currently less used in China.

Key words Postmenopausal endometrial thickening, Postmenopausal bleeding, Endometrial histological sampling

First Live Birth in China after Ovarian Tissue Cryopreservation and Transplantation for Prevent Iatrogenic POI

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In order to promote the standard application of ovarian tissue cryopreservation in China, and to provide effective scientific medical services of fertility preservation for patients, In 2018, the First Chinese Guideline of Ovarian Tissue Cryopreservation and Transplantation is established according to the agreements between gynecologists, embryologists, oncologists, pediatricians, breast oncologists, hematologists, and experts on Traditional Chinese Medicine (TCM), based on already successful treated cases within Beijing Obstetrics and Gynecology Hospital, Capital Medical University, China, and based on already existing international guidelines on fertility preservation including important publications in this field. The guideline includes selection criteria, evaluation, and indications; SOPs of ovarian tissue removal, transportation, preparation, freezing, and thawing; approaches of ovarian tissue transplantation and follow-up; practical recommendations for ovarian tissue cryopreservation and transplantation including recommendations of the diseases where this method could be available, and treatment of menopausal symptoms during the peri-transplantation period (time between cryopreservation and transplantation). The aim of this guideline was to be scientific, practical, and operable.

Major indications: Ovarian tissue cryopreservation can preserve fertility and ovarian endocrine function, so it is suitable for patients with tumors and nonmalignant diseases. Good indications are prepubertal patients, patients whose chemoradiation treatment cannot be delayed, and patients with Malignancies and Nonmalignant diseases need of chemotherapy, radiotherapy, or stem cell transplant, et al.

The gonadal toxicity of anti-cancer treatments causes severe damage to survivors' ovarian function, especially those for hematologic diseases after hematopoietic stem cell transplantation (HSCT). To safeguard the fertility of young patients at high risk of premature ovarian insufficiency (POI), ovarian tissue cryopreservation and transplantation (OTCT) has been offered as a routine clinical technique. Until 2020, the cumulative number of live births after OTCT exceeded 200 worldwide. The first ovarian tissue cryobank in China was established in 2012 by our centre, in which nearly 400 cases of cryopreservation and 10 cases of transplantation have been successfully performed. One of these patients diagnosed with myelodysplastic syndrome (MDS) became pregnant spontaneously and delivered recently, and we report on this first pregnancy and live birth resulting from OTCT in China.

Funding Supported by Beijing Natural Science Foundation (7202047); Capital's Funds for Health Improvement and Research (2020-2-2112); Beijing Municipal Administration of Hospitals' Ascent Plan (DFL20181401).

Key words Ovarian Tissue Cryopreservation

Otosclerosis analysis of contraindications to MHT

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Menopause related short-term symptoms and long-term complications perplex the majority of elderly women. With the extension of life expectancy, more and more women are perplexed by menopause symptoms. According to the statistics of the World Health Organization, there were 160 million postmenopausal women in China in 2010, and this number will increase to 280 million by 2030. Menopausal hormone therapy (MHT) is a therapeutic measure for ovarian failure. It is the most effective method to alleviate climacteric symptoms.

MHT is a medical activity. There are some precautions that need to be taken under the advice of a specialist. According to 《the guidelines for the management of menopause and menopausal hormone therapy (2018) in China》, the otosclerosis is MHT contraindication. The incidence rate of otosclerosis is higher in women than in men. The ratio is about 1.4:1-2:1, which is the main reason for the inclusion of contraindications. However, the incidence rate of this disease is related to race and male onset. This suggests that sex hormones are not decisive for the disease. Therefore, the effect of estrogen and progesterone on otosclerosis should be reassessed. The benefits brought by MHT make MHT overcome many difficulties and make MHT more and more widely used, which is also the driving force of this research. Due to the lack of direct evidence, the relationship between estrogen and progesterone and otosclerosis was evaluated with the help of pregnancy and contraceptives. The results suggest that pregnancy and oral contraceptives are not associated with otosclerosis symptoms obviously, and the use of low-dose estrogen and progesterone in MHT may have less impact.

In 1991, a literature reported the relationship between MHT and otosclerosis. The original text was not published online. However, most international guidelines and statements in the later stage did not include otosclerosis as a contraindication. It is speculated that it did not clearly support MHT to aggravate the symptoms of otosclerosis.

Key words MHT

Sleep disorder in peri-post menopause

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As the global population of postmenopausal women continues to increase, it is significant to explore the differences between eastern and western postmenopausal population in menopause related health problems.

Menopausal symptoms vary. There are differences in symptoms between eastern and western postmenopausal women. Hot flashes and night sweats are probably the most common symptom among Western women. Oriental women may be more physical symptoms, such as fatigue, bone pain

Sleep disturbance is a common symptom in postmenopausal people. The main performance is difficult to fall asleep, difficulty maintaining sleep, early awakening and sleep after no recovery, and can cause bodily dysfunction or apparent discomfort. In addition to leading to short-term daytime discomfort, fatigue, etc., affecting the quality of life. Sleep disorders are also related to cardiovascular and cerebrovascular diseases in the long term. The incidence of sleep disorders varies in different countries and regions. Other symptoms associated with menopause also have mixed effects on sleep disorders. Postmenopausal women and menopausal health care providers have different perceptions of sleep disorders associated with menopause. A study conducted by the World Health Organization shows that sleep disorders remain an under-appreciated and under-addressed public health problem worldwide.

Key words Sleep disorder, peri-post menopause

Expert consensus on female vulvar lichen sclerosis

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Female vulvar lichen sclerosis (vulvar lichen sclerosis, VLS) is a common chronic inflammatory dermatosis that may lead to scarring of the vulva. Although the exact prevalence is unknown, VLS is most common in postmenopausal women (mean age 52.6 years). The main characteristics of this disease are ivory white atrophic plaques with a waxy texture, resorption of the labia, narrowing of the introitus, and distortion of the vulvar architecture, with chronic progression and recurrent attacks. The most common symptoms of VLS are pruritus, dyspareunia, or vulvar pain. The goals of treatment are to alleviate symptoms of itching and pain, prevent anatomic changes due to scarring. Although there is no cure for VLS, there are a number of treatment options which have been explored to achieve remission and prevent progression of disease. The topical moisturizing lubricant is basically used as the long-term maintenance treatment of VLS. The topical glucocorticoid is the current first line for treating VLS, which is divided into two stages: induction of remission and maintenance treatment. In the remission induction stage, topical glucocorticoid ointment or cream daily is recommended for continuous 3 to 4 months, then maintenance therapy, which local low-dose glucocorticoid ointment or cream at one time per week for lifetime is recommended. Emerging treatment including high-intensity focused ultrasound, the fractional CO₂ laser, photodynamic and other physical therapy methods are currently being studied to find more effective, and minimally invasive, and become alternative treatments for VLS. Surgical treatment is suitable for patients to restoring anatomy with vulvar adhesions and suspicious malignant changes. Surgical resection alone cannot achieve the satisfactory outcomes, and drug treatment is generally required after surgery. Long-term follow-up of VLS is extremely important. The follow-up time is generally 3, 6, and 12 months after treatment, and then every 6 to 12 months.

Key words VLS

Cervical cancer screening in perimenopausal and menopausal women

lin wang

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According to the 2019 World Health Statistics, the life expectancy of women is 74.2 years, but the average menopausal age of women has not changed. Due to the sharp decline of estrogen in the perimenopausal period and the occurrence of perimenopausal syndrome, the patient's mentality is extremely unstable, and the poor psychological state can improve the probability of patients suffering from malignant tumors, especially the perimenopausal period, which is the high incidence age of cervical cancer. As the only malignant tumor that can be prevented, the incidence rate of cervical cancer has decreased over time. However, there are some problems in cervical cancer related research of perimenopausal and menopausal women: first, 19.7% of women aged 65 and above were diagnosed and diagnosed, and the proportion did not change significantly over time. 2、 For some reasons, such as the reduced screening compliance of middle-aged and elderly women, the insufficient understanding of the risk of diseases, the fear of gynecological examination caused by vaginal atrophy of postmenopausal women, and the desire for treatment is not as strong as that of young women, the proportion of women without regular cervical cancer screening is also increasing as they approach the "stop age" of cervical screening; 3、 At present, cervical cancer screening guidelines recommend that people over 65 years old can stop cervical cancer screening, but the study found that perimenopausal and menopausal women can still benefit from cervical cancer screening. With the continuous increase of research data and different medical and health levels in various countries, the current cervical cancer screening strategy for middle-aged and elderly women is not enough to realize the desire to eliminate cervical cancer, suggesting that we need to analyze and consider various situations.

Key words Cervical cancer screening

Study on Ovarian Aging, Advances and Challenges

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Aging is an inevitable process in all people. Ovarian aging is clearly defined by the age-specific decline of ovarian reserve and function until failure. At the core of this process is functional failure, which is typically manifested as menopause. The essence of diminished ovarian reserve (DOR), primary ovarian insufficiency (POI) and poor ovarian response (POF) is the premature decline of ovarian function, representing different stages of ovarian aging. Ovarian aging is a multifactorial pathological process. The etiology and influencing factors of ovarian aging involve genetics, environmental exposure, lifestyle and medical interventions. According to various etiology, influencing factors, pathogenesis and pathological stages, three-grade prevention can be employed to take corresponding, personalized and comprehensive management for patients with “already failed”, “about to fail” and “no failure” of ovarian function. Ovarian preservation and protection strategies should be applied in a timely and appropriate manner for cancer patients with reproductive requirements. Relevant potential treatment strategies include artificial ovary, stem cell therapy, gene therapy, ovarian in vitro activation, etc. Currently, the clinical applications of these interventions are still limited. In addition, the pathological process of ovarian aging regulated by internal and external factors remains to be elucidated in most cases. The early warning system of ovarian function aging needs to be established. Effective intervention methods of ovarian aging need to be explored and translated into clinical practice. Thus, ovarian aging still requires further study.

Key words Ovarian aging, pathological process, three-grade prevention

Hereditary gynecologic cancers and HT

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Cancer remains a major public health problem in the world today, Approximately 5 – 10% of all cancers can be attributed to hereditary cancer syndromes. The most common conditions associated with gynecologic cancers include Hereditary Breast and Ovarian Cancer (HBOC) and Lynch (Hereditary Nonpolyposis Colorectal Cancer or HNPCC) syndromes. Both are inherited in an autosomal dominant pattern. HBOC is characterized by pathogenic variants in tumor suppressor genes (BRCA1 and BRCA2) that increase the risk of breast, ovarian, pancreatic, and prostate cancer. Lynch Syndrome is associated with pathogenic variants in one of a family of mismatch repair genes. Lynch Syndrome is associated with an increased risk of colorectal cancer as well as endometrial, stomach, breast, ovarian cancers and many other cancers.

For HBOC, prophylactic measures include chemoprevention and risk reducing surgery. Risk-reducing Salpingo-oophorectomy (RSO) is the most effective way to reduce the risk of ovarian cancer in high-risk women, but it can cause iatrogenic premature menopause in patients. Women considering RSO should be informed about the common sequelae of surgical menopause. Hormone therapy (HT) can prevent and alleviate many of the symptoms associated with surgical menopause. The use of HT after oophorectomy in women at increased risk for gynecologic (and breast) cancers is controversial. Therefore treatment of menopausal symptoms should be individualized and consider the potential risk versus benefit, medical history and therapeutic goals.

Total hysterectomy and bilateral salpingo-oophorectomy has been demonstrated to decrease the risk of endometrial and ovarian cancer in women with Lynch Syndrome. Patients should be informed of the adverse consequences of premature menopause before surgery, and HT should be recommended for patients without contraindications.

Key words hereditary gynecological cancer syndrome, menopause, hormone therapy

Lower urinary tract symptoms and menopause

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Genitourinary syndrome of menopause (GSM) includes genital symptoms of dryness, burning, and irritation, urinary symptoms and conditions of dysuria, urgency, and recurrent urinary tract infections (UTIs), and sexual symptoms of pain and dryness. The International Continence Society (ICS) defines OAB as the presence of “urinary urgency, usually accompanied by frequency and nocturia with or without urgency urinary incontinence (UUI) in the absence of urinary tract infection or other obvious pathology. The combined result of six trials of systemic administration (of oral systemic oestrogens) resulted in worse incontinence than on placebo (risk ratio (RR) 1.32, 95% CI 1.17 to 1.48). There was some evidence that oestrogens used locally (for example vaginal creams or pessaries) may improve incontinence (RR 0.74, 95% CI 0.64 to 0.86). Urinary tract infections (UTIs) are common in women, and appropriate antibiotics are the mainstay of treatment of acute infections. Recurrent UTIs (RUTIs) are defined as at least two episodes of UTIs within 6 months or three episodes within 1 year. An important pathogenesis of RUTIs in these women is hormonal deficiency. Compared with placebo, vaginal estrogen treatment could reduce the number of RUTIs and lower the vaginal pH. China consensus or Guidelines: Topical vaginal estrogens are recommended for GSM, stress urinary incontinence, OAB, pelvic organ prolapse pessary placement, Mesh-related infections and mesh exposure after pelvic organ prolapse repair surgery.

Key words lower urinary tract symptoms

Menopause Symptoms, East vs. West

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With the continued sustained growth of menopausal and postmenopausal women across the world, it is meaningful to explore the differences between the East and the west in terms of menopausal symptoms.

Firstly, the age of the onset of the menopause in the west is slightly higher than in the East, so is the onset time of menopausal symptoms.

The symptom spectrum of menopause in the East and the West are different, the most two common menopausal symptoms in Western countries are hot flashes and sleeplessness. However, Asian women mostly report somatic symptoms, with a higher frequency observed in postmenopausal symptoms as opposed to perimenopausal ones.

Hot flashes, sleep disruption, depression and irritability, headaches/migraine, cognitive symptoms, reduced libido, vaginal dryness, urinary incontinence and joint pain are varied in the East and the West as well as in different countries/regions.

The prevalence of hot flashes in the west is higher than in the East, and there are significant differences between different countries/regions even within Asia.

Prevalence of sleep disruption is not obviously different between the East and the West. Prevalence of depression/irritability and urinary incontinence vary among different countries/regions. Prevalence of headaches/migraine, reduced libido, vaginal dryness and joint pain in the East is higher than in the West. Non-Hispanic Asians have significantly lower total numbers and total severity scores in Cognitive Symptoms compared to other racial/ethnic groups.

The reported prevalence of menopausal symptoms varied widely and differed substantially among studies. It may be related to research methods, sample size, ethnicity, culture, socio-economic differences, menopausal status and other factors.

Key words Age of menopause, Menopausal symptoms

Multidisciplinary interventions on diminished ovarian reserve

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Lanzhou university

Ovarian reserve refers to the quality and quantity of oocytes retained in the female ovary, which is an important indicator of female reproductive potential. Because of age, inflammation, immunity, heredity, iatrogenic factors, environmental lifestyle and mental and psychological factors, the quality and quantity of oocytes retained in the ovary is declined, in order to improve the ovarian reserve, it is necessary to carry out systemic and individual comprehensive interventions as early as possible to improve the fertility and solve the reproductive problems.

Key words diminished ovarian reserve, multidisciplinary interventions, individualized

An update on menopause management in Zhejiang

Zhifen Zhang
Hangzhou Women's Hospital

The foundation of Zhejiang menopause academic branch, which has been led by Professor Zhang since 2014, is the first provincial menopause academic group in China and has provided with a good exchange platform for scholars and colleagues engaged in health care of perimenopausal women.

Aiming at popularizing of proper menopause management (hormonal, non-hormonal and complementary options), escalating medical practitioners' skills and maximizing the benefit among general population in Zhejiang. Continuous training programs, academic seminars and multi-form community education workshops have been conducted regularly since 2014.

Although there has been conflicting information about the safety of menopausal hormone therapy (MHT), MHT is by far the most effective treatment for menopausal symptoms. Focusing on the major provincial project "Perimenopausal and postmenopausal women's hormonal therapy and the basic and clinical research on the relationship between estrogen and anti-aging", We managed to set up perimenopausal clinics in over 30 cooperative hospitals for suitable crowd recruitment and long-term follow up. By developing follow-up software and promoting its application through out Zhejiang, we have managed to familiarize the characteristics of perimenopausal patients, evaluate the benefits and risks of different MHT programs at different age groups in our local area.

Our research achievements won the first prize of medical and health science and technology of Zhejiang province in 2017, the second prize of science and technology progress award of Zhejiang province in 2020 and have been shared at international and domestic academic seminars.

Menopause is a time of significant change for women and an opportune time to assess and promote health. At present, we, Hangzhou women's hospital, are focusing on the major provincial project "perimenopausal and postmenopausal women's osteoporosis genotyping and risks prediction model" with cooperates of other 30 hospitals in Zhejiang using multi-center model aiming at optimizing MHT and improving bone health of perimenopausal women.

Key words menopause management, Zhejiang

Individualized menopausal hormone therapy for perimenopausal women

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Menopause is a physiological process that all elderly women will go through. From the perimenopausal period, fluctuating or falling levels of estrogen may cause a series of physical and mental symptoms. After menopause, the risk of cardiovascular disease and osteoporosis increases. Menopause seriously affects women's quality of life and health. Menopausal hormone therapy (MHT) is considered to be the most effective way to treat vasomotor symptoms (VMS), menopausal genito-urinary syndrome of menopause (GSM), and can prevent bone loss and broken. However, unreasonable use of MHT may also increase the risk of some diseases and even malignant tumors. How to maximize the benefits and minimize the risks of MHT? First of all, the first principle is that there are indications for MHT but no contraindications for MHT. According to the symptoms, underlying diseases, and treatment needs of menopausal women, individualized MHT regimen, including type, route, dosage, and duration of use can help to achieve the best therapeutic effect and minimize side effects of MHT.

Key words MHT, Estrogen, Individualization

