Management of menopausal physiological symptoms

Yuxin Su [1,†], Danyang Zhang [2,*,†]

[1] Kunming NO.1 High School International Division, Kunming, China

[2] School of Social and Political Science, University of Edinburgh, Edinburgh, United Kingdom

* Corresponding Author Email: S1901322@ed.ac.uk

[†]These authors contributed equally.

Abstract. With the development of our society, people are putting more and more emphasis on women's health. Perimenopause is a period that women must experience. When women are in perimenopause, their hormone levels will change greatly, resulting in obvious physiological changes, such as hot flashes, night sweats and other physical symptoms,such as muscle and joint problems, urinal system, and cardiac problems.In fact, there will be a series of psychological changes, such as depression, anxiety and so on, but most of the symptoms will be covered up by physical symptoms, leading to misdiagnosis and missed diagnosis. When patients have negative emotions, they will continue to have an impact on the development of the disease, and even accelerate the development of the disease, gradually forming a vicious circle.It is very important for perimenopausal women to do a good job in hormone supplementation and mental health care, and it is also the key to help perimenopausal women alleviate the physiological and psychological changes caused by menopause. MHT is the first-line recommended treatment, which can also be supplemented by other treatments, such as physical exercise, yoga, warm acupuncture, etc

Keywords: Menopause, Perimenopause, Physiological Symptoms, Menopause Hormone Therapy

1. Introduction

Menopause refers to the period from the beginning of ovarian function decline to the last menstruation. It can start at the age of 40 and last as short as 1-2 years and as long as 10 years. It is a transitional period for women from maturity to old age.Take a closer look, menopause could be divided into three sub-periods, including premenopausal, perimenopausal, and postmenopausal stages Before 40 years old, women experience the regular menstruation cycle every month, in a long period called premenopause.However, starting from the age of 40, females may observe subtle changes in the length of menstruation cycles, in the transition period of perimenopause. The final stage, the postmenopausal state comes after 1 months of pausimenia[1-3].

Flushing, menstrual changes, depression, fatigue, palpitations, irritability, emotional instability, anxiety, etc. are the main manifestations of women after menopause. According to relevant European survey data, 94% of women suffer from one or more menopausal symptoms, and 2/3 of menopausal women will be affected by symptoms, affecting their quality of life and rhythm.With the passage of menopause,other severe symptoms such as joints disorders, cardiac problems and cognitive disorders also arise.

Clinically, it is common for postmenopausal women to complain of autonomic nervous dysfunction symptoms such as paroxysmal hot flashes, which masks emotional symptoms. In fact, menopausal psychological problems have seriously affected women's family and life. Patients and doctors are prone to pay attention to physical diseases and ignore the management of menopausal syndrome and emotional disorders. In recent years, with the deepening of related research, psychological problems have been paid more and more attention in clinic[3-6].Studies have shown that women in perimenopausal states have higher possibilities of being depressed, compared to women in premenopausal state. These psychological uneasiness caused negative impacts on women's daily life more or less [3].

It is still unclear that ultimately which factor directly cause the psychological problems.Factors contributing to menopausal psychological problems include fluctuations in hormone levels, changes

in neurotransmitters,certain mental stress, reactions to anxiety and negative life pattern ot status, socialeconomical changes, and health crisis.

Menopausal hormone therapy(MHT) is a treatment measure taken by making up for ovarian failure. After years of practice,it has been proved that the scientific application of MHT can effectively alleviate menopause related symptoms, and the use in early menopause can also prevent the occurrence of chronic diseases in the elderly to a certain extent.However, due to the influence of many factors such as general concept and education level, the majority of postmenopausal women do not pay enough attention to the arrival of menopause and menopause; In addition, the public rejects all treatment methods, especially the long-term use of hormones, which makes the progress of MHT difficult. Even if MHT is carried out, it is difficult to persist for a long time.Other intermediate therapies include yoga, warm acupuncture, dietary therapy (N-3, for example) [7-9]. Though relieving serious symptoms for a moment, those therapies have no way to alter the state of hormone deficiency. In this essay, we would provide a comprehensive perspective of menopause or relevant researchers and women world-wide suffering from menopausal symptoms, by analyzing typical psychological disorders and comparing corresponding therapies.

It is generally known that emotions or other psychological disorders may be multifarious, for example, social status and economic performance would influence women's metal health. However, few studies have specifically examine about the exact reasons causing these downsides and the helpful treatments. Currently therapy treating menopausal uncomfortness, such as estrogen plus progestogen therapy (EPT), which generates negative impacts on human health by altering female hormone levels, warm acupuncture, and N-3 dietary therapy just have effects alleviating serious symptoms [1,4,7-9].

This paper will take psychological problems as the main starting point,and introduce the pathogenesis and management measures of psychological symptoms in detail

2. Menopause psychological problems

2.1. The definition of menopause

At the age of about 40, women start entering a so-called physiological state called climacteric with or without awareness [10].Shortly before the formal climacteric period, women are in the premenopausal status, with a regular menstruation cycle every month, or discover some subtle changes in the menstruation [11]. After the premenopausal status, women enter the perimenopausal state followed by the postmenopausal state. Gynecologic experts define the perimenopausal state as a persistent difference of 7 days of a change in the length of one menstruation cycle, namely women in this state may experience the menstruation cycle longer or shorter than usual. Despite changes in the periodic length, women would also encounter excessive bleeding and painful periods. Meanwhile, a postmenopausal state refers to amenorrhea longer than 12 months [10].

2.2. Psychological problems

With the development of society, diagnosis and treatment of menopausal symptoms are no longer limited to arrays of physiological disorders, and psychological disorders occurring during menopause get more and more emphasis. Specifically, symptoms like depression, sleeping disorder, and the loss of confidence and interest are researched the most, as researchers have found people in the climacteric period are susceptible to psychological issues such as stress, anxiety, and depression.

Indeed, an apposite understanding of climacteric and menopause could effectively reduce those negative feelings [12].The most common uncomfortable somatic symptoms occurred during menopause include joint and muscle disorders, fatigue, sleep disorders, and hot flashes or sweating [13].Then the symptoms of urogenital tract atrophy gradually occur, and chronic diseases such as osteoporosis and cardiovascular and cerebrovascular diseases will occur in late menopause[14].A systematic retrospective study included 23 articles on the prevalence of menopausal symptoms in Asian women. The final sample size was 18166.The purpose was to evaluate the prevalence of

menopausal symptoms in Asian women. The final results showed that menopausal symptoms were mainly somatic symptoms, followed by psychological symptoms, vasomotor symptoms and sexual symptoms[16]. Studies about the symptoms like depression, sleeping disorder, and the loss of confidence and interest are becoming more and more, as researchers have found people in the climacteric period are susceptible to psychological issues such as stress, anxiety, and depression. In addition, stressors or depression could influence sleep quality. Inadequate sleep would then cause negative health problems and psychological issues, while researchers found that stress from income and occupational status has an impact on sleep quality. In this case, patients are easy to be trapped in the vicious spiral of sleep disorder and depression[10,12,13].

Previous research has suggested associations between menopausal status and the severity of symptoms. More specifically, women in perimenopausal states and postmenopausal states reported more serious symptoms in both somatic and psychological aspects.A study investigating New-Zealand women before has found a subtle relation between menopausal status and occupational status, whereby women at an age of 40 in the perimenopausal and postmenopausal states are found in low occupational families (at an age of 40 with Low occupational status defined by New Zealand Socio-Economic Index, NZSEI, the percentages of women in premenopause, perimenopause and postmenopause are 10.4, 17.9, and 20.0, respectively) [10]. Other findings have suggested that menopausal status is irrelevant to social well-being, psychological functions, and education level [13].

2.3. Factors contributing to psychological symptoms

2.3.1 Hormones level

With the increase in age, the ovary follicles' conditions start deteriorating in aspects of depletion of the stored oocytes in the ovaries, which in turn, leads to the decrease in the level of estrogen and progesterone and an increase in the level of follicle-stimulating hormones (FSH) secreted [12]. This alteration of hormone levels would directly contribute to symptoms such as vasomotor and urogenital disorders [6]. Moreover, the decline of estrogen levels would result in microstructural changes in white matters in the insula, and then further makes women vulnerable to depression [11].

It may seem surprising that male hormones also play a role in psychological symptoms during climacteric. While gonads are known to produce male hormones like androgen, the brain has been found to have the capability to produce androgen, as well.The androgen could induce nervous reactions in spine synapses in the hippocampus. Moreover, similar to estrogens, androgens have neuroprotective effects. Through complex mechanisms involved in the hormone-neuron interactions, anxiety could be effectively reduced; cognitive deficits, as well as psychotic and depressive symptoms, would be augmented.

2.3.2 Neurotransmitters

Taking a closer look at how hormones alter the function of neuroendocrine could find a clear explanation for the occurrence of psychological symptoms concerning hormones.A type of sex hormone that has an impact on neurons is called neurosteroids.These hormones function through receptors in the nucleus and mitochondria of synaptic cells, especially in spines. Use actions estrogen exerts on the brain as an example.The means estrogen employs include neurotrophic and neuroprotective actions, which may, in turn, improve synaptic plasticity and neurite growth, and form a protecting barrier against cell damage and autolysis.By acting on mitochondria, estrogen helps the adenosine triphosphate (ATP) production and thus improves human respiration and adjusts metabolic activities. In this way, with estrogen deficit, women would often feel enervated or sleepy, due to inadequate production of ATP, the energy currency circulating through human bodies[16].

Another route estrogen takes to influence nervous activities is through the genetic pathway. Estrogen may bind to operons responsible for the production of C-reactive proteins, a kind of inflammatory marker, in a length of DNA molecule. The excessive C-reactive proteins produced may be related to impeded cognitive functions.This provides a theoretical ground to explain that with

difficulties in memorizing and communication, females develop psychological symptoms derived from anxious and self- contemptuous feelings.

2.3.3 Social interaction

When nervous system functions and emotional activities are fragile and unstable, some encountered psychosocial factors are easy to play a pathogenic role. Perimenopausal women are in the period of role transformation, with specific psychological tension, social factors, stress, negative living conditions and status.Self-reports and interviews have shown that the reason why women normally view menopause negatively is that they consider themselves losing sexuality and attractiveness.The idea that menopausal transition and aging are synonymous further makes females stressed. Moreover, it is noticeable that women with higher social security may give positive ratings when viewing judging body images. Factors like stress, educational level, ethnicity, and partner status may directly influence the menopausal symptoms, which are correlated to depressive disorders, with a positive relationship that the severer menopausal symptoms, the severer the depressive disorders are [12].

2.4. Evaluations of psychological symptoms

As commonly known, psychological problems would cause negative results, then how to numerically measure these symptoms in daily life becomes crucial. In this way, questionnaires providing numerical values become the key to assessing the psychological symptoms. The one with the most international reputation is the Beck Depression Scale (BDS), which appraises the severity of depression with a maximum score of 63, and a score above 17 points needs a more accurate diagnosis to discern depression [12].Another questionnaire that would be employed to assess depressive symptoms is the PHQ-9 questionnaire, a brief and self-explanatory questionnaire, which was used to evaluate the presence of depressive symptoms during the past 14 days, with the score ranging from 0 to 27 [11].A score less than 5 points could be regarded as having no depressive symptoms, while a point of 5 behaves like a critical point.Scores ranging from 5 to 9 are classified as mild, 10-14 as moderate, 15-19 as moderately severe, and scores above 20 as severe.

To evaluate the severity of menopausal symptoms and their effect on the quality of life, researchers in a previous study researching menopausal symptoms and sleeping disorders used the Menopause Rating Scale (MRS) can be used, which includes 11 items and has three subscales consisting of somatic, psychological, and urogenital symptoms, and the Pittsburgh Sleep Quality Index (PSQI), a self-reported scale evaluating the sleep quality [13]. The results from the MRS may provide a reference for patients to decide whether the symptoms are so serious that need to see a doctor. Also, PSQI provides a criterion that a score above 5 indicates poor sleep quality.

3. Therapeutic measures

3.1. Menopause hormone therapy (MHT)

The MHT is a treatment measure adopted through compensating the ovarian function failure. According to decades of research, women in menopause scientifically apply the MHT could efficiently improve the menopausal-related symptoms. In addition to the advantages of MHT, starting earlier to take it could also help women to prevent the chronic diseases of the elderly, as well as the benefits of primary prevention of osteoporotic fractures. At present, MHT varies from drug selection to drug route, and different individuals have different suitable schemes. Therefore, patients need to take drugs under the guidance of specialists. Therefore, Zhi et al. suggests climacteric women start to take the MHT once the ovarian declined and persist the standardized drug use as long as the benefits outweigh the risks. However, it is not rigorous to claim that the MHT is beneficial for all women without explaining its limitations. Women who known or probable pregnancy, severe liver or kidney insufficiency, etc. could not adopt the MHT, or in careful cases, such as uterine fibroids, endometrial hyperplasia, thrombosis tendency and so on, should be prudent when applying it. Thus, MHT must

be individualized - selecting the type, dose, compatibility, medication route and using time of sex hormones based on factors including the need to treat symptoms, benefit risk evaluation, relevant test results, personal preference and treatment expectations.

To realize the individualization of MHT, the first step is to assess patients' health conditions and medical history, deciding to proceed with MHT or non-MHT treatments then, and regular follow-up visits and follow-up visits will be made during the medication phase at the final stage. The medicines - mainly including natural estrogen, such as 17β-estradiol, estradiol valerate, conjugated estrogen,estradiol/didrogesterone tablets, estradiol valerate tablets, estradiol valerate tablets, cycloproterone acetate tablets, estradiol/drospirone tablets, and tibulone (which can help with low mood and libido in climacteric women).

3.2. Phytoestrogens

The phytoestrogens is a compound, which is biologically active, synthesize and isolate from plants. As the phytoestrogens has similar chemical structure with estrogen produced by the body, it could interplay with the estrogen in human cells directly. A paper assessed if climacteric women eating the cereal bar that including phytoestrogens could help them to improve the menopausal symptoms,which was developed by the Nutrition Technology and Food Technology Laboratory in Federal University of Fronteira Sul, main ingredients are textured soy protein and crushed golden flaxseed, along with rice flakes, raisins and cinnamon, binding agents are water, brown sugar and soy lecithin.

Frigo et al.differentiated participating women into two groups to assess the efficacy of cereal bar - experiment group (provided with phytoestrogens) and control group (provided with placebo). The research shows that those negative mental symptoms triggered by women's estrogen decline, especially the emotional changes, are less after the intervention period, such as depression, anxiety and sleeping problems. The amounts of intervention are 50mg/day and 500ml/d soy drinks and 160mg/d soy protein isoflavones. Although the research results prove the safety and validity of those chemical compounds in practical, there are still some side effects that should be noticed, especially the effects on the gastrointestinal tract. And the research period is not long enough so that it could not provide conclusive evidences, thus, the specific side effects of phytoestrogens intake are needed to be further observed.

3.3. Exercise and phytoestrogen supplementation

Fotvieille et al. focused on assessing if the exercises plus phytoestrogen could positively affect overweight women in menopause in health-related quality of life (HRQoL) and in climacteric symptoms. Research showed that those negative climacteric symptoms have relativity with low physical activities. In addition to consider in the long term, doing precious few exercises will worsen the physical conditions in menopausal women. In contrast, those women who doing regular physical activities (>30 min/d) proved the improvements in the mental, social and environmental aspects of HRQoL and in climacteric symptoms.

3.4. Yoga

Many researches demonstrated that yoga has strong effects on enhancing menopausal women's mental and physical health, therefore.In the assessment of if yoga is beneficial in improvement on climacteric symptoms in this paper, He used control experiment to arrange 126 menopausal women into experimental group which having at least 12 yoga lessons and control group which doing individual arrangements. The results show that, women who reported to have depression in yoga group improved more than the control group, though women in control group did some other exercises instead of doing nothing. To be specific, women in yoga group had explicitly better physiological levels than control group after 18 weeks of experiment, systolic and diastolic blood pressure were close to normal and the physical quality apparently tended to normal physiological state as well. According to the statistics about depression improvement, 93.65% women in yoga group reported not having depression, however, there are only half of women in control group reported not

having depression, next half of women had mild (23.81%), moderate (15.87%) and even major (7.93%) depression.

As excessive exercises could make climacteric women having worse physical fitness, yoga becomes more appropriate choice for the women,which bring benefits to menopausal women in both physical and mental aspects. Firstly, yoga is an quiet exercise doing in an quiet environment, women's body is totally relaxing, which relieves tension in the brain's nervous system, this is beneficial for women to improve the subjective pressure brought by the menopause. Secondly,yoga could help regulate endocrine self-help function to relieve hot flashes, sweating, insomnia and other psychological conditions caused by decreased estrogen secretion due to the gradual decline of ovarian function during menopause. Finally, as yoga pursue the harmony between human and nature, it emphasizes the perfect cooperation between movement and breathing, which helps women in promoting circulation and gastrointestinal digestive function, so it also plays a role in the prevention and treatment of menopause constipation.

3.5. Food intake

Many previous studies have shown that Omega-3 (N-3) has huge wide of effects in maintain women's mental health, as high-level depression is relevant to insufficiency of N-3 intake. According to some studies, it is due to the nutrition materials included in N-3 could improve the menopausal symptoms.However, more significant thing is that there are plenty of studies noticed its importance, it needs further observation. One study surprisedly found that women without symptoms of depression were more likely to get enough polyunsaturated fatty acids (PUFA), with 65.3% of women without symptoms of depression reported they got the recommended intake, almost twice as many as women with symptoms of depression (34.7%). According to the data in general, micronutrient deficiency plays vital role in the development of menopausal depression, including PUFA, magnesium, zinc, vitamin C, D and B12, the intake differences in women with/without depression cannot be overstated.

3.6. Warm needle acupuncture

Warm needle acupuncture (WNA) is one of typical traditional Chinese medicine therapies, it is valid and safe as it combines the advantages of acupuncture. The WNA have been barely found harmful side effects in heating stimulates acupuncture points. Some studies have shown that WNA may be effective for menopausal women with insomnia, also, the influence of insomnia on people cannot be ignored as the morbidity of insomnia will grow follows aging, that could cause huge adverse effect to women's health and daily life. At the same time, it can improve immunity, improve blood circulation, and have a significant impact on disease prevention.Xu et al.observed 7 electronic databases to investigate the randomized controlled trials (RCTs) of WNA on improving the insomnia of menopausal women. Women in experimental group used WNA no mater what type and how long the needles in use, it can also be used with other conventional treatments; whereas the control group could only take conventional treatments. Assessment references including Pittsburgh Sleep Quality Index (PSQI), Kupperman score, serum hormone level and TCM syndrome score. The results of this study provided evidences of curative effect and safety of WNA, and other data, such as untoward effects (these statistics are not shown in details in this paper though), which could as references in clinicians' decision-making.

Some studies show that those women with higher education, good job and strong economic strength lives better life and have less menopausal symptoms than women without [5,18]. Education gives women more peace in mind as they will consider menopause as a chance to boost creativity; better education gives women jobs, which give them social status and social relations to have a sense of worth and drive away from loneliness; jobs give women more stable source of finance, it helps women to have better medical treatment than women who live in poor economical condition.

The essence of menopause is estrogen deficiency, so MHT is still the first-line recommended treatment, and other schemes can be used as adjuvant treatment or as a management strategy to

prevent menopausal symptoms.The rest, whether exercise or drug/food supplement therapy, will also have benefits in alleviating menopausal symptoms in women within the scope of scientific use. It is worth noting that adopting measures after fully understanding its standard application method could avoid unnecessary side effects in the use process.

4. Conclusions

With the decline of ovarian function, the fluctuation of hormone levels, the changes of neurotransmitters, and the influence of social and psychological factors, women will have a variety of psychological problems, which seriously endanger women's quality of life, but they are often not recognized. Due to self-esteem and other cultural consideration, women face difficulty in taking an initiative to ask for help. The lack of knowledge of relatives makes them even harder to understand women's encounters, which increases the social tensions even more.

Menopausal women should pay attention to the management of menopausal psychological problems. MHT is an effective method to treat vasomotor symptoms and menopausal emotional disorders. At the same time, it can assist some other treatments, such as yoga, physical exercise, etc. At the same time, people should make it clear that the treatment of menopausal syndrome can not be solved simply by taking drugs. Psychological problems are actually the key problems that perplex women. Women need to have enough confidence in themselves. This confidence needs to be built on the premise of personality, not on appearance. In addition, more participation in social activities, so that women can feel their own value, thereby reducing anxiety. But one thing to be clear is that for serious psychological problems, it is still necessary to refer to the specialist clinic.

References

[1] Frigo, M., de Barros, E., Dos Santos, P. C. B., Peres, G. L., Weber, J., Zanelatto, C., & Koehnlein, E. A. (2022). Effects of a Cereal Bar with a Combination of Phytoestrogens on the Climacteric Symptoms: A Placebo-Controlled, Randomized Trial. Journal of the American Nutrition Association, 41(3), 325-332.

[2] World Health Organization. (1981). Research on the menopause: report of a WHO scientific group [meeting held in Geneva from 8 to 12 December 1980]. World Health Organization.

[3] Oldra, C. M., Benvegnú, D. M., Silva, D. R. P., Wendt, G. W., & Vieira, A. P. (2020). Relationships between depression and food intake in climacteric women. Climacteric, 23(5), 474-481.

[4] He, L. (2020, August). Effect of yoga on physical and mental health of climacteric women in the context national fitness. In 2020 International Conference on Sports Sciences, Physical Education and Health (ICSSPEH 2020) (pp. 117-120). Atlantis Press.

[5] Monterrosa-Blanco, A., Monterrosa-Castro, Á., & González-Sequeda, A. (2021). Online assessment of the perception of loneliness and associated factors in Colombian climacteric women during the COVID-19 pandemic: A cross-sectional study. Health Promotion Perspectives, 11(2), 230.

[6] Prados, M. (1967). Emotional factors in the climacterium of women. Psychotherapy and Psychosomatics, 231-244.

[7] Fontvieille, A., Dionne, I. J., & Riesco, E. (2017). Long-term exercise training and soy isoflavones to improve quality of life and climacteric symptoms. Climacteric, 20(3), 233-239.

[8] Oldra, C. M., Lazarotto, A. K., Wendt, G. W., Ferreto, L. E., Follador, F. A. C., & Vieira, A. P. (2022). Depression mediates the links between climacteric symptoms and food and nutritional insecurity. Climacteric, 25(3), 311-315.

[9] Xu, H. W., Du, W., He, L., & Kuang, X. (2019). Effectiveness and safety of warm needle acupuncture on insomnia in climacteric women: protocol for a systematic review and meta-analysis. Medicine, 98(20).

[10] G. F. H. McLeod, L. Cleland, J. Welch, J. K. Spittlehouse, A. Fenton, J. M. Boden & L. J. Horwood (2022) Menopause status and climacteric symptoms in a birth cohort of mid-life New Zealand women, Climacteric, 25:3, 271-277, DOI: 10.1080/13697137.2021.1948005

[11] X. Y. Wang, L. H. Wang, J. L. Di, X. S. Zhang & G. L. Zhao (2021): Association of menopausal status and symptoms with depressive symptoms in middle-aged Chinese women, Climacteric,

[12] Nülüfer Erbil (2018) Attitudes towards menopause and depression, body image of women during menopause, Alexandria Journal of Medicine, 54:3, 241-246.

[13] Ferdane Koçoğlu, Semra Kocaöz, Pınar Kara & Özlem Aşcı (2022): Relationship between menopausal symptoms and sleep quality in women during the climacteric period: a cross-sectional study, Journal of Obstetrics and Gynaecology.

[14] Xiangyan Ruan, Yamei Cui, Juan Du, Fengyu Jin & Alfred Otto Mueck (2017) Prevalence of climacteric symptoms comparing perimenopausal and postmenopausal Chinese women, Journal of Psychosomatic Obstetrics & Gynecology, 38:3, 161-169.

[15] Janine M. Simmons, Lois Winsky, Julia L. Zehr & Joshua A. Gordon (2021) Priorities in stress research: a view from the U.S. National Institute of Mental Health, Stress, 24:2, 123-129.

[16] Islam MR, Gartoulla P, Bell RJ, Fradkin P, Davis SR. Prevalence of menopausal symptoms in Asian midlife women: a systematic review. Climacteric. 2015 Apr;18(2):157-76.

[17] Zhi, Z. F. C. K. Z. (2018). 2018 Chinese guideline on menopause management and menopause hormone therapy. Med J Peking Union Med Coll Hosp, 53(11), 729-739.

[18] Szadowska-Szlachetka, Z., Stasiak, E., Leziak, A., Irzmańska-Hudziak, A., Łuczyk, M., Stanisławek, A., ... & Domżał-Drzewicka, R. (2019). Intensity of menopausal symptoms and quality of life in climacteric women. Menopause Review/Przegląd Menopauzalny, 18(4), 217-221.