Archives of Gynecology and Obstetrics (2020) 302:657–664
https://doi.org/10.1007/s00404-020-05628-w

GENERAL GYNECOLOGY

Effect of zinc supplementation on quality of life and sleep quality in young women with premenstrual syndrome: a randomized, double-blind, placebo-controlled trial

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Received: 21 December 2019 / Accepted: 30 May 2020 / Published online: 8 June 2020

Abstract

Introduction Premenstrual syndrome is a prevalent disorder affecting a large number of women in their reproductive ages. Nutritional importance of zinc has been known for a long time and studies have shown that zinc can positively affect psychological disorders.

Purpose The aim of this study was to evaluate the effects of zinc supplementation on quality of life and sleep quality of young women diagnosed with premenstrual syndrome.

Methods This randomized, double-blind, placebo-controlled trial was carried out on 60 young university women that were allocated into two groups of intervention who took 30 mg/day of elemental zinc or placebo for three months. Pre- and post-intervention, participants completed the questionnaires of quality of life and Pittsburgh sleep quality.

Results After supplementation, quality of life score in the intervention group was increased ($+9.185 \pm 7.29$, $P < 0.001$), however, in comparison with the control group, results were not significant; Physical aspects of quality of life score were significantly enhanced ($+5.55 \pm 3.71$ vs. $+0.13 \pm 2.87$, $P < 0.001$). Sleep quality was marginally improved just in the zinc group (-1.48 ± 4.12, $P = 0.07$).

Conclusion Zinc supplementation for 12 weeks had beneficial effects on physical aspects of quality of life in young women with premenstrual syndrome.

Keywords Zinc supplement · Sleep · Premenstrual syndrome · Quality of life

Introduction

Premenstrual syndrome or PMS includes series of recurrent physical and psychological symptoms that affect a large number of women in their reproductive ages. These symptoms including mood swing, fatigue, irritability, depression, food craving and tender breast occur during the last days of luteal phase and persist for 2–4 days after starting the menses [1, 2]. The onset of PMS is usually during late adolescence, but the symptoms remain unrecognized and untreated so they can negatively affect the quality of life, work and social functions [3, 4]. Premenstrual dysphoric disorder (PMDD) is a more severe form of PMS, that impairs the patients' normal functions and cause disruption of personal relationships [5]. It is believed that about 85% of women go through at least one of mild PMS symptoms in their lives, 20–25% experience moderate to severe symptoms and about 5% suffer from PMDD [6]. Based on a systematic review and meta-analysis, it is estimated that worldwide prevalence of PMS is about 48% [1]. Some studies report that the prevalence of women suffering from PMS in Egypt [7], northern Ethiopia [8] and Poland [9] are: 65, 37 and 76.39%, respectively. It has been reported that PMS prevalence in Iran varies between 30 and 99.5% [10]. The etiology of PMS is unknown, but several studies suggested that cyclical changes in ovarian hormones levels initiate the symptoms [11–13].

Abnormal sex hormones fluctuations probably associated with increased inflammatory and oxidative stress and over activation of the renin–angiotensin–aldosterone

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system that results in physical symptoms of PMS [14]. It has been stated that PMS symptoms negatively affect quality of life (QOL) of these women [3]. WHO defined QOL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" [15]. Health-related quality of life (HRQOL) determines how a chronic illness interfere one's life. HRQOL is significantly lower in women with PMS than non-affected women [16]. In a study by Borenstein et al. health-related burden of PMS was estimated to be comparable to major depression and cyclothymia disorder [17]. It has been reported that PMS symptoms not only impairs quality of life of the women, but can also negatively affect their interpersonal relationships, social activities, sexual function and job performances [18]. Based on an epidemiologic survey conducted in Sao Paulo (EPISONO), the PMS group had poorer sleep quality than the control group [19]. Women with PMS complain about insomnia, fatigue, nightmares and poor sleep quality [20–22]. Usual sleep problems related to PMDD are repeated night time awakenings, sleep onset insomnia and non-restoration of sleep; these sleep difficulties can lead to daytime sleepiness, poor concentration, declined alertness and weak performance at work and study [23].

Although it is suggested that some minerals deficiency may partially play a role in pathogenesis of PMS and PMDD, this role has not been fully explored [24, 25]. Serum concentration of some metallic ions such as zinc changes during menstrual cycle. Zinc is an essential mineral that is involved in numerous physiological pathways [26]. Women who suffer from PMS have significantly lower serum zinc than normal women [27–29]. Zinc deficiency leads to abnormal glucocorticoid's production that can result in some neuropsychological symptoms such as irritability, depression and emotional instability, similar to some of PMS symptoms [30, 31]. Several studies showed that supplementation with zinc may have a positive effect on sleep disorders in children, childhood hyperactivity, attention and mental disorders such as depression [32–34]. To our knowledge, except for case–control studies that support the idea of supplementation with zinc in PMS [27, 29, 35], there is only one clinical trial published on the effect of zinc on quality of life of women with PMS and their symptoms, showing positive effect of zinc supplementation in PMS [36]. Previously, we observed that zinc supplementation can alleviate PMS symptoms, improve total antioxidant capacity and BDNF levels in these patients [37]. Accordingly, we aimed to examine the effects of 12 weeks of supplementation with 30 mg/day elemental zinc in the form of zinc gluconate on sleep quality in addition to quality of life in women with PMS.

Methods

Participants

This double-blind randomized and placebo-controlled trial was conducted at the Isfahan University of Medical Sciences girls' dormitories between June 2017 and June 2018 using a parallel design. Inclusion criteria included healthy single young women with regular menstrual cycle of 21–35 days, aged 18–30 years old, BMI between 18.5–24.9, not taking any oral contraceptives or any medications, not exercising professionally, not taking zinc supplement in the last 3 months, not being depressed or having anxiety. Exclusion criteria were: not filling out the daily record questionnaire, taking less than 80% of the zinc or placebo pills, getting married and not willing to continue the study. Students who met the inclusion criteria were initially diagnosed using a 30 item questionnaire consisted of physical and psychological symptoms of PMS [38].

Study design

We conducted this study in 2 phases. In the first phase, 200 young women who met the inclusion criteria were asked to fill out a questionnaire consisting of 30 symptoms of PMS. Girls who experienced 5 or more PMS symptoms with at least one psychological symptom, 7 days prior to 4 days after onset of menses, were initially diagnosed with PMS. These young women were asked to fill out the Beck's anxiety and depression questionnaires. Those with scores of depression and anxiety lower than 4 and 15, respectively, were eligible to participate in the study.

In the second phase, after explaining the study, participants gave their written consent and completed food frequency questioner (FFQ) with the help of a trained nutritionist. To obtain participants' zinc intakes, we used customized Nutritionist IV software (N-Squared Inc., San Bruno, CA, USA). Women who were temporarily diagnosed with PMS, recorded their symptoms for 2 consecutive months pre-intervention, using Daily Symptoms Record form. The form included 30 most prevalent psychological and physical symptoms of PMS based on DSM-V [38, 39] that was validated by Pakgohar et al. using content validity. They also stated a Pearson's correlation coefficient of $r = 0.92$ for the reliability of this questionnaire [40]. Participants with definite diagnosis of PMS, were randomly allocated into 2 groups of 30; one group took zinc gluconate tablets (contained 30 mg of elemental zinc) and the other group consumed the placebo tablets that contained starch. Both zinc gluconate and

placebo tablets were provided by Dine Iran Pharmaceutical Company (Tehran, Iran) in identical appearance. Women were asked not to change their physical activity and diet and not to take any supplements during the trial. All participants nor had specific diets neither followed special regimens before and during the study. In the second and third months, along with the packages of tablets, same daily record questionnaires were given to them to fill out.

Sample size calculations

To calculate the sample size, we used the standard equation for parallel clinical trials considering the type one error (α) of 0.05 and type two error (β) of 0.10 (power of 90%). Based on previous study [41], we used 2.71 and 2.32 as SD and 2.66 as the difference in mean (d) of sleep quality score as the key variable. Based on this study and considering the dropouts, we recruited 30 women in each group.

Outcome measure

Participants that were eligible for the trial completed the Pittsburgh sleep quality questionnaire (PSQI) and the Persian version of WHO quality of life questioner (WHOQOL-BREF) in luteal phase of their menstrual cycle pre- and post-intervention. Pittsburgh sleep questionnaire (PSQI) is one of the most applicable questionnaires about quality of sleep used in studies that investigates subject's attitude about their sleep in the past 4 weeks. PSQI includes 19 self-rated questions containing seven components: subjective quality of sleep, sleep latency, duration, efficiency, disturbance, use of sleep medication and daytime dysfunction. Each component is scored from 0 to 3 and total score would be between 0 and 21 [42]. Scores above 5 indicate poor quality of sleep. Sensitivity and specificity of PSQI are 90 and 87%, respectively [43]. Another questionnaire was the Persian version of (WHOQOL-BREF) that has been validated in Iranian population [44]. The (WHOQOL-BREF) questionnaire contains 26 questions based on 4 domains including: physical health, psychological health, social and personal relationships and environmental aspect of life [44]. Participants recorded their symptoms severity on the scale of (0 = not having the symptoms) to (3 = sever symptom prevents the person from taking part in normal daily activities). PMS was diagnosed according to diagnostic criteria of American Psychiatry Association [40]. To avoid diurnal variations, blood samples were collected after an overnight fasting from individual's cubital vein. The samples were then centrifuged at 5000 rpm for 15 min and serums were removed and then stored at − 80 °C until further measurements. Serum zinc levels were measured by a colorimeter using 5-BR-PAPS method. Biochemical kits (Biosystems S.A., Barcelona, Spain) were applied to determine serum zinc. Results obtained from this technique are correlated well with those by atomic absorption spectrophotometry [45, 46].

Statistical analysis

We applied Kolmogorov–Smirnov test to verify the normal distribution of variables. To detect differences in basic variables between the two groups, we used independent t test and to determine the effects of zinc supplementation on sleep quality and health-related quality of life score, multivariate analysis of covariance (MANCOVA) test was applied with adjustment for the baseline confounders. P value below 0.05 was considered statistically significant. We used Statistical Package for Social Science version 16 (SPSS Inc., Chicago, IL, USA) to perform statistical analysis (Fig. 1).

Results

In this study, out of 200 students who met the inclusion criteria and were initially diagnosed with PMS, 60 women whose Beck's scores for depression and anxiety were respectively less than 4 and 15 and recorded their symptoms for 2 consecutive menstrual cycles were allocated into 2 groups of 30. In the second phase of the study, 3 participants in the intervention group dropped out due to personal reasons. The participants took 87 and 90% of the tablets in placebo and intervention groups, respectively. Both zinc and placebo pills were well tolerated and no sensible side effects were reported following the intervention. No significant differences were seen in the baseline parameters (Table 1). As

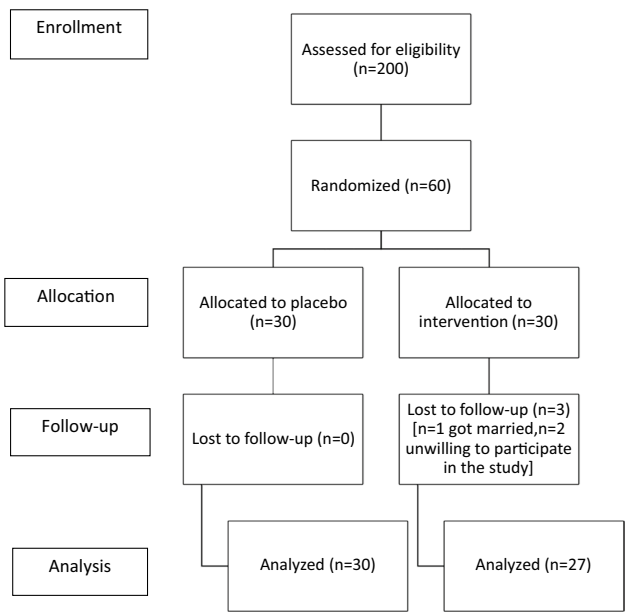

Fig. 1 Summary of patient flow diagram

Table 1 Basic characteristics of study participants

Variables	Placebo group ($n=30$)	Zinc supplementation group ($n=27$)	P value*
Age (years)	22.53 ± 1.85	23.04 ± 2.97	0.063
Weight at study baseline (kg)	56.50 ± 5.81	57.05 ± 7.28	0.748
BMI at study baseline (kg/m^2)	21.03 ± 1.90	21.39 ± 2.00	0.668
Age at menarche (years)	12.26 ± 1.36	12.10 ± 1.21	0.133
Duration of cycle (days)	27.56 ± 2.92	27.73 ± 2.53	0.814
Duration of menstruation (days)	6.23 ± 1.19	6.56 ± 0.77	0.205
Zinc intake (mg/day)	8.00 ± 0.96	7.8 ± 1.16	0.56
Depression Beck's score	2.53 ± 1.77	3.03 ± 1.60	0.25
Anxiety Beck's score	8.23 ± 3.43	7.86 ± 4.03	0.70

Data are mean ± SDs

* Obtained from independent-samples t test

shown in the Table 1, there was no significant difference in dietary zinc intake between the two groups. After 12-week intervention, zinc supplementation significantly increased the serum zinc levels ($P<0.001$). Moreover, this group demonstrated increased score of the first domain of quality of life indicating improved physical aspects ($P < 0.001$). Based on independent t test, quality of life total score of intervention group significantly increased, however, after comparing with those of placebo group using MANCOVA test, no significant changes were observed. Moreover, no significant changes were seen in social and personal relationships, environment aspect of life and psychological aspects of quality of life of the groups pre- and post-supplementation. Sleep quality of the intervention group improved marginally (− 1.48 ± 4.12, $P=0.07$) after supplementation, however, scores were not different between the groups (Table 2).

Table 2 Metabolic profiles at baseline and after the 12-week intervention in subjects with premenstrual syndrome

Variables	Group	Baseline*	Week 12**	Change	P value***
Serum zinc (µg/dL)	Intervention	75.50 ± 11.72	110.42 ± 17.14	34.56 ± 17.17	< 0.001†
	Placebo	85.55 ± 26.75	88.69 ± 14.45	3.13 ± 23.36	0.46
	P value	0.065	< 0.001†		
Sleep quality score	Intervention	8.00 ± 3.23	6.14 ± 3.58	− 1.48 ± 4.12	0.073
	Placebo	7.86 ± 4.46	6.86 ± 4.94	− 1 ± 4.39	0.223
	P value	0.895	0.328		
Quality of life	Intervention	78.46 ± 6.98	86.88 ± 10.06	9.185 ± 7.29	< 0.001†
	Placebo	81.96 ± 8.62	83.70 ± 8.71	1.73 ± 3.77	0.018†
	P value	0.089	0.206		
Quality of life D1 (physical health)	Intervention	23.53 ± 2.92	28.81 ± 2.63	5.55 ± 3.71	< 0.001†
	Placebo	24.23 ± 3.85	24.10 ± 3.95	0.13 ± 2.87	0.801
	P value	0.431	< 0.001†		
Quality of life D2 (psychological health)	Intervention	20.20 ± 3.50	21.70 ± 2.75	1.59 ± 3.53	0.27
	Placebo	19.13 ± 4.33	20.50 ± 4.60	1.36 ± 6.05	0.227
	P value	0.299	0.144		
Quality of life D3 (social and personal relationships)	Intervention	10.06 ± 1.31	10.11 ± 2.08	0.07 ± 2.12	0.858
	Placebo	10.23 ± 1.79	11.06 ± 1.77	0.83 ± 2.36	0.063
	P value	0.683	0.259		
Quality of life D4 (environmental aspect of life)	Intervention	25.56 ± 3.50	26.7 ± 6.55	1.48 ± 5.19	0.151
	Placebo	26.93 ± 4.60	27.86 ± 4.45	0.93 ± 3.63	0.171
	P value	0.201	0.578		

All values are means ± SDs

* PValue obtained from independent-samples t test; **obtained from MANCOVA [adjustment for changes in baseline values of biochemical parameters (i.e., serum zinc)]; *** Pvalue obtained from paired-samples t test; †P value < 0.05

Discussion

PMS is one of the most prevalent disorders among premenopausal women. In the present study, after 12 weeks of treatment with zinc, total score of quality of life and sleep quality increased in the intervention group, yet these changes were not significantly different from those of placebo group. In addition, first domain of quality of life indicating the physical aspects of quality of life in PMS woman was improved. There are limited therapies to relieve PMS symptoms [47]. Therapies suggested for this disorder include psychiatric, anovulatory, supplements, herbal and non-pharmacological treatments [48]. Selective serotonin reuptake inhibitors, in spite of their side effects such as weight gain, sexual dysfunction and sleep disturbances, are the first-line medicine being used to alleviate the symptoms of PMS and PMDD [48]. Despite overwhelming prevalence of PMS, its underlying mechanisms are yet to understand. It is suggested that some minerals such as zinc might have a role in the etiology of PMS. Serum zinc level fluctuates across the menstrual cycle [49] and is lower in women with PMS [27, 29]. There have been some case–control studies that support supplementation with zinc in PMS. Zinc is concentrated in hippocampus and in PMS patients its level is lower than normal women; this can lead to isolation and depression [50]. Chocano-Bedoya et al., in a nested case–control study, showed that high intake of zinc from supplements was marginally associated with lower risk of PMS [35]. There is scarce evidence on the effect of zinc supplementation on PMS symptoms and patients' quality of lives. In a study conducted by Siahbazi et al., supplementation with 50 mg/day elemental zinc improved the PMS symptoms and physical and psychological aspects of health related quality of life in these patients [36]. Previously, we found that supplementation with zinc could alleviate physical symptoms of PMS [37] as well as the fact that improved zinc status could enhance the psychological aspects of this syndrome, serum levels of BDNF and TAC in subjects with PMS [37]. In another study by Ribeiro et al. oral zinc supplementation 45 days prior and up to 12 weeks post-chemotherapy for colorectal cancer prevented worsening of fatigue symptoms and preserved quality of life [51]. It has been proposed that irregular response to normal hormonal fluctuations might be responsible for this syndrome. Fluctuating gonadal hormones negatively affect certain neurotransmitters [48]. Estrogen has excitability effect on neurotransmitters whereas progesterone exhibits inhibitory effect on neurotransmitters through increasing monoamine oxidase activity, decreasing serotonin and stimulation of GABA receptors [13]. Allopregnanolone, major metabolite of progesterone, is a positive modulator of GABA-A receptors [6]. As GABA system is one of the strongest inhibitory systems in the CNS, allopregnanolone has anxiolytic, anesthetic, and sedative effect in response to the stressors [6, 13]. Women with PMS have lower alopregnanolone levels than women who are not affected by the syndrome [52]. These affected women after stimulation with gonadotropin releasing hormone (GnRH) in luteal phase, seem to have decreased production of progesterone and allopregnanolone, resulting in PMS [53]. SSRIs enhance allopregnanolone's production and GABA-A receptors function [54]. It has been documented that zinc functions as an agonist on GABA system, so that it can relieve PMS symptoms and increases quality of life [55].

It is well documented that sleep quality and hormonal changes are related, therefore, PMS can affect women's quality of life and sleep [22]. Poor sleep quality is a common feature of sever PMS [56]. Ji and Liu reported that sufficient zinc concentration is associated with good sleep quality in children [57]. In our study, we did not detect any significant change in sleep quality post-supplementation, in spite of these results, the scores in intervention group improved from 8.00 ± 3.32 indicating low sleep quality to 6.14 ± 3.58 being marginally better sleep quality. Gholipour Baradari et al. demonstrated that supplementation with 220 mg/day zinc sulfate, improves sleep quality in ICU nurses [41]. Rondanelli et al. observed that administration of nightly melatonin, magnesium and zinc improved the sleep quality and quality of life in long-term care facility residents with primary insomnia [58]. This discrepancy might be due to different study designs, dosage and form of zinc administration as well as duration of the study and combination of zinc with other supplements. Zinc, as an important micronutrient, exerts important role in more than 300 enzymes in human body [59] and it is concentrated in hippocampus in the brain. Low zinc concentration in hippocampus results in dysregulation of glucocorticoid secretion that can cause some neuropsychological dysfunctions such as isolation and depression that are known as common symptoms of PMS [50]. The possible role and mechanisms in which zinc regulates sleep is still unclear. It is hypothesized that zinc's inhibitory effect on glycinergic neurons excitation projecting to orexin neurons in lateral hypothalamus involved in maintenance of wakefulness, might be the possible pathway in which zinc involves in sleep regulation [60]. In addition, zinc is required for production and inflection of melatonin and GABA that help regulating dopamine function [61]. Zinc also increases melatonin and serotonin synthesis, therefore, it can improve violent behavior and impulsivity [62].

PMS is a prevalent disorder among women in their reproductive ages that interferes with women's personal relationships, studies or work. One of the most significant concerns about PMDD, sever form of PMS, is potential development of suicidal thoughts, so treatments are needed

[63]. Further studies with longer duration could be helpful to improve women's lives affected by PMS.

Our study had some limitations such as lack of measurement of sex hormones to confirm the menstrual cycle phases and also relatively short duration to detect any possible side effects of zinc supplementation in long-term course.

As the final point, our findings revealed that zinc supplementation in PMS women for 12 weeks positively influenced the physical aspect of quality of life but did not affect sleep quality of women with PMS.

Acknowledgements We wish to thank all the participants who kindly cooperated in the trial. This study was extracted from Fatemeh Jafari's MSc dissertation that was approved and supported by a granted from Vice-Chancellor for Research, Isfahan University of Medical Sciences under the registration code: (IR.MUI.REC.1396.3.247).

Author contributions FJ: Developed the project and did the data collection, Manuscript writing, RA: Proposed the subject, supervised the project development and edited the manuscript. MJT: Did the data analysis, AF: Helped with lab works.

Funding This study was financially supported by a grant from the Vice-chancellor for Research of Isfahan University of Medical Sciences (code: 39627).

Compliance with ethical standards

Ethical approval All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 (in its most recently amended version). The study protocol was approved by the Medical Ethics Committee at the Isfahan University of Medical Sciences (code: IR.MUI.REC.1396.3.247) and it was registered in the official website for Iranian registration of clinical trials (https://www.irct.ir) under the registration number IRCT20180215038738N1.

Informed consent Written Informed consents were obtained from all participants for all the procedures and to allow data collection and analysis for research purpose and publication.

Conflict of interest None.

References

1. Direkvand-Moghadam A, Sayehmiri K, Delpisheh A, Kaikhavandi S (2014) Epidemiology of premenstrual syndrome (PMS)—a systematic review and meta-analysis study. J Clin Diagn Res JCDR 8(2):106
2. Kleinstäuber M, Schmelzer K, Ditzen B, Andersson G, Hiller W, Weise C (2016) Psychosocial profile of women with premenstrual syndrome and healthy controls: a comparative study. Int J Behav Med 23(6):752–763
3. Rapkin AJ, Winer SA (2009) Premenstrual syndrome and premenstrual dysphoric disorder: quality of life and burden of illness. Expert Rev Pharmacoecon Outcomes Res 9(2):157–170
4. Dennerstein L, Lehert P, Heinemann K (2012) Epidemiology of premenstrual symptoms and disorders. Menopause Int 18(2):48–51
5. Chung S-H, Kim T-H, Lee H-H, Lee A, Jeon D-S, Park J, Kim Y (2014) Premenstrual syndrome and premenstrual dysphoric disorder in perimenopausal women. J Menopausal Med 20(2):69–74
6. di Scalea TL, Pearlstein T (2017) Premenstrual dysphoric disorder. Psychiatr Clin 40(2):201–216
7. Abdelmoty HI, Youssef MA, Abdallah S, Abdel-Malak K, Hashish NM, Samir D, Abdelbar M, Hosni AN, Ghafar MA-E, Khamis Y, Seleem M (2015) Menstrual patterns and disorders among secondary school adolescents in Egypt. A cross-sectional survey. BMC Womens Health 15(1):70. https://doi.org/10.1186/s12905-015-0228-8
8. Tolossa FW, Bekele ML (2014) Prevalence, impacts and medical managements of premenstrual syndrome among female students: cross-sectional study in college of health sciences, Mekelle University, Mekelle, Northern Ethiopia. BMC Womens Health 14(1):52. https://doi.org/10.1186/1472-6874-14-52
9. Drosdzol A, Nowosielski K, Skrzypulec V, Plinta R (2011) Premenstrual disorders in Polish adolescent girls: prevalence and risk factors. J Obstet Gynaecol Res 37(9):1216–1221. https://doi.org/10.1111/j.1447-0756.2010.01505.x
10. Ranjbaran M, Samani RO, Almasi-Hashiani A, Matourypour P, Moini A (2017) Prevalence of premenstrual syndrome in Iran: a systematic review and meta-analysis. Int J Reprod Biomed 15(11):679
11. Hammarbäck S, Bäckström T, Hoist J, von Schoultz B, Lyrenäs S (1985) Cyclical mood changes as in the premenstrual tension syndrome during sequential estrogen-progestagen postmenopausal replacement therapy. Acta Obstet Gynecol Scand 64(5):393–397
12. Kumar P, Sharma A (2014) Gonadotropin-releasing hormone analogs: understanding advantages and limitations. J Hum Reprod Sci 7(3):170
13. Halbreich U (2003) The etiology, biology, and evolving pathology of premenstrual syndromes. Psychoneuroendocrinology 28:55–99
14. Rosenfeld R, Livne D, Nevo O, Dayan L, Milloul V, Lavi S, Jacob G (2008) Hormonal and volume dysregulation in women with premenstrual syndrome. Hypertension 51(4):1225–1230
15. Groupt W (1993) Study protocol for the World Health Organization project to develop a Quality of Life assessment instrument (WHOQOL). Qual Life Res 2(2):153–159
16. Pearlstein TB, Halbreich U, Batzar ED, Brown CS, Endicott J, Frank E, Freeman EW, Harrison WM, Haskett RF, Stout AL, Yonkers KA (2000) Psychosocial functioning in women with premenstrual dysphoric disorder before and after treatment with sertraline or placebo. J Clin Psychiatry 61(2):101–109
17. Borenstein J, Chiou C-F, Dean B, Wong J, Wade S (2005) Estimating direct and indirect costs of premenstrual syndrome. J Occup Environ Med 47(1):26–33
18. Wallenstein GV, Blaisdell-Gross B, Gajria K, Guo A, Hagan M, Kornstein SG, Yonkers KA (2008) Development and validation of the Premenstrual Symptoms Impact Survey (PMSIS): a disease-specific quality of life assessment tool. J Womens Health 17(3):439–450
19. Nicolau ZFM, Bezerra AG, Polesel DN, Andersen ML, Bittencourt L, Tufik S, Hachul H (2018) Premenstrual syndrome and sleep disturbances: results from the Sao Paulo Epidemiologic Sleep Study. Psychiatry Res 264:427–431. https://doi.org/10.1016/j.psychres.2018.04.008
20. Halbreich U, Endicott J, Nee J (1983) Premenstrual depressive changes: value of differentiation. Arch Gen Psychiatry 40(5):535–542
21. Moos RH, Kopell BS, Melges FT, Yalom ID, Lunde DT, Clayton RB, Hamburg DA (1969) Fluctuations in symptoms and moods during the menstrual cycle. J Psychosom Res 13(1):37–44

22. Baker FC, Kahan TL, Trinder J, Colrain IM (2007) Sleep quality and the sleep electroencephalogram in women with severe premenstrual syndrome. Sleep 30(10):1283–1291
23. Jehan S, Auguste E, Hussain M, Pandi-Perumal SR, Brzezinski A, Gupta R, Attarian H, Jean-Louis G, McFarlane SI (2016) Sleep and premenstrual syndrome. J Sleep Med Disord 3(5):1061
24. Andrea J, Sharon A (2009) Premenstrual syndrome. Winer Expert Rev Pharmacoecon Outcomes Res 9(2):157–170
25. Do Kaur G, Gonsalves L, Thacker HL (2004) Premenstrual dysphoric disorder: a review for the treating practitioner. Clevel Clin J Med 71(4):303
26. Hara T, Takeda T-a, Takagishi T, Fukue K, Kambe T, Fukada T (2017) Physiological roles of zinc transporters: molecular and genetic importance in zinc homeostasis. J Physiol Sci 67(2):283–301
27. Posaci C, Erten O, Üren A, Acar B (1994) Plasma copper, zinc and magnesium levels in patients with premenstrual tension syndrome. Acta Obstet Gynecol Scand 73(6):452–455
28. Chuong CJ, Dawson EB (1994) Zinc and copper levels in premenstrual syndrome. Fertil Steril 62(2):313–320
29. Fathizadeh S, Amani R, Haghighizadeh MH, Hormozi R (2016) Comparison of serum zinc concentrations and body antioxidant status between young women with premenstrual syndrome and normal controls: a case–control study. Int J Reprod BioMed 14(11):699
30. Sowa-Kućma M, Legutko B, Szewczyk B, Novak K, Znojek P, Poleszak E, Papp M, Pilc A, Nowak G (2008) Antidepressant-like activity of zinc: further behavioral and molecular evidence. J Neural Transm 115(12):1621
31. Levenson CW (2006) Zinc: the new antidepressant? Nutr Rev 64(1):39–42
32. de Moura JE, de Moura ENO, Alves CX, de Lima Vale SH, Dantas MMG, de Araújo SA, Das Graças Almeida M, Leite LD, Brandão-Neto J (2013) Oral zinc supplementation may improve cognitive function in schoolchildren. Biol Trace Elem Res 155(1):23–28
33. Kordas K, Siegel EH, Olney DK, Katz J, Tielsch JM, Kariger PK, Khalfan SS, LeClerq SC, Khatry SK, Stoltzfus RJ (2009) The effects of iron and/or zinc supplementation on maternal reports of sleep in infants from Nepal and Zanzibar. J Dev Behav Pediatr JDBP 30(2):131
34. Akhondzadeh S, Mohammadi M-R, Khademi M (2004) Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial [ISRCTN64132371]. BMC Psychiatry 4(1):9
35. Chocano-Bedoya PO, Manson JE, Hankinson SE, Johnson SR, Chasan-Taber L, Ronnenberg AG, Bigelow C, Bertone-Johnson ER (2013) Intake of selected minerals and risk of premenstrual syndrome. Am J Epidemiol 177(10):1118–1127
36. Siahbazi S, Behboudi-Gandevani S, Moghaddam-Banaem L, Montazeri A (2017) Effect of zinc sulfate supplementation on premenstrual syndrome and health-related quality of life: clinical randomized controlled trial. J Obstet Gynaecol Res 43(5):887–894
37. Jafari F, Amani R, Tarrahi MJ (2020) Effect of zinc supplementation on physical and psychological symptoms, biomarkers of inflammation, oxidative stress, and brain-derived neurotrophic factor in young women with premenstrual syndrome: a randomized, double-blind, placebo-controlled trial. Biol Trace Elem Res 194(1):89–95
38. Ebrahimi E, Motlagh SK, Nemati S, Tavakoli Z (2012) Effects of magnesium and vitamin b6 on the severity of premenstrual syndrome symptoms. J Caring Sci 1(4):183
39. Dadkhah H, Ebrahimi E, Fathizadeh N (2016) Evaluating the effects of vitamin D and vitamin E supplement on premenstrual syndrome: a randomized, double-blind, controlled trial. Iran J Nurs Midwifery Res 21(2):159
40. Pakgohar M, Mehran A, Salehi Sormaghi M, Akhondzadeh S, Ahmadi M (2003) Effect of hypericum flowers in treatment of premenstrual syndrome in students living in dormitories of Tehran University of Medical Sciences and Tehran University [MSc Thesis]. Tehran: School of Nursing and Midwifery, Tehran University of Medical Sciences
41. Gholipour Baradari A, Alipour A, Mahdavi A, Sharifi H, Nouraei SM, Emami Zeydi A (2018) The effect of zinc supplementation on sleep quality of ICU nurses: a double blinded randomized controlled trial. Workplace Health Saf 66(4):191–200
42. Cheng S-H, Shih C-C, Yang Y-K, Chen K-T, Chang Y-H, Yang Y-C (2013) Factors associated with premenstrual syndrome—a survey of new female university students. Kaohsiung J Med Sci 29(2):100–105
43. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 28(2):193–213
44. Nedjat S, Montazeri A, Holakouie K, Mohammad K, Majdzadeh R (2008) Psychometric properties of the Iranian interview-administered version of the World Health Organization's Quality of Life Questionnaire (WHOQOL-BREF): a population-based study. BMC Health Serv Res 8(1):61
45. Homsher R, Zak B (1985) Spectrophotometric investigation of sensitive complexing agents for the determination of zinc in serum. Clin Chem 31(8):1310–1313
46. Tetsuo M, Saito M, Horiguchi D, Kina K (1982) A highly sensitive colorimetric determination of serum zinc using water-soluble pyridylazo dye. Clin Chim Acta 120(1):127–135
47. Braverman PK (2007) Premenstrual syndrome and premenstrual dysphoric disorder. J Pediatr Adolesc Gynecol 20(1):3–12
48. Maharaj S, Trevino K (2015) A comprehensive review of treatment options for premenstrual syndrome and premenstrual dysphoric disorder. J Psychiatr Pract 21(5):334–350
49. Das K, Chowdhury A (1997) Metallic ion concentration during menstrual cycle in normally menstruating women. Indian J Med Sci 51(2):52–54
50. Takeda A, Tamano H (2009) Insight into zinc signaling from dietary zinc deficiency. Brain Res Rev 62(1):33–44
51. Ribeiro SMdF, Braga CBM, Peria FM, Martinez EZ, Rocha JJRd, Cunha SFC (2017) Effects of zinc supplementation on fatigue and quality of life in patients with colorectal cancer. Einstein (Sao Paulo) 15(1):24–28
52. Bernardi F, Pluchino N, Begliuomini S, Lenzi E, Palumbo M, Luisi M, Genazzani A (2004) Disadaptive disorders in women: allopregnanolone, a sensitive steroid. Gynecol Endocrinol 19(6):344–353
53. Monteleone P, Luisi S, Tonetti A, Bernardi F, Genazzani AD, Luisi M, Petraglia F, Genazzani AR (2000) Allopregnanolone concentrations and premenstrual syndrome. Eur J Endocrinol 142(3):269–273
54. Pearlstein T, Steiner M (2008) Premenstrual dysphoric disorder: burden of illness and treatment update. J Psychiatry Neurosci JPN 33(4):291
55. Carver CM, Chuang S-H, Reddy DS (2016) Zinc selectively blocks neurosteroid-sensitive extrasynaptic δGABAA receptors in the hippocampus. J Neurosci 36(31):8070–8077
56. Mauri M (1990) Sleep and the reproductive cycle: a review. Health Care Women Int 11(4):409–421
57. Ji X, Liu J (2015) Associations between blood zinc concentrations and sleep quality in childhood: a cohort study. Nutrients 7(7):5684–5696
58. Rondanelli M, Opizzi A, Monteferrario F, Antoniello N, Manni R, Klersy C (2011) The effect of melatonin, magnesium, and zinc on primary insomnia in long-term care facility residents in Italy: a double-blind, placebo-controlled clinical trial. J Am Geriatr Soc 59(1):82–90. https://doi.org/10.1111/j.1532-5415.2010.03232.x

59. Sandstead HH (1994) Understanding zinc: recent observations and interpretations. J Lab Clin Med 124(3):322–327
60. Cherasse Y, Urade Y (2017) Dietary zinc acts as a sleep modulator. Int J Mol Sci 18(11):2334
61. Parry BL, Berga SL, Mostofi N, Klauber MR, Resnick A (1997) Plasma melatonin circadian rhythms during the menstrual cycle and after light therapy in premenstrual dysphoric disorder and normal control subjects. J Biol Rhythms 12(1):47–64
62. Hosie AM, Dunne EL, Harvey RJ, Smart TG (2003) Zinc-mediated inhibition of GABA A receptors: discrete binding sites underlie subtype specificity. Nat Neurosci 6(4):362
63. Wittchen H-U, Becker E, Lieb R, Krause P (2002) Prevalence, incidence and stability of premenstrual dysphoric disorder in the community. Psychol Med 32(1):119–132