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Original Article

Comparing the Effects of Selenium-Enriched Yeast and Sodium Selenite Supplementation on Postpartum Depression and Sexual Satisfaction: A Triple-Blind Controlled Clinical Trial

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Abstract

Introduction: Postpartum depression (PPD) is the most prevalent postpartum complication, significantly diminishing sexual function in marital life. It may result in visible developmental delays, social and interactive challenges in infants, and marital stress leading to divorce. The present study aimed to examine the effect of organic selenium (*Saccharomyces cerevisiae* yeast enriched with sodium selenite) and sodium selenite on PPD and sexual satisfaction.

Methods: A triple-blind controlled clinical trial was conducted on 108 women after childbirth. Participants were randomly assigned into two intervention groups and one placebo group in a 1:1:1 ratio. Participants were given single, identical 250 mg oral capsule containing 200 µg of organically derived selenium or 200 µg of sodium selenite or placebo daily for 8 weeks. They completed Beck's depression inventory and the sexual satisfaction questionnaire before and after the intervention white one-way analysis of variance (ANOVA) and analysis of covariance (ANCOVA) tests. The mean score of PPD and sexual satisfaction were assessed.

Results: All three groups exhibited identical personal and social profiles**.** PPD scores were significantly reduced in the intervention groups of organically derived selenium (adjusted mean difference [AMD] = -2.77; 95% CI: -0.97 to -4.57; $P = 0.003$) and organic selenium (AMD = -1.77; 95% CI: -0.00 to -3.53; $P = 0.04$) compared to control group by adjusting the baseline values. No significant difference was observed in the sexual satisfaction of intervention groups compared to the placebo at the end of intervention ($P = 0.19$).

Conclusion: Both organically derived and inorganic selenium could improve PPD. However, the decline rate was greater in the group receiving yeast-derived selenium. No statistically significant changes were observed in sexual satisfaction following supplementation.

Introduction

Substantial concern surrounds the rising prevalence of mental disorders globally.[1] According to WHO's projections, depression is expected to become a prevalent condition in the coming years.[2,3] Postpartum depression (PPD), a form of major depressive disorder, is one of the most common postpartum complications.[4] Approximately 10%-15% of women experience PPD.[5] According to evidence, PPD has severe effects on the quality of life of all family members and may increase the risk of suicide child harm.[6] PPD destroys the relationship between mother and infant during the vital period of initial brain development. It also leads to significant obvious developmental delay, social and interactive problems, poor speech development, long behavioral problems, child neglect, and marital stresses that leads to divorce.[7]

Various factors influence the depression pathophysiology, including genetic, environmental, and social factors, as well as biological factors such as hormonal effects (ovarian hormones, thyroid hormones, hypothalamus-pituitary-adrenal axis function), oxidative stress, immune system

function, neurotransmitters function, and malnutrition.[8,9] According to assessments, mental and psychological symptoms in women during the postpartum period considerably associate with decreased sexual function.[10] Sexual issues are the most important challenges in marital life, and compatibility in sexual relationships and balance between couples is the most crucial factor for successful marriage and overall well-being.[11]

Selenium is an essential micronutrient for mammals that play a vital role in the brain's natural function, and depression is significantly associated with selenium levels.[12] Selenium provides antioxidant and protective features.[13,14] Oxidative stress markers return to their natural state with the use of antidepressants. Therefore, drugs with antioxidant potential hold significant promise for treating depressive disorders. Organic selenium (Selenium-enriched yeast, Se-yeast) exists in the form of selenoprotein, such as selenomethionine. It is actively absorbed through amino acid pathways. Body tissues store organic selenium for use in emergencies, such as stress. Organic selenium is beneficially stored in the body. Inorganic selenium exists as mineral salts and is mostly excreted from the body after consumption, and only a small amount of inorganic selenium moves towards the body's proteins. Inorganic selenium is rarely stored in the body.[15] In experiments with weanling rats, the chronic toxicity of se-yeast has been reported to be lower compared to sodium selenite. Accordingly, the safety record of Se-yeast is excellent: no cases of accidental Se poisoning have been reported in the three decades of its use as a feed additive and in nutritional supplements.[16,17] Of about one dozen supplementation studies, none has shown evidence of toxicity even up to an intake level of 800 mg selenium over a period of years.[18]

Regarding the importance of maternal and child health care, PPD may put the health of the mother and baby at risk in absence of treatment. According to previous studies, selenium plays a vital role in the body and many reactions. However, no comprehensive study has been done to compare the effect of organic and inorganic selenium on PPD. Moreover, some studies have proved the effect of selenium on the sexual function of men and female rat models. Therefore, this study aimed to examine the effect of selenium on PPD and sexual satisfaction among women who have given birth to compare the effects of organic and inorganic selenium.

Materials and Methods

This study was a randomized controlled clinical trial with three parallel arms. The present study examined 108 women aged 15-45 years old who were within 15th-90th day after childbirth. The target population encompassed all women who had given birth and were referred to the healthcare center of Tabriz City, Iran. The participants were selected from different social-economic backgrounds. Following approval from the regional ethics committee (IR.TBZMED.REC.1400.342) and enrollment of the study in the Iranian Registry of Clinical Trials (IRCT), sampling permission was acquired from the research deputy. Convenient sampling was used to select samples.

Inclusion criteria consisted 15-45 years old women, recently low-risk pregnancies, willingness to participate in the study, having health records, and being on the 15th-90th day after childbirth. Exclusion criteria included depression before childbirth based on the mother's statement, a Beck's inventory score lower than 16 and higher than 46, the experience of depression or any kind of psychological disorder, death of the infant, or hospitalization of the mother because of postpartum complications, undesired incidents such as hospitalization or death of relatives or divorce over past three months, suffering from chronic diseases, such as liver and kidney diseases, experiencing repetitive abortions and infertility record, having a child with mental and physical disabilities, and being allergic to mushrooms and yeast.

Eligible women were selected based on the eligibility criteria checklist. The author then explained the research objectives, advantages, and disadvantages and asked them to voluntarily sign a consent letter and participate in the study. The studied participants completed their personal-social profile, Beck's depression inventory, and sexual satisfaction questionnaire, and gave them to the researcher in the next step.

Upon collection of data from all participants, the results were analyzed through SPSS 24 software. Data normality was examined using the Kolmogorov-Smirnov test, which indicated that data were normally distributed. The chi-square test, Fisher's exact test, and one-way ANOVA were used to examine personal-social profile similarity between groups. One-way analysis of variance (ANOVA) and analysis of covariance (ANCOVA) were used by adjusting the base values to compare the score of depression and sexual satisfaction groups obtained before and after the intervention. A P value less than 0.05 was considered significant. All analyses were done based on Intention-to–Treat approach.

The eligible participants were assigned into two intervention groups (the group of Se-yeast and the group of sodium selenite) and one control group (placebo) using a randomized block design with three and six blocks using a 1:1:1 allocation ratio. The allocation sequence was generated through Random Allocation Software (RAS), by the researcher. Identical, sealed, opaque envelopes numbered from 1 to 108 were used to conceal the allocation, prepare the envelopes, and assign drugs based on the allocation sequence by a person not involved in the study. Participants received envelopes from 1 to the last one based on the inclusion sequence. The researcher, patient, data analyst, and result checker were unaware of the envelopes' content and type of received intervention.

The intervention was implemented as follows:

the first intervention group (n = 36) received 250mg *Saccharomyces cerevisiae* yeast enriched with 200 µg selenium (selenoprotein), the second intervention group (n = 36) received 250 mg capsule containing sodium selenite, and the third group received daily 250 mg placebo. All capsules had a similar appearance. The placebo-based intervention was done for 8 weeks. Participants refilled Beck's depression inventory and sexual satisfaction questionnaire at the end of the intervention. Two envelopes containing 30 drugs were allocated to each person to keep admission. The capsules were sufficient for one month and the researcher asked them to bring their envelopes to subsequent follow-ups to verify the remaining capsules**.** The envelopes were collected in addition to daily use and side effect checklists during follow-up visits. Patients received 8-week interventions, and the researcher inquired about the participants' satisfaction with the drugs using a questionnaire.

According to a previous on-phone agreement with participants, the researcher collected the completed questionnaires after 8 weeks of intervention. It should be noted that subjects were followed-up on phone for two weeks.

The Se-yeast was the product of aerobic fermentation of *S. cerevisiae* in the selenium-rich medium. The basic culture medium contained sugarcane molasses or beet, and vitamins, nutrients, and other growth factors were added to it to promote maximum cellular mass. Selenium was introduced to the culture medium in the form of selenium selenite. Temperature, pH, the concentration of selenium source, the time of injecting it into the culture medium, aeration, inoculation liquid quantity, and the time of adding it to the medium, and the base culture medium were all factors affecting the optimal growth of yeast and selenium uptake efficiency. Fermentation in a selenium-enriched medium results in binding of the organic form of this element and yeast. After fermentation, the yeasts were isolated from the culture medium using a centrifuge, and the cellular mass was thoroughly washed and dried to remove inorganic selenium bonded to the cellular wall. The Se-yeast capsule was produced as a 250mg capsule containing 200µg of organic selenium. The ICP mass. According to this method, the selenium content in the synthesized sample was equivalent to 12600 PPM (12 600 µg/kg) and each 250 mg capsule contained 16mg synthesized selenium powder in organic form, with the remaining amount being filled by yeast.

To prepare inorganic selenium supplement, 250 mg capsule containing 200 µg of inorganic selenium (sodium selenite) was utilized, and the remaining amount was filled with *S. cerevisiae* yeast. The placebo capsule was produced as a 250 mg capsule containing *S. cerevisiae* yeast with the same color, shape, and weight as two previous tablets prepared at the Nutrition Research Center of Tabriz.

Personal and demographic information questionnaire: The basic and demographic information questionnaire was made by the researcher based on the research goals. It had items such as age, education level, income, etc. The questionnaire was completed by the participants in the study, after entering the study.

*Beck's Depression Inventory***:** This study used the Beck scale to measure PPD. This inventory was introduced by Ghassemzadeh et al. This tool comprises 21 self-report items with responses scored on a 0-3 scale. The items were designed based on some contexts, including sadness, pessimism, feelings of failure, guilty feelings, sleep disturbance, loss of appetite, self-dislike, and so forth. Two items were categorized as affective, 11 as cognitive, 2 as overt behavioral, 5 as somatic symptoms, and 1 as interpersonal symptomology. The lowest and highest scores equaled 0 and 63, respectively. This scale measures different levels of depression, ranging from mild to extreme levels. Scores lower than 16 indicate the absence of depression, a score between 16 and 46 signifies mild to moderate depression, and scores exceeding 46 indicate severe depression. This study selected participants with a score range of 16-46.[19] The reliability of the Iranian version of this inventory was confirmed based on Cronbach's alpha coefficient of 0.87, and the reliability of the retest equaled 0.74.[19]

Sexual Satisfaction Questionnaire: Larson's sexual satisfaction questionnaire was used to evaluate sexual satisfaction. For this purpose, 25 items were asked about sexual affections, emotions, tendencies, and expectations of sexual relationships. The items were scored based on the 5-point Likert scale: never (1), rarely (2), usually (3), mostly (4), and always (5). The overall score of this questionnaire varied between 25 and 125. A higher score signifies higher sexual satisfaction. Sexual satisfaction was classified as sexual dissatisfaction (< 50), low sexual satisfaction (51-75), moderate sexual satisfaction (76-100), and high sexual satisfaction (> 101). Bahrami et al examined the psychometric specifications of the Persian version of this questionnaire and reported 0.82 and 0.74 values for the reliability of positive items of the scale and the reliability of negative items of the sexual satisfaction scale, respectively.[20]

In this research, participants completed the checklist for side effects of medicine and satisfaction with the received drug. Checklists were collected at the end of the intervention.

Based on the study conducted by Ivanbaqa et al. on the effect of omega-3 on postpartum depression, it was concluded that people receiving omega-3 had less severe depression than the group receiving placebo. The mean severity of depression before treatment decreased from 9.2 ± 35.4 in the omega-3 group to 7.0 ± 17.6 after treatment, which was statistically significant ($P < 0.0005$). The average severity of depression before treatment changed from 8.4 ± 34.2 in the placebo group to 9.3 ± 33.6 after treatment, which was not statistically significant (P=0.57). The reduction of depression severity score after

treatment in two groups showed a statistically significant difference ($P < 0.001$).[21]

Results

This study examined 200 women of which 108 members were eligible, and 92 members did not have inclusion criteria. One sample loss occurred in the first intervention group due to the side effects of drugs. Finally, 107 members were analyzed (Figure 1).

The mean (standard deviation, SD) value of participants' age was 25.65 (5.85), 29.77 (6.34), and 29.97 (5.98) years in placebo, organic selenium, and inorganic selenium groups, respectively ($P = 0.61$). The mean (SD) value of participants' BMI was 26.08 (3.63), 27.46 (4.13), and 27.51 (3.31) kg/m^2 in placebo, organic selenium, and inorganic selenium groups, respectively ($P = 0.18$). More than three fourth of individuals in the organic selenium (94.42%), inorganic selenium group (94.44%), and placebo (88.88%) groups breastfed their infants ($P = 0.46$). No significant difference existed between the demographic and social characteristics of women in intervention and control groups ($P > 0.05$; Table 1).

No significant difference was observed between organic selenium 20.91(4.90), inorganic selenium 20.91(3.60), and placebo 23.48(5.32) groups in terms of the mean (SD) of Beck's depression score before intervention ($P = 0.05$).

After the intervention, mean (SD) values of Beck's depression score was statistically significant in organic selenium 7.94 (3.57), inorganic selenium 8.94 (3.41), and control 11.00 (4.09) groups ($P = 0.01$). A significant reduction was observed in depression scores after intervention received by the organic selenium group compared to the control group (adjusted mean difference [AMD] = -2.77; 95% confidence interval [CI]: -0.97 to -4.57; $P = 0.003$) and also a decline was seen in the inorganic selenium (AMD = -1.77; 95% CI: -0.00 to -3.53; $P = 0.049$) compared to control group. However, no significant difference was observed between organic and inorganic selenium groups (AMD = -1.00; 95% CI -2.70 to -0.70; $P = 0.24$) (Table 2).

The mean (SD) value of the sexual satisfaction score was similar in organic selenium 97.91(11.84), inorganic selenium 94.70(9.71), and control 93.91(10.14) groups before intervention ($P = 0.25$).

The mean (SD) value of sexual satisfaction score was 96.02(10.10), 93.08(10.90), and 96.65(7.41) in organic

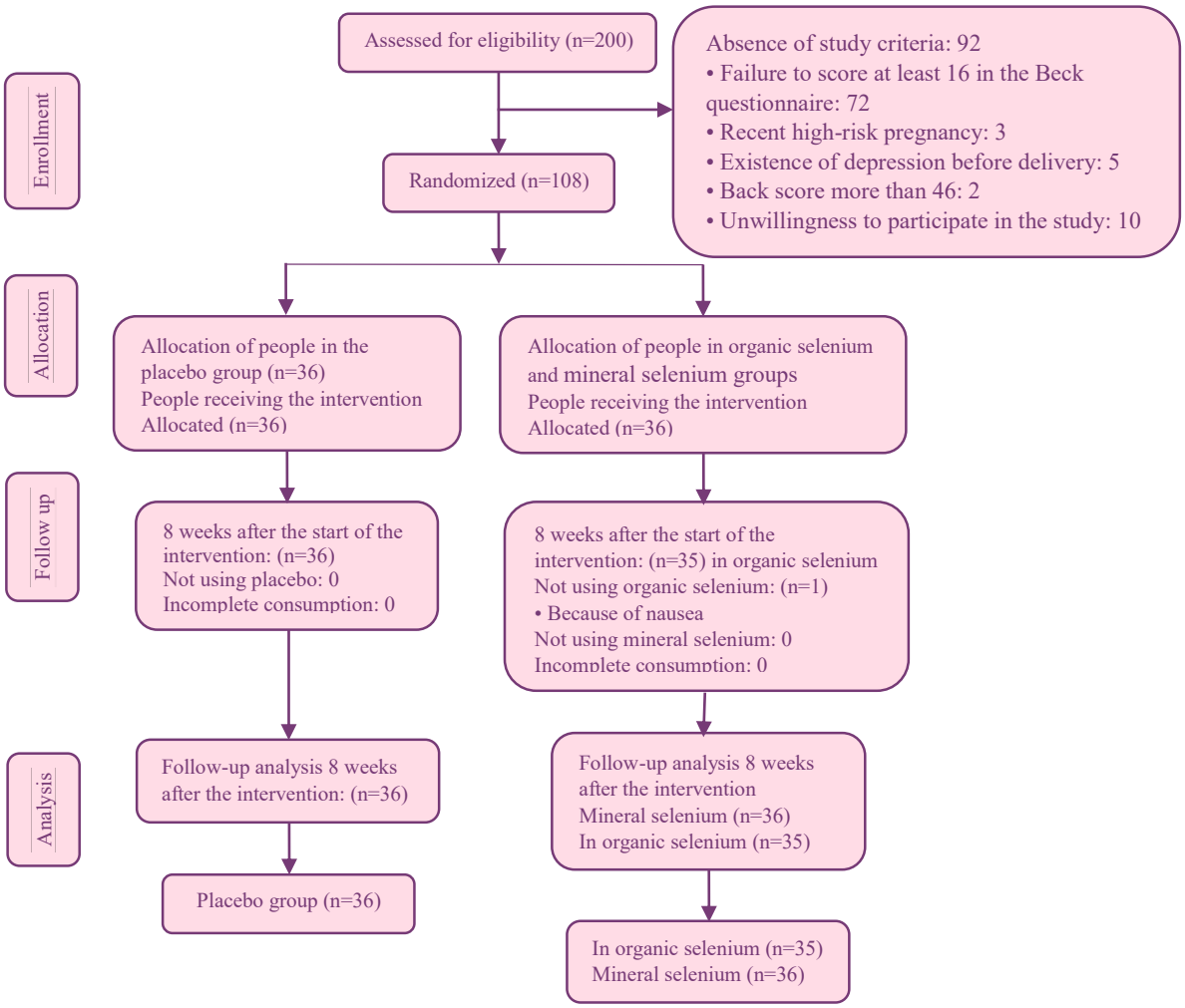

Figure 1. Flowchart of participants

Table 1. Individual and social characteristics of the participants in the study groups

Variables	Organic selenium (n=35)	Mineral selenium (n=36)	Placebo (n=36)	*P* value
	No. (%)	No. (%)	No. (%)	
Age				
15 to 25	10 (28.6)	8 (22.22)	12 (34.3)	0.61[a] 0.59[b]
26 to 35	17 (48.6)	21 (58.33)	20 (55.55)	
36 to 45	8 (22.9)	7 (19.44)	4 (11.11)	
Weight	70.58 (10.57)	70.48 (8.08)	67.08 (8.91)	0.19[a]
Height	160.41 (4.94)	160.13 (6.25)	160.54 (6.12)	0.95[a]
BMI				
<18.5	0 (0.0)	0 (0.0)	2 (5.55)	0.18[a] 0.24[b]
18.5 to 25	11 (31.42)	9 (25.00)	16 (44.44)	
25 to 30	15 (42.85)	17 (47.22)	12 (5.55)	
>30	9 (25.71)	10 (27.77)	6 (8.33)	
Education				
Illiterate	4 (11.4)	6 (16.66)	1 (2.77)	0.64[d]
Diploma and lower	17 (48.6)	21 (58.33)	29 (80.55)	
Academic	14 (40.0)	9 (25.00)	6 (16.66)	
Job				
Housewife	27 (77.1)	28 (77.77)	31 (86.11)	0.61[b]
Have a job	8 (22.9)	8 (22.22)	5 (13.58)	
Husband's Job				
Self-employment	20 (57.1)	18 (50.0)	20 (55.55)	0.93[f]
Employee	11 (31.4)	15 (41.66)	13 (36.11)	
Worker	3 (8.6)	3 (8.33)	2 (5.5)	
Unemployed	1 (2.9)	0 (0.0)	1 (2.77)	
Husband's education				
Illiterate	11 (31.42)	10 (27.77)	12 (33.33)	0.91[c]
Non- academic	2 (5.71)	2 (5.55)	4 (11.11)	
Academic	22 (62.85)	26 (72.22)	20 (55.55)	
Income				
Low	8 (22.85)	1. (2.8)	5 (13.88)	0.43[c]
Medium	24 (68.57)	32 (88.9)	27 (75.00)	
High	3 (8.57)	3 (8.3)	4 (11.11)	
Smoking of husband				
Yes	8 (22.9)	12 (33.33)	8 (22.9)	0.56[b]
No	27 (77.1)	24 (66.66)	27 (77.1)	
Living with husband family				
Yes	1 (2.9)	7 (19.44)	6 (16.66)	0.08[b]
No	34 (97.1)	29 (80.55)	30 (83.33)	
The number of family members				
1-3	19 (54.58)	19 (52.8)	10 (27.77)	0.13[b]
4-6	16 (45.71)	17 (47.2)	25 (69.44)	
>6	0.00	0 (0.0)	1 (2.77)	
Gravida				
1	16 (45.7)	20 (55.55)	13 (36.11)	0.68[b]
2	13 (37.1)	8 (22.22)	14 (38.88)	
3	5 (14.3)	7 (19.44)	7 (19.44)	
>4	1 (2.9)	1 (2.77)	2 (5.55)	
Gender of newborn				
Girl	7 (20.00)	2 (5.55)	6 (16.66)	0.39[b]
Boy	28 (80.00)	34 (94.44)	30 (83.33)	
Breastfeeding				
Yes	32 (91.42)	34 (94.44)	32 (88.88)	0.46[b]
No	3 (8.57)	2 (5.55)	4 (11.11)	

[a] One-way ANOVA; [b] Chi-square test; [c] Pearson chi-square; [d] Chi-square test.

selenium, inorganic selenium, and control groups, respectively, after the intervention, which was not statistically significant ($P=0.19$). No significant difference was observed between organic selenium and control groups ($P=0.38$, AMD = -1.82, 95% CI: 2.34 to -6.00), inorganic selenium and control groups ($P=0.07$, AMD = -3.73, 95% CI: 0.33 to -7.81), organic and inorganic selenium groups ($P=0.35$, AMD = 1.90, 95% CI: 5.99 to –2.17) (Table 3). One participant (2.8%) in the first intervention group (organic selenium) experienced nausea and vomiting two weeks later and dropped out of the study.

In the group organic selenium group, 15 (42.85%) individuals, in the inorganic selenium group 17 (47.22%), and in the placebo group 21 (58.33%) individuals were satisfied with the drugs. A total of 76 (71.02%) participants in all groups were satisfied or very satisfied with the drugs used. None of the participants were dissatisfied or very dissatisfied with the use of medications. According to the Kruskal-Wallis test, there was no statistically significant difference in terms of satisfaction.

According to the medication consumption checklist and the counting of medication envelopes at the end of the intervention, the compliance rate was over 90% among study groups.

- Based on a 5-point Likert scale (very satisfied, satisfied, equally satisfied, dissatisfied, dissatisfied, very dissatisfied) was used to evaluate the satisfaction with the drug.
- In the group receiving organic selenium, 15 people (42.85%), in the mineral selenium group 17 people (47.22%), and in the control group 21 people (58.33%) were satisfied with the drugs.
- A total of 76 (71.02%) participants in all groups were satisfied and very satisfied with the drugs. According to the Kruskal Varis test, there was no statistically significant difference in terms of satisfaction (Table 4).

Table 2. Comparison of the mean score of depression in the study groups

Groups	Before intervention	*P* value[a]	After intervention	*P* value[b]
	Mean (SD)		Mean (SD)	
Organic selenium (n=35)	20.91 (4.90)		7.94 (3.57)	
Mineral selenium (n=36)	20.91 (3.60)	0.05	8.94 (3.41)	0.01
Placebo (n=36)	23.48 (5.32)		11.00 (4.09)	
Comparison between groups	**aMD (95% CI)**	***P* value[c]**	**aMD (95% CI)**	***P* value[b]**
Organic selenium with control	-2.57 (-5.21 to 0.07)	0.05	-2.77 (-4.57 to -0.97)	0.003
Mineral selenium with control	-2.56 (-5.17 to 0.04)	0.05	-1.77 (-3.53 to -0.00)	0.04
Organic with mineral selenium	-0.004 (-2.61 to 2.60)	1.000	-1.003 (-2.70 to 0.70)	0.24

aMD, Mean difference adjusted to baseline values; CI: confidence interval; SD, standard deviation.
[a] One way ANOVA; [b] ANCOVA; [c] Tukey's test.

Table 3. Comparison of the mean score of sexual satisfaction the study groups

Groups	Before intervention	*P* value[a]	After intervention	*P* value[b]
	Mean (SD)		Mean (SD)	
Organic selenium (n=35)	97.91 (11.84)		96.02 (10.10)	
Mineral selenium (n=36)	94.70 (9.71)	0.25	93.08 (10.90)	0.19
Placebo (n=36)	93.91 (10.14)		96.65 (7.41)	
Comparison between groups	**aMD (95% CI)**	***P* value[c]**	**aMD (95% CI)**	***P* value[b]**
Organic selenium compared to control	4.00 (-2.02 to 10.02)	0.25	-1.82 (-6.00 to 2.34)	0.38
Mineral selenium compared to control	0.78 (-5.15 to 6.72)	0.94	-3.73 (-7.81 to0.33)	0.07
Organic selenium to mineral selenium	3.21 (2.72 to 9.15)	0.40	1.90 (-2.17 to 5.99)	0.35

aMD, Mean difference adjusted to baseline values; CI: confidence interval; SD, standard deviation.
[a] One way ANOVA; [b] ANCOVA; [c]Tukey's tes

Table 4. Comparison of the level of satisfaction with the drug used among the study groups

Satisfaction	Organic selenium (n=35)	Mineral selenium (n=36)	Placebo (n=36)	*P* value
Very satisfied	10 (28.75)	5 (13.88)	8 (22.22)	
Satisfied	15 (42.85)	17 (42.22)	21 (58.33)	
Equal amount of satisfaction and dissatisfaction	10 (28.57)	14 (38.88)	7 (19.44)	0.70
Dissatisfied	0 (0)	0 (0)	0 (0)	
Very displeased	0 (0)	0 (0)	0 (0)	

- In the present study, out of 108 participants, only one person was excluded from the sampling due to reporting nausea and itching after two weeks.

Discussion

This study investigated for the first time the impact of *S. cerevisiae* yeast enriched with selenium and sodium selenite compared to placebo on PPD and sexual satisfaction. The results of the present study indicated that both considered selenium supplements reduced the mean PPD compared to placebo. This reduction was more pronounced in the Se-yeast group, while no significant difference was illustrated between sexual satisfaction's mean scores in the studied groups. This finding aligns with previous studies. For instance, Banikazemi et al found a relationship between selenium use and lower depression.[22] Moreover, the medical department of Zagreb University conducted a review study and found that selenium deficiency led to significant depression in animal models by affecting neutrophiles' activity and immune system function, including cellular immunity.[23] Li et al conducted a cross-sectional study in the US and found a reverse significant association between depression and zinc, copper, iron, and selenium intake.[24] According to results of a systematic study and meta-analysis conducted by Sajjadi et al no significant difference was observed in serum selenium levels among patients with depression and healthy individuals. Moreover, they found no significant correlation between serum selenium levels and depression scores. However, a negative significant association existed between high selenium intake and the risk of PPD. Moreover, selenium supplements considerably reduced depression symptoms.[25]

Brüning et al examined female mice and found that the selenium-based compound m-trifluoromethyl-diphenyl diselenide (m CF3–PhSe) 2 significantly reduced depression symptoms, evident from a reduction in immobility time during the forced swimming test

(FST), suggesting its antidepressant efficacy.[2] According to the results of a case-control study conducted by Pasco et al lower selenium intake leads to a higher risk of major depressive disorder.[26]

Mokhber et al conducted an interventional study in Mashhad and concluded that selenium supplement intake during pregnancy is associated with elevated serum selenium levels and lower scores on Edinburgh Postnatal Depression Scale (EPDS) compared to those who received a placebo.[27] Yousefi et al conducted a study on the effect of selenium-enriched *S. cerevisiae* on male rats and found a subsequent reduction in lipid peroxidation but a considerable increase in fertilization and subsequent fetal growth rate. Due to its strong anti-seizure and antioxidant properties, Se-yeast could reduce the destructive effects of stress and can be used to treat many mental and psychological diseases.[28]

Harati et al conducted an interventional study in Tehran on the effects of oral consumption of aqueous chamomile extract and selenium on the experimental model of PPD and plasma oxidant-antioxidant system in mice. Chamomile and selenium exhibited antidepressant effects in the experimental model of PPD induced by progesterone.[29]

All of the abovementioned studies confirmed the results of the present study on PPD. Few studies have conducted a clinical trial on postnatal depression, and no study examined the effect of organic selenium on postnatal depression.

According to studies conducted, selenium could affect the thyroid sexual hormones, and many studies have confirmed the effect of these hormones on depression. From another viewpoint, the side effects of antidepressants on infants and breastfeeding can be reduced by treating PPD. Some studies have indicated a reduction in serum selenium concentration during pregnancy and breastfeeding since it is transmitted to the fetus. Therefore, selenium deficiency in pregnant women can be considered an etiological factor causing PPD.[30]

A balance exists between oxidant-antioxidant systems of organisms under physiological conditions, while the balance is destroyed in favor of oxidant factors under oxidative stress, and this condition is seen in the pathophysiology of several neurological-psychological diseases, including major depression.[31] It has been proved that oxidative stress markers return to their natural state using antidepressants. Therefore, those drugs that are potential antioxidants can be used to treat depressive disorders. Because selenium is used as a cofactor in an active antioxidant enzyme (Glutathione peroxidase), it provides an antioxidant and protective feature for the nervous. Oxidative stress occurs when reactive oxygen species (ROS) and other radicals produce too much or insufficient consumption or overuse of antioxidants exists. ROS may be produced in the mitochondrial respiratory chain and exposed to alcohol, cigarette smoke, and environmental pollutants. Antioxidants, including vitamins C, and E, and antioxidant cofactors, such as selenium, zinc, and copper can modify or suppress ROS formation. Therefore, selenium can probably reduce depression severity through this mechanism.[32]

Elsayed conducted a study on the effect of selenium on sexual satisfaction and concluded that a low-concentration nano-selenium supplement could considerably improve the sexual behavior of quail chicks.[33] Deletion of the selenoproteins gene indicated that lack of this supplement during spermatogenesis leads to abnormal sperm that, in turn, affect the quality of semen and fertility. Change in optimal values of selenium (increase or decrease) may cause abnormal multiple sperms affecting mobility and fertility. Moreover, selenium can increase sexual desire or libido. The optimal value of selenium is necessary to keep the reproductive performance of men and prevent their fertility.[34] Zagrodzki and Ratajczak conducted a study entitled the status of selenium and sex hormones and thyroid hormones and found a balance between selenium and sex hormones in young women during the luteal menstrual cycle.[35] Lanza di Scalea et al conducted a study entitled "sexual dimorphism in selenium metabolism and selenoproteins and found that selenium supplement has better efficiency in female mice rather than male ones in selenium deficiency status, ad GPX plasma level is increased,[10] which confirms the higher selenium absorption in women rather than men. Few studies have been conducted on the sexual satisfaction or activity of women. The present study indicated that selenium could not affect sexual satisfaction in women while could significantly reduce the depression score. In general, previous studies and the association between depression and better quality of sexual relationships in a marital relationship indicate that sexual concerns are affected by depression improvement rather than the side effects of antidepressants among women during the postpartum period.[36] According to this theory, it was expected that sexual satisfaction would be improved in groups that received the intervention. However, the extant study was limited by sample size and time constraints. Therefore, it is possible that the observed improvement in sexual satisfaction may persist in women over the long term during the postnatal period. On the other hand, sexual dissatisfaction during this period can be attributed to a number of factors, such as pain, insomnia, breastfeeding (high prolactin levels), dyspareunia, and other issues that may arise in the postpartum period.

According to the results of the present study, the average depression score was significantly reduced in both intervention groups (organic and inorganic selenium groups) compared to the placebo group. Although this decline was greater in the organic selenium group, the difference between these two groups was not statistically significant. No significant relationship was observed in the sexual satisfaction of both groups.

Zhang et al conducted a study to examine the effect of different types of organic and inorganic selenium on goats' milk yield and concluded that the group that received organic selenium had a higher effect on mammals' bodies due to better function and bioavailability.[37] Jamali Kohshahi et al conducted a study on survival immune function and body composition of Oncorhynchus mykiss under the effect of organic and inorganic selenium and nano-selenium and found the higher effect of selenium compound on nanoparticles and organic forms rather than other selenium forms on innate immune reactions of Oncorhynchus mykiss.[38]

Despite the limited number of studies investigating the superior bioavailability of organic selenium over inorganic selenium, this study achieve this goal with a larger sample size, longer duration, or maximum allowable dose. Therefore, the present study's findings cannot conclusively rule out the possibility of better bioavailability for organic selenium. Additionally, due to financial restrictions, this study did not measure the selenium levels in participants' serum before and after intervention. This constraint could be considered a significant factor for validating the results.

The subjects of the study were selected from those who referred to health-treatment centers in different urban levels, so that the results of this study can be generalized to all women in the society in terms of socio-economic conditions. Using the method of random allocation of study subjects to prevent selection bias. Use of blinding in order to reduce the risk of bias in data collection. Failure to select women with severe depression or non-depressed based on the Beck questionnaire. Telephone follow-up of the participants and use of the daily record table of drug consumption by individuals and answering their questions in order to ensure that the pills are taken and to ensure that the consumption continues during the follow-up period. Our study is a guide and a good basis for citing future studies.

Conclusion

This study indicated that organic and inorganic selenium supplementation significantly reduced depression compared to placebo during the postnatal period without affecting sexual satisfaction. Although depression scores in the organic selenium group were considerably lower compared to the inorganic selenium group, statistical analysis between two groups indicated that organic selenium did not significantly reduce depression scores compared to inorganic selenium. Results indicate selenium supplementation can be prescribed as a routine dietary supplement, in addition to other supplements, for the mental health of mothers referred to healthcare centers.

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Research Highlights

What is the current knowledge?

- Regarding the importance of maternal and child health care, PPD may put the health of the mother and baby at risk in absence of treatment.
- According to previous studies, selenium plays a vital role in the body and many reactions.
- However, no comprehensive study has been done to compare the effect of organic and inorganic selenium on PPD.
- Moreover, some studies have proved the effect of selenium on the sexual function of men and female rat models.
- Therefore, this study aimed to examine the effect of selenium on PPD and sexual satisfaction among women who have given birth to compare the effects of organic and inorganic selenium.

What is new here?

- There are two types of selenium (organic or inorganic selenium - inorganic or inorganic selenium) that we examined their differences in this study.
- On the other hand, for the first time in our study, this substance was examined in the postpartum period, previous studies of consumption during pregnancy and done on animals which are discussed in the section.

Authors' Contribution

Conceptualization: Mahnaz Shahnazi.
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Formal analysis: Azizeh Farshbaf-Khalili.
Funding acquisition: Mahnaz Shahnazi.
Investigation: Azizeh Farshbaf-Khalili, Parnian Rahimi.
Methodology: Mahnaz Shahnazi.
Project administration: Mahnaz Shahnazi.
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Supervision: Alireza Ostarahimi, Mahnaz Shahnazi.
Validation: Azizeh Farshbaf-Khalili.
Visualization: Azizeh Farshbaf-Khalili, Parnian Rahimi.
Writing–original draft: Parnian Rahimi.
Writing–review & editing: Azizeh Farshbaf-Khalili, Parnian Rahimi.

Competing Interests

The authors declare that they have no competing interests.

Data Availability Statement

The datasets are available from the corresponding author on reasonable request.

Ethics Approval

The protocol of study was approved by the Regional Ethics Committee (IR.TBZMED.REC.1400.342). All participants consented to participate and signed an informed consent.

Funding

The protocol of the study was registered and approved by the Research Vice Chancellor of Tabriz University of Medical Sciences (Research ID: 67579).

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