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Short communication

Antepartum/postpartum depressive symptoms and serum zinc and magnesium levels

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Abstract:
In the present study, we investigated the relationship between depressive symptoms and serum zinc and magnesium level in antepartum and postpartum women. All women received standard vitamin, zinc and magnesium supplementation. Sixty-six pregnant women in the Czerwiakowski Hospital in Kraków were assessed for prepartum depressive symptoms using the Beck Depression Inventory (BDI). Sixty-two and fifty-eight women were also assessed for postpartum depressive symptoms (using Edinburgh Postnatal Depression Rating Scale, EPDRS) at 3 and 30 days after delivery, respectively. Serum zinc and magnesium levels were also determined at these time points, however, the number of examined subjects were diminished. A significantly higher EPDRS score (by 45%), indicating severity of depressive symptoms, was found on the 3rd day after childbirth compared with the 30th postpartum day. Moreover, the early post-delivery period (3rd day) was characterized by a 24% lower serum zinc concentration than that found on the 30th day after childbirth. BDI scores assessed a month before childbirth revealed mild depressive symptoms, which was accompanied by a serum zinc concentration similar to that found on the 3rd day after delivery. No significant alterations were found in the magnesium levels between these time points. The present results demonstrated a relationship between severity of depressive symptoms and decreased serum zinc (but not magnesium) concentration in a very specific type of affective disorder, the postpartum depression.

Key words:
antepartum, postpartum, depression, serum, zinc, magnesium

Introduction

Depression is a psychiatric disorder with high morbidity and mortality, leading to a significant percentage of suicidal attempts in humans [14]. Prevalence of depression is estimated at 10–15% and is almost twice as common in women than in men. Although mood changes (maternity blues) are not rare in the early postpartum period, only 10–20% of women develop more severe depressive symptoms, i.e. postpartum depression [15, 38, 43]. However, the low diagnostic rate (50%) limits proper treatment of women suffering from this disorder. Apart from affecting psychophysiology of a mother, the postpartum depression also disturbs the emotional and cognitive development of a child. Thus, the postpartum depression, which develops in a very important and difficult period for both mother and the child, creates significant social and psychological problems [43, 47].

Zinc is a trace element involved in a variety of biochemical processes that modulate the function of the central nervous and immune systems [9, 10, 35, 44]. Alterations in blood zinc homeostasis may reflect mood disturbances as well as functions of the immune system (see [25, 28, 29] for review). Zinc has been shown to exhibit antidepressant-like activity in animal preclinical tests/models [16, 17, 30]. It is interesting to note that very low, ineffective doses of zinc administered together with low, ineffective doses of an antidepressant (imipramine or citalopram) exhibited antidepressant-like effects in mouse and rat forced swim test [16, 39]. Moreover, our preliminary data suggest enhanced efficacy of antidepressant therapy by zinc in human depression [26]. On the other hand, repeated administrations of imipramine or citalopram induce a 20% increase in the ratio of zinc concentration in the hippocampus and other regions of the brain [27]. This finding may indicate a significant "redistribution" of the brain zinc pool following chronic antidepressant treatments. Chronic electroconvulsive treatment, the most effective antidepressant therapy, induces an increase in zinc concentrations in the hippocampus with a similar, although less significant effect in the cortex and cerebellum [27]. It has also been demonstrated (using Timm's method for zinc staining) that chronic treatment with electroconvulsive shock induces hippocampal mossy fibre sprouting [45]. This data suggest an increase in the vesicular zinc level in the hippocampus following electroconvulsive treatment.

These findings suggest that zinc homeostasis is implicated in affective disorders, and serum concentration of this ion may be a sensitive marker of depression.

Magnesium is also involved in the pathophysiology and therapy of depression. This ion exhibits antidepressant-like activity in animal tests, and magnesium deficiency induced depression-like behavior in mice [5, 34, 37]. Moreover, beneficial clinical efficacy of magnesium was demonstrated in patients with different affective-like mood disorders (mania, rapid cycling bipolar disorders, chronic fatigue syndrome/atypical depression, or premenstrual syndrome) [2, 3, 7, 8, 13, 33, 40]. However, the data from clinical studies, which examined magnesium blood concentrations, are not so unequivocal. Depending on the type of affective disorders, no alterations, and decrease as well as increases in blood magnesium concentration were demonstrated (see [24] for review).

The aim of this study was to compare serum zinc and magnesium concentration in antepartum and postpartum women and to relate them to depressive symptoms.

Subjects and Methods

Participants were 140 pregnant women who were admitted to and delivered at the Czerwiakowski Hospital in Kraków. Sixty-six of them (62%) were finally accepted for the study. All accepted women were 31 ± 1 years old, in good physical health, without history of psychotic or affective disorders. We investigated depressive symptoms in 66 pregnant women a month before delivery. However, only 62 and 58 of them were examined in the 3rd and 30th day of postdelivery period, respectively. Moreover, we determined the serum zinc and magnesium concentration at these time points. The study was approved by the Ethics Committee of Collegium Medicum, Jagiellonian University and Institute of Pharmacology PAS, and informed consent was obtained from all participants. Psychopathological status was assessed using the Beck Depression Inventory (BDI) a month before childbirth and with the Edinburgh Postnatal Depression Rating Scale (EPDRS) on the 3rd and 30th day

after delivery. When patients fulfilled diagnostic criteria for postpartum depression, the 9/10 EPDRS cut-off score served to distinguish between healthy and depressed subjects [4, 6]. Blood samples were collected from antepartum and postpartum women between 9.00 and 10.00 on the day when BDI and EPDRS questionnaires were completed. All women received standard vitamin and mineral supplementation [daily (between 12.00 and 14.00 h) intake of 25 mg Zn (from 4th month of pregnancy) and 2–3 times a day 470 mg magnesium lactate + Vit B6 (from 7th month)].

The zinc concentration in serum was determined using flame atomic absorption spectrometry (Unicam Solaar 939 with deuterium background correction). The aqueous standard for serum was $Zn(NO_3)_2$ (Polish Committee for Standardization, Measures and Analysis Control, Poland). Validate-N ser. B5-308 (Organon Teknika, USA.) was used as a serum control for the zinc measurement.

The magnesium content in the serum was estimated colorimetrically using the Mann and Yoe reaction (Biochemtest – POCH, Gliwice, Poland) [22].

Group differences were assessed using Student's *t*-test (EPDRS scores) or ANOVA followed by Bonferroni test. Relationships between variables were assessed using the Spearman rank order correlation coefficient.

Results

On the 3rd day postpartum, 26 of 62 women (42%) exhibited 9 and higher EPDRS scores. However, on the 30th day, only 17 women (29%) were qualified for postpartum depression (9 and higher EPDRS scores).

The mean of EPDRS scores on the 30th day after delivery were by 32% lower (significant) in comparison with the scores determined on the 3rd day ($p < 0.05$; Tab. 1).

The serum zinc concentration on the 30th day after delivery was statistically significantly higher by 33% or 25% than that measured on the 3th postpartum day or 1 month before delivery, respectively ($p < 0.05$; Tab. 2), and was similar to our previous data derived from non-pregnant women (0.86 ± 0.02 mg/l). There was a significant correlation between serum zinc and EPDRS scores measured on 3rd and 30th day of post delivery period ($r = –0.2968$, $p = 0.014$; Fig.1).

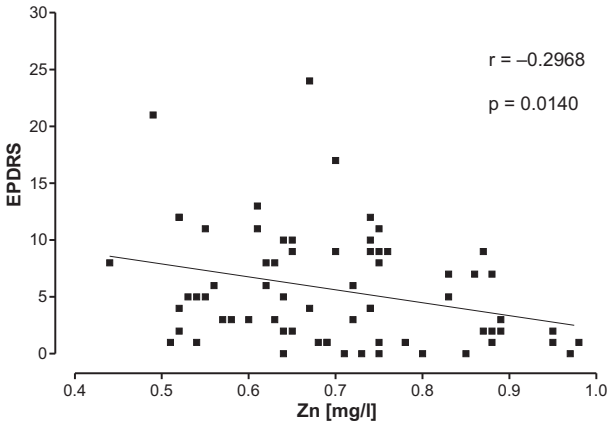

Fig. 1. The relationship between serum zinc concentration and Edinburgh Postnatal Depression Rating Scale (EPDRS) scores on the 3rd day and at 1 month after delivery. Variables were assessed using Spearman rank order analysis

Tab. 1. Beck Depression Inventory (BDI), Edinburgh Postnatal Depression Rating Scale (EPDRS) scores at 1 month before delivery and on the 3rd and 30th day of the post delivery period

Time of examination	Score (mean ± SEM)	n
1 month before (BDI)	7.26 ± 0.66	66
3 days after (EPDRS)	7.77 ± 0.69	62
30 days after (EPDRS)	5.36 ± 0.66*	58

* $p < 0.05$ *vs.* "3 days after" time point (Student's *t*-test)

Tab. 2. Serum zinc and magnesium concentrations at 1 month before delivery and on the 3rd and 30th day of the post delivery period

Time of determination	Concentration (mean ± SEM)	n
Zinc (mg/l)		
1 month before	0.64 ± 0.01	39
3 days after	0.61 ± 0.01	36
30 days after	0.80 ± 0.02*	32
Magnesium (mg/100 ml)		
1 month before	3.67 ± 0.22	36
3 days after	3.34 ± 0.22	31
30 days after	3.50 ± 0.21	27

ANOVA: $F(2,104) = 44.84$, $p < 0.0001$ for zinc and $F(2,91) = 0.5994$, $p = 0.5513$ for magnesium assay. * $p < 0.05$ *vs.* "1 month before" and "3 days after" time points (Bonferroni test)

There were no significant differences in magnesium concentrations between all time points (Tab. 2). Moreover, magnesium content in serum at all times studied was higher then normal control range (2.24 ± 0.06 mg/100 ml, our own data obtained previously in non-pregnant women).

Discussion

Our study demonstrated 29% prevalence of postpartum depression, which is similar to the data described previously (23%) [6]. There are discrepancies in literature concerning the prevalence rate, e.g. 10–20% was presented by Josefsson et al. [15]. This may be due to more restricted 9/10 EPDRS scores cut-off applied in the present and the Dennis' [6] studies, compared to 10/11 scores cut-off used by others (e.g. [15]).

In the present study, we found lowered serum zinc concentrations in the late antepartum and early postpartum period, which increased a month after delivery. In addition, the means of BDI or EPDRS scores were significantly higher than those found a month after delivery. The increase in zinc concentration at a later point in time was accompanied by alleviation of depressive symptoms. Since there was negative correlation between serum zinc and EPDRS scores, this indicated a relationship between serum zinc and depression symptoms in postpartum period. What is important, standard supplementation, which includes zinc salt, did not prevent hypozincemia. Most studies have reported that in unipolar depression, the severity of the illness measured by the Hamilton Depression Rating Scale (HDRS) is negatively correlated with the serum level of this ion [18, 19, 23, 31, 36]. However, another study of Maes et al. [21] did not find a correlation between these two parameters (HDRS scores and zinc). Therefore, we expect that a lower serum zinc level will accompany depressive symptoms in unipolar and postpartum depression, while its relationship with the severity of the illness varies with the population of depressive patients. Alterations in zinc homeostasis in unipolar depression are at least partly related with disorganized immunological system. The increased inflammatory response system (increased CD4+/CD8+ T cell ratio, serum neopterin and interleukin-6) and impaired function of cell immunity (reduced T-cell cytokine production) were demonstrated in this disorder (see [29] for review). Also, similar mechanism(s) may exist in postpartum depression [20]. The reduced blood zinc level may represent such reduction in the zinc brain pool, although such relationship between central and peripheral zinc was not demonstrated in affective disorders. As was previously proposed [29], the mechanism of antidepressant zinc action involves NMDA/glutamate system. Moreover, effect on glycogen synthase kinase-3β and immune systems should also be considered in antidepressant activity of zinc [29]. Thus, mechanism(s) of zinc deficiency-induced mood alterations may implicate the above mentioned systems.

As indicated in the Introduction, the relationship of the depressive symptoms with blood magnesium concentration is not quite clear and vary between specific types of affective disorders (see [24] for review). The low serum/plasma magnesium level was demonstrated in depressed patients (unipolar affective disorders; [11, 12, 46]). The other studies, however, reported increased or no alterations in magnesium level and this variability seems to be dependent of clinical subtypes of affective disorders (e.g. [1, 32, 41, 42]). In our present study, serum magnesium concentration was not altered at different time points, although it was increased presumably due to standard magnesium supplementation.

The present results demonstrated a relationship between severity of depressive symptoms and decreased serum zinc (but not magnesium) concentration in a very specific type of affective disorder, the postpartum depression.

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