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DETERMINING THE RELATIONSHIP BETWEEN THE LEVEL OF OXYTOCIN IN HUMAN BLOOD AND POSTPARTUM DEPRESSION (PPD) IN PREGNANT WOMEN REFERRING TO GOVERNMENTAL HOSPITALS AFFILIATED TO AHWAZ UNIVERSITY OF MEDICAL SCIENCES IN 2015

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ABSTRACT

Introduction: Postpartum depression (PPD) affects approximately 19% of women. According to the DSM-5™ Diagnostic Criteria, postpartum depression is a component of major depressive disorder that is diagnosed during pregnancy or during the 4 weeks postpartum. **Method:** 85 pregnant women with 37 and 42 weeks of pregnancy were randomly selected. 46 patients were entered into the study using the Beck Depression Inventory (BDI)[1], and diagnosing the absence of postpartum depression. Blood samples were collected before delivery and transferred to the laboratory and centrifuged, and the plasma was stored in the freezer. Again, the Edinburgh Postnatal Depression Scale (EPDS) was distributed among the same women, during the 2nd to 6th week after delivery and oxytocin plasma concentration was measured by the kit (ZellBio GmbH, Germany) and ELISA Microplate Reader. **Results**: According to the results of the Edinburgh Postnatal Depression Scale (EPDS), 26 of the participants were healthy and 20 of them were depressed. No significant difference was observed between the concentration of oxytocin before delivery in two groups of healthy and depressed. Plasma oxytocin concentration was significantly increased in comparison with prepartum, but its level in the depressed group was significantly lower than the healthy group. **Conclusion**: In some women, depression may develop after delivery, called postpartum depression, which can be directly related to the lack of increasing oxytocin plasma levels sufficiently after delivery.

KEYWORDS: Postpartum depression, oxytocin, Edinburgh test.

INTRODUCTION

There are steps during each woman's life that have significant effects on her life, including pregnancy and after it, which are associated with significant psychological and hormonal changes.[1]

In the post-pregnancy period, especially in the first month, women experience the highest levels of stress throughout their lives, so that mental disorders one month after childbirth is 18 times more prevalent than pregnancy, and stress from the birth of the first child in psychosocial stress tables is classified as a severe stress, and women requires comprehensive support to spend their time in good health.[2] Postpartum mood disorders cause functional and emotional disturbances and can have significant effect on the family depending on the severity of the problem. Failure to diagnose and treat these disorders may be associated with chronic emotional **disorders**, poor mother-to-child attachment, marital conflicts, suicide, child neglect, and drug abuse.[3]

Postpartum depression is considered as a clinical syndrome that is more severe than sadness after childbirth and has a greater impact on the family. This syndrome is a combination of physical, emotional illnesses and behavioral changes that some women experience after childbirth.[4]

Research has shown that of every 4 million births that occur annually, approximately 40% of women experience different forms of postpartum mood

disorders.[5] It has reported that the prevalence of postpartum depression in the world is 10% to 20%.[6]

Although true cause of this disorder has not yet been proven, but many researchers during various studies concluded that a set of psychological, midwifery and hormonal factors can be considered as causes of mood disorders.[7] Sudden changes in levels of progesterone, estrogen, prolactin, cortisol, thyroxine, vasopressin and oxytocin after delivery can be considered as the cause of depression and mood changes.[8]

Fiske et al. (1984), during a study conducted in the United States, and concluded that salivary estradiol and progesterone concentrations were significantly higher in women with postpartum depression and no significant difference was observed between these women with healthy women in terms of their salivary estradiol.[9] Also, Harris et al. (1994), conducted a study in Austria, and concluded that women with postpartum depression had higher progesterone concentrations than healthy women in the pre-natal period, while progesterone concentrations in the first to fifth day after delivery among these women were lower than healthy women.[10]

Victoria Hendrik, conducted a study on 147 women aged 6-8 weeks after delivery in Poland, and concluded that depressed women had lower levels of prolactin than healthy women, but did not evaluate the levels of oxytocin and vasopressin.[11]

The change in plasma levels of oxytocin in mood disorders has been proven.[12] In studies on postpartum, it has been reported that oxytocin has an antidepressant and anti-stress effect. In animals, oxytocin can reduce glucocorticoid secretion and anxiety.[13] In humans, oxytocin can reduce anxiety in lactating mothers.[14] Oxytocin reduction in depressed patients due to lack of adjustment of the hypothalamic-pituitary-adrenal axis may cause the symptoms.[15]

Oxytocin is a peptide hormone and neuropeptide, which is normally produced by the paraventricular nucleus of the hypothalamus and stored and secreted in the posterior pituitary. The gene for this hormone is located on chromosome 20. The main function of this hormone is secretion and milk excretion by contraction in the myovipillion cells, located around the alveoli, in the mammary glands.[16] Oxytocin is released from the posterior pituitary by the mother's nipple stimulation by the baby. From the physiological point of view, the other function of oxytocin is uterus stimulation, with no doubt, release of oxytocin plays an important role in childbirth. The hormone is used synthetically to exacerbate birth constipations.[17]

Oxytocin (OT) is also secreted in the testicles. It has not yet been proven that the hormone is produced or accumulated by leydig cells. However, it has been observed that in mice, it plays an important role in seminal duct movement and may stimulate spermatogenesis.[18]

The physiological role of oxytocin in the central nervous system is still unknown, but the behavioral effects of this peptide is somehow clear, which may be due to oxytocin metabolites.[19]

Pharmacological and non-pharmacological activity of oxytocin may be an important way to treat anxiety.[20] According to the results of studies, there is a significant relationship between oxytocin and secretion of serotonin. That is, oxytocin is released in response to treatment with selective serotonin reuptake inhibitors (SSRI) and balances the effect of serotonin.[21]

Considering the postpartum depression complications for mother and family, and the known mechanism of oxytocin in human behavior, the researcher decided to conduct a study aimed to determine the relationship between the level of oxytocin and postpartum depression in pregnant women. If this relationship is confirmed, the synthetic oxytocin can be used for the treatment of postpartum depressed mothers.

MATERIALS AND METHODS

Population, sampling and research design

The population included mothers who referred to Imam Khomeini and Razi hospitals in Ahwaz for prenatal and postnatal care. In the present study, the convenience and purposive sampling methods were used, ie the units were selected according to the inclusion and exclusion criteria.

Data were collected from interviews, patients' records and completion of the questionnaire as well as the blood samples of the subjects. These included:

1. A researcher-made questionnaire was used in this study, which includes the following:

Individual factors: Name, Last name, Age, nationality, marriage age, Type of marriage, Education level, Job.

Midwifery factors: number of births, abortion history, history of stillbirth, delivery method, gestational age, history of premenstrual syndrome, obstetric events, infertility history, history of hospitalization during pregnancy, postpartum hemorrhage, duration of delivery, duration of hospitalization after delivery.

Neonatal factors: infant weight, infant admission, infant gender, mother and father's satisfaction with the infant gender.

2. **Beck's Depression Inventory:** It is used for measuring depression during pregnancy. Beck test has a high sensitivity and specificity in the pre-natal period. So that its sensitivity in this period is 80-82% and its specificity is 78-82%.

3. **Edinburgh Postnatal Depression Scale:** It is used to measure postpartum depression. In Iran, this questionnaire has been validated by researchers by content validity method. This questionnaire has a high sensitivity and specificity.

4. **Blood samples taken for testing:** Blood samples were centrifuged for 2 hours and immediately stored in the freezer, and then plasma oxytocin was measured using the ZB-11046-H9648. Human oxytocin, OT ELISA Kit. ZB-11047-H9648. The lowest limit of plasma oxytocin measurement was 9.4 pg / ml. The coefficient of variation (V) of the internal measurement was less than 10%. The range of measurement was 15.6- 1000 pg / ml.

5. **Determining the validity and reliability of the tool**

Content validity method was used to determine the validity of a questionnaire including individual, midwifery, and neonatal factors. The necessary corrections have been made to the questionnaire with the opinion of ten faculty members.

In order to determine the confidence of the questionnaire, a two-part test method was used. After the initial study, 30 subjects were divided into two groups. Spearman-Brown correlation coefficient of 79% was obtained based on the results of the table.

Inclusion criteria in research

• **Having consent to participate** in a **research study**
• Resident in Ahvaz city
• Age 18 to 35 years old
• Pregnancy: 37 to 42 weeks
• Lack of first birth
• Lack of unwanted pregnancy
• Deaths of loved ones or first-degree relatives during the past 6 months have not occurred
• Not having a physical or mental illness known in the mother
• Non-use of analgesics and anesthetics
• Lack of alcohol, cigarettes and drugs
• No history of severe depression and special medications during the interview
• No history of infertility
• No history of abortion
• Lack of early or late delivery
• No history of hospitalization during pregnancy
• No history of
• No history of dead baby

6. **Exclusion criteria**

• Presence of anomalies in the baby
• The birth of the dead baby
• The birth of baby who require special care
• Birth of a baby with weight less than 2500 grams
• Dissatisfaction with the baby's gender
• Postpartum hemorrhage
• Occurrence of incidents during childbirth
• Prolonged admission after childbirth
• Cesarean delivery

This study was conducted analytically. After referring to the Imam and Razi Hospitals, pregnant women with inclusion criteria, who did not have any exclusion criteria, were selected to participate in this study. The inclusion and exclusion criteria are listed separately.

85 pregnant women with gestational age of 42-47 weeks were first selected. After interviewing and explaining the purpose of the study and the benefits of this study and the possible complications, they were given the discretion to choose whether to participate or not to participate in this research, finally 46 pregnant women were entered into this study. At first, demographic information in the questionnaire was asked from the patients and collected. Then, using Beck's Depression Inventory, non-depression of the pregnant women was evaluated during entering the study. Blood samples were taken at the same time and transferred to the laboratory according to scientific principles. They were centrifuged for 2 hours and the plasma was stored in the freezer at -70°C until the measurement of oxytocin concentration. Again, the same women were visited 2 to 6 weeks after delivery. After completing the Edinburgh questionnaire, the blood samples were taken from the same subjects again and transferred to the laboratory and, like the first one, the patient's plasma was prepared and stored in the freezer at -70°C. Then, the oxytocin concentration was measured and recorded by the ELISA reader ELX808 and the Human Oxytocin ELISA kit, Germany.

RESULTS

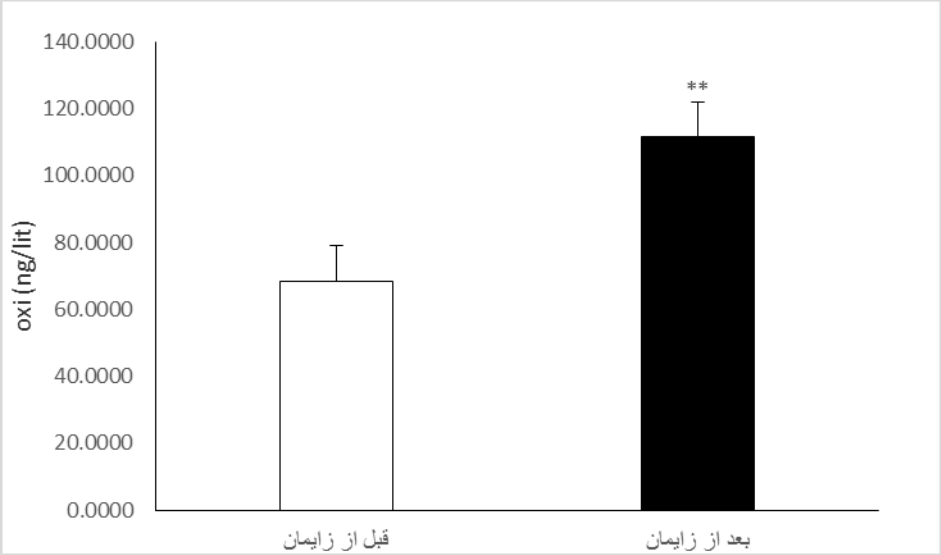
In the present study, 85 pregnant women with a gestational age of 37 to 42 weeks were first selected. Beck test was done on these people in order to differentiate healthy people from depressed ones. Of these, 19 have been diagnosed with depression with a score of less than 32 and were excluded from the study, and 66 were diagnosed as healthy people. with a score of over 32 and entered into the study. The blood samples were taken from 59 women from 66 pregnant women in the third trimester of pregnancy and the serum oxytocin concentration in the pre-natal period was measured. 8 people were excluded from study due to cesarean delivery. Edinburgh test were performed on 48 women of the remaining 58 after delivery, and the blood samples were taken from 46 of them to determine the oxytocin concentration after delivery. A total of 46 women remained in the study, so that the results of the Edinburgh test and the oxytocin blood concentration were available simultaneously before and after delivery.

The score of Edinburgh Perinatal/Postnatal Depression Scale (EPDS) of the subjects studied

26 people (52.56%) of the subjects with scores less than 12 were diagnosed as healthy people and 44 people (43.4%) with a score of more than 12 were diagnosed as depressed ones.

The oxytocin concentration in the subjects studied

The plasma oxytocin concentration in the studied population was 68.46 ± 10.72 ng / L. Concentration of this factor after dlivery was 11.46 ± 10.51 ng / L, which was significantly increased (P <0.01) in comparison with before delivery (Figure 1).

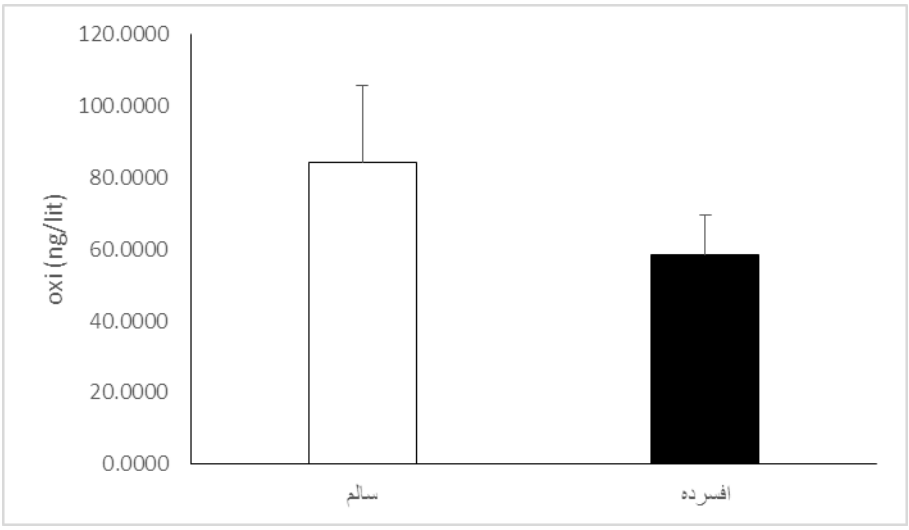


Before delivery, after delivery

Figure 1, shows the serum oxytocin concentration in subjects before and after delivery. Paired t test was used for comparison of the two groups statistically. Results are expressed as mean ± SEM. P < 0.01 * *P has significant levels compared with before delivery.

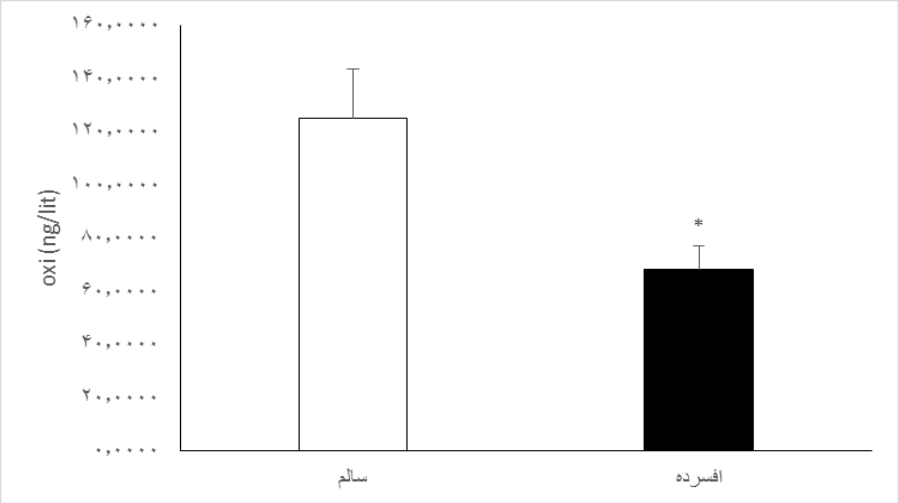
Relationship between blood oxytocin levels and postpartum depression

The pre-natal oxytocin concentration was 84.4 ± 21.48 in healthy subjects and in depressed subjects was 58.50 ± 11.00, which no significant differences was observed between the two groups (Fig. 2). Postpartum oxytocin levels in the healthy group reached 125.33 ± 18.36 and in the depressed group was 68.11 ± 8.81, which was significantly lower than healthy group (P <0.05) (Fig. 3).



Healthy, depressed people

Fig 2, Shows the serum oxytocin concentration in healthy group and depressed group before delivery. Unpaired t test was performed for statistical comparison between two groups. Results are expressed as mean ± SEM.



Healthy, depressed people

Fig 3, Shows the serum oxytocin concentration in healthy and depressed group after delivery. Unpaired t test was performed for statistical comparison between two groups. Results are expressed as mean ± SEM. * P <0.05 is considered as significant levels compared to healthy group.

DISCUSSION

85 pregnant women with 37 and 42 weeks of pregnancy were randomly selected. 66 patients were entered into the study using the Beck Depression Inventory (BDI), and finally 46 people entered into this study, so that the results of the Edinburgh test and the oxytocin blood concentration were available simultaneously before and after delivery.

According to the results of Edinburgh test, after the delivery, the subjects were divided into two groups: healthy and depressed. The oxytocin concentration before delivery was the same and no significant difference was observed. After delivery, serum oxytocin concentration significantly increased in comparison with before delivery, but it was significantly lower in depressed group than in healthy subjects.

In the present study, healthy pregnant women were studied by Beck test and diagnosis of mental health and absence of depression. However, after childbirth, by performing the Edinburgh test, the incidence of depression in some of these women was proven. Postpartum depression is considered as a clinical syndrome that some women experience after delivery.[4] The prevalence of this postpartum disorder in the world has been reported between 10% - 20%[6] and this disorder has been 43.48% in this study.

Although true cause of this disorder has not yet been proven, but many researchers during various studies concluded that a set of psychological, midwifery and hormonal factors can be considered as causes of mood disorders (7 and 8).

In this study, serum oxytocin concentration significantly increased after delivery, in comparison with after delivery. Oxytocin is a peptide hormone and neuropeptide, which is normally produced by the paraventricular nucleus of the hypothalamus and stored and secreted in the posterior pituitary. The main function of this hormone is secretion and milk excretion.[16] From the physiological point of view, the other function of oxytocin is uterus stimulation. Therefore, its plasma level increases during and after delivery.[17] The results of this study also confirmed this fact.

However, the level of this hormone in the depressed group was significantly lower than in healthy group. In studies on postpartum, it has been reported that oxytocin has an antidepressant and anti-stress effect. In animals, oxytocin can reduce glucocorticoid secretion and anxiety.[13] In humans, oxytocin can reduce anxiety in lactating mothers.[14] Oxytocin reduction in depressed patients due to lack of adjustment of the hypothalamic-pituitary-adrenal axis may cause the depression symptoms.[15]

According to the results of studies, there is a significant relationship between oxytocin and secretion of serotonin. That is, oxytocin is released in response to treatment with selective serotonin reuptake inhibitors (SSRI) and balances the effect of serotonin.[21]

Therefore, lack of oxytocin increase during and after childbirth sufficiently, which can lead to depression in women, which is consistent with the results of this study. In other studies, this relationship has been proven, so that Skrundz et al during a study on pregnant women in Switzerland, concluded that there is a significant relationship between the oxytocin concentration in pregnant women and the incidence of postpartum depression symptoms, so that those who were at risk of postpartum depression, had the serum oxytocin concentration lower than those without risk of depression.[22]

Also, Zelkowitz et al conducted a study on pregnant women in Canada, and concluded that there is a reverse relationship between postpartum oxytocin concentration and the Edinburgh score (-0.115), as well Sandraluz et al during a study on pregnant women in Chicago, concluded that 21% of women developed depression during the first 8 weeks after delivery.

In those women who had stopped breastfeeding, the oxytocin concentration was lower than those who hadn't stopped breastfeeding, but were not depressed[23], and Lindsey et al. during a study on African-American women, concluded that depressive symptoms were observed in 15.6% of people with low oxytocin concentration, 12.4% with moderate oxytocin concentration, and 5.3% of those with high oxytocin concentrations, so that depression symptoms were higher in women with low oxytocin concentration.[24] Finally, the results of the present study are consistent with the results of these studies.

CONCLUSION

In some women, depression may develop after delivery, called postpartum depression, which can be directly related to the lack of increasing oxytocin plasma levels sufficiently after delivery.

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