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Investigation and Analysis of Emotional State and Oxytocin Level in Patients with Postpartum Depression

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Abstract

Background: Postpartum depression (PPD) is a common mental disorder in postpartum women, negatively impacting physical and mental health. Correlation analysis can predict the relationship between variables. By detecting the abnormal level of oxytocin, clinicians can timely know the emotional states of parturients to guide clinical practice. This study aimed to investigate the relationship between emotional states and oxytocin (OT) levels in patients with PPD.

Materials and Methods: The medical records of 166 PPD patients admitted to Cangzhou Central Hospital from May 2020 to March 2023 were retrospectively analyzed. After excluding 9 patients who did not meet the inclusion criteria, the remaining 157 patients were included in this study. The 7-item Generalized Anxiety Disorder Scale and Patient Health Questionnaire-9 items were used to evaluate the emotional states of 157 patients, and the included subjects were grouped according to the results of the scale. The serum OT levels of patients was measured, and the relationship between the OT levels and emotional states was analyzed.

Results: In this study, 75 patients were included in the mild anxiety group, and 82 patients were included in the moderate and severe anxiety group. Seventy-nine patients were selected as the mild depression group, and 78 patients were included in the moderate and severe depression group. The mild anxiety group had a higher OT level than the moderate and severe anxiety group ($Z = -10.121$, $p < 0.001$). The mild depression group had a higher OT

level than the moderate and severe depression group ($Z = -9.758$, $p < 0.001$). OT level was negatively correlated with anxiety and depression scores ($r = -0.676$, $r = -0.665$, $p < 0.001$).

Conclusion: There is a specific relationship between the emotional states of PPD patients and the OT levels in the body, and active clinical management strategies need to be implemented.

Keywords

postpartum depression; emotional state; oxytocin; investigation and analysis

Introduction

Postpartum depression (PPD) is a common mental disorder in postpartum women, with clinical manifestations including perinatal crying, irritability, frustration, sadness, hallucinations, and even suicide [1,2]. PPD has high incidence, especially in developing countries [3]. The perinatal period is a period of dramatic fluctuations in hormone levels and women's psychological vulnerability [4]. According to the survey data, 4%–39% of postpartum women have negative emotions such as anxiety and depression after delivery, which are often ignored [5]. The occurrence of PPD has a negative impact on patients and their offspring. On the one hand, PPD causes patients to suffer from insomnia, self-blame, self-incrimination, injury to infants, and other problems; on the other hand, it also has a negative impact on the social emotions and cognition of future generations [6].

Oxytocin (OT) is a peptide hormone secreted by the posterior pituitary gland and synthesized by the hypothalamus's paraventricular and supraoptic nuclei. OT is a cir-

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Table 1. GAD-7 scale.

Projects	Options			
	0 point	1 point	2 points	3 points
1. Feeling nervous, anxious, or urgent	Never	Several days	More than a week	Almost every day
2. Unable to stop or control worry	Never	Several days	More than a week	Almost every day
3. Worrying too much about all kinds of things	Never	Several days	More than a week	Almost every day
4. Hard to relax	Never	Several days	More than a week	Almost every day
5. Unable to sit still due to anxiety	Never	Several days	More than a week	Almost every day
6. Becoming dysphoric or irritable	Never	Several days	More than a week	Almost every day
7. Feeling as if something terrible will happen and being afraid	Never	Several days	More than a week	Almost every day

GAD-7, 7-tiem Generalized Anxiety Disorder Scale.

Table 2. PHQ-9 scale.

Projects	Options			
	0 point	1 point	2 points	3 points
1. Lack of motivation and energy when doing things	Never	Several days	More than half of the days	Almost every day
2. Feeling low, depressed, or desperate	Never	Several days	More than half of the days	Almost every day
3. Difficulty in falling asleep, restless or oversleeping	Never	Several days	More than half of the days	Almost every day
4. Feeling tired or lacking vitality	Never	Several days	More than half of the days	Almost every day
5. Loss of appetite or overeating	Never	Several days	More than half of the days	Almost every day
6. Feeling bad or failing, or disappointing oneself or family	Never	Several days	More than half of the days	Almost every day
7. Difficulties in focusing on things, such as reading newspapers or watching TV	Never	Several days	More than half of the days	Almost every day
8. Moving or speaking slowly until others have already noticed, or just the opposite, becoming more restless or restless than usual, moving around	Never	Several days	More than half of the days	Almost every day
9. Lack of interest in doing things	Never	Several days	More than half of the days	Almost every day

PHQ-9, Patient Health Questionnaire-9 items.

culating peptide composed of 9 amino acids and acts on the peripheral and central nervous systems [7,8]. In addition, OT can also reduce the level of stress hormones such as adrenal ketone in the human body to reduce blood pressure [9]. OT, as a neurotransmitter, acts on the central nervous system and is synthesized by the hypothalamus and projected to various regions of the brain and a wide range of brain regions in the brainstem and limbic system, such as the striatum, hippocampus, and amygdala. It acts on different social behaviors of human beings, such as social cognition and maternal behavior [10,11]. The OT level can affect the physiological indexes of parturient women and play a specific role in regulating emotions, cognition, and behavior. The study of Yoon and Kim [12] has shown that OT positively affects anti-anxiety. OT acts as a stress molecule, anti-inflammatory molecule and antioxidant, especially with protective effects in adversity or trauma [13]. Few studies have confirmed the relationship between emotional changes and OT levels in PPD patients at present. This study hopes to analyze the relationship between the two and provide more directions for selecting and formulating clinical treatment schemes.

Materials and Methods

Sources of Research Subjects

All PPD patients admitted to Cangzhou Central Hospital from May 2020 to March 2023 were selected as research subjects in this study. This study included 157 samples in total. This study, conforming to the Declaration of Helsinki (2013) [14], has been approved by the ethics committee of Cangzhou Central Hospital (approval No.: 2022-094-02(z)). This study was a retrospective analysis; all patients included had informed consent and signed relevant agreements. Inclusion criteria. (1) Patients conformed to the diagnostic criteria for depression in the Chinese Classification of Mental Disorders (Third Edition) [15]. (2) The Edinburgh Postnatal Depression Scale score was >15 points [16]. (3) Patients were in the period of breastfeeding. (4) Patients were 21–38 years old. (5) Patients had complete medical records. Exclusion criteria. (1) Patients with secondary depression caused by organic diseases or other mental disorders; (2) patients with a history of depression or other mental illness before pregnancy; (3) patients with

heart, liver, kidney, and brain organic lesions; and (4) patients without complete medical records.

Evaluation of Emotional State

Patients' anxiety was assessed by the 7-item Generalized Anxiety Disorder Scale (GAD-7) [17]. This scale consisted of 7 items and adopted a 4-level scoring method (0 points, never; 1 point, several days; 2 points, more than a week; 3 points, almost every day). The total score range was 0–21 points. A score of 5–9 points indicated mild anxiety, 10–14 points showed moderate anxiety, and ≥ 15 points showed severe anxiety. The higher score indicated more severe anxiety.

Patients' depression was assessed by the Patient Health Questionnaire-9 items (PHQ-9) [18]. The scale consisted of nine items, using a four-level scoring method (0 points, never; 1 point, several days; 2 points, more than half of the days; 3 points, almost every day). The total score range of this scale was 0–27 points. A score of 5–9 points indicated mild depression, 10–14 points showed moderate depression, and ≥ 15 points showed severe depression. Higher scores showed more severe depression, as detailed in Table 1 and Table 2.

Detection of OT Level

The detection of OT level was performed at 8:00 a.m. In this study, 3 mL of fasting peripheral venous blood was collected from research subjects and centrifuged at 3000 r/min for 5 min to obtain the supernatant. Serum OT level was measured using enzyme linked immunosorbent assay. The reagent kits (manufacturer: Elabscience Biotechnology Co., Ltd.; serial number: E-EL-0029; origin: Wuhan, China) were purchased from Elabscience Biotechnology Co., Ltd., and all operations were implemented according to the manufacturer's instructions.

Statistical Methods

SPSS 26.0 statistical software (Armonk, NY, USA), produced by IBM, was used for data analysis. Firstly, the Shapiro-Wilk method was used to test whether the continuous variables conformed to the normal distribution. The continuous variables that did not conform to the normal distribution were indicated by $M (P_{25}, P_{75})$ and detected by the Mann-Whitney U test. The continuous variables were indicated by $[n (\%)]$, detected by the χ^2 test. The correlation analysis was as follows. When the two columns of variables conformed to the normal distribution in general,

Pearson product-moment correlation was adopted. When the two columns of variables did not conform to the normal distribution, the Spearman rank correlation was used. $p < 0.05$ indicated that the difference was statistically significant.

Results

General Data

A total of 157 subjects were included in this study. According to the scores of anxiety and depression, all research subjects were divided into mild anxiety group, moderate and severe anxiety group, mild depression group, and moderate and severe depression group. The results showed that there was no significant difference in age, body mass index (BMI), educational level, residence, and other general data between the mild anxiety group and the moderate and severe anxiety group ($p > 0.05$). No significant difference existed in age, BMI, educational level, residence, and other general data between the mild depression group and the moderate and severe depression group ($p > 0.05$). The comparison of general data among different groups is shown in Table 3 and Table 4.

Comparison of OT Levels under Different Emotional States

Comparison of OT Levels under Different Anxiety States

By comparing the OT levels under different anxiety states, the results showed that the mild anxiety group had higher OT levels than the moderate and severe anxiety group ($p < 0.001$), as detailed in Table 5.

Comparison of OT Levels in Different Depression States

When analyzing OT levels in different depression states, the study found that the mild depression group had higher OT levels than the moderate and severe depression group ($p < 0.001$), as detailed in Table 6.

Correlation Analysis

Spearman correlation analysis showed that OT level was negatively correlated with anxiety and depression scores ($r = -0.676$, $r = -0.665$, all $p < 0.001$), indicating that there was a moderate negative correlation between OT levels and anxiety and depression scores.

Table 3. Comparison of general data of patients with different degrees of anxiety.

Indicators	Mild anxiety group (n = 75)	Moderate and severe anxiety group (n = 82)	Z/ χ^2	p
Age [years old, M (P ₂₅ , P ₇₅)]	28.00 (25.00, 33.00)	30.00 (25.75, 34.00)	-0.736	0.462
BMI [kg/m ² , M (P ₂₅ , P ₇₅)]	22.79 (20.80, 24.12)	22.65 (20.90, 24.53)	-0.603	0.547
Educational level			0.431	0.512
Senior high school and below	35 (46.67)	34 (41.46)		
College and above	40 (53.33)	48 (58.54)		
Residence			0.252	0.616
City	40 (53.33)	47 (57.32)		
Countryside	35 (46.67)	35 (42.68)		
Gestational weeks [week, M (P ₂₅ , P ₇₅)]	38.00 (37.00, 40.00)	38.00 (37.00, 40.00)	-0.105	0.916
Birth weight of infants [g, M (P ₂₅ , P ₇₅)]	2941.00 (2415.00, 3501.00)	2927.00 (2403.50, 3467.00)	-0.170	0.865
Gender of infants			0.033	0.857
Male	41 (54.67)	46 (56.10)		
Female	34 (45.33)	36 (43.90)		
Duration after delivery [month, M (P ₂₅ , P ₇₅)]	3.00 (2.00, 6.00)	4.00 (2.00, 5.25)	-0.169	0.866
Breastfeeding			0.082	0.775
Yes	51 (68.00)	54 (65.85)		
No	24 (32.00)	28 (34.15)		

BMI, body mass index.

Table 4. Comparison of general data of patients with different degrees of depression.

Indicators	Mild depression group (n = 79)	Moderate and severe depression group (n = 78)	Z/ χ^2	p
Age [years old, M (P ₂₅ , P ₇₅)]	28.00 (24.00, 33.00)	30.00 (26.00, 34.00)	-1.423	0.155
BMI [kg/m ² , M (P ₂₅ , P ₇₅)]	22.71 (20.80, 24.12)	22.90 (20.90, 24.76)	-1.036	0.300
Educational level			0.306	0.580
Senior high school and below	33 (41.77)	36 (46.15)		
College and above	46 (56.23)	42 (53.85)		
Residence			0.154	0.695
City	45 (56.96)	42 (53.85)		
Countryside	34 (43.04)	36 (46.15)		
Gestational weeks [week, M (P ₂₅ , P ₇₅)]	38.00 (37.00, 40.00)	38.00 (37.00, 40.00)	-0.964	0.335
Birth weight of infants [g, M (P ₂₅ , P ₇₅)]	2895.00 (2414.00, 3555.00)	2957.50 (2438.75, 3431.00)	-0.126	0.899
Gender of infants			0.005	0.943
Male	44 (55.70)	43 (55.13)		
Female	35 (44.30)	35 (44.87)		
Duration after delivery [month, M (P ₂₅ , P ₇₅)]	4.00 (2.00, 6.00)	3.00 (2.00, 5.00)	-1.218	0.223
Breastfeeding			0.202	0.653
Yes	51 (64.56)	53 (67.95)		
No	28 (35.44)	25 (32.05)		

Discussion

Depression is one of the most severe mental disorders in the world [19]. Females are more likely to suffer from this mental illness, and the morbidity of depression in females is usually 1 time that of males [20]. The survey data have shown that the probability of PPD is getting higher and higher in postpartum women, and the incidence has reached 15%–30% [21]. PPD's effect involves in women's physiological and psychological functions and extends to part-

ner, family, and mother-infant interaction, so its threat to women's health and family happiness cannot be ignored. Therefore, the etiology and treatment of PDD have become the focus of attention in basic and clinical medicine, neuroscience, and psychology. Study has shown that OT levels are predictors of PDD during pregnancy and after delivery [22]. Based on the mechanism of OT, a study was conducted in 157 PPD patients, aiming to explore the relationship between the emotional state of PPD patients and OT level, namely, to investigate whether the OT level was

Table 5. Comparison of OT levels under different anxiety states.

Groups	Cases	OT level [mIU/L, M (P ₂₅ , P ₇₅)]
Mild anxiety group	75	74.00 (61.00, 87.00)
Moderate and severe anxiety group	82	37.00 (27.00, 48.00)
Z		-10.121
p		<0.001

OT, oxytocin.

Table 6. Comparison of OT levels in different depression states.

Groups	Cases	OT level [mIU/L, M (P ₂₅ , P ₇₅)]
Mild depression group	79	72.00 (57.00, 87.00)
Moderate and severe depression group	78	37.00 (26.75, 47.25)
Z		-9.758
p		<0.001

different in different emotional states. This study adopted the GAD-7 scale and PHQ-9 scale to evaluate the anxiety and depression of research subjects. The test results of the GAD-7 scale showed that 75 cases had mild anxiety and 82 cases had moderate and severe anxiety among 157 subjects. The test results of the PHQ-9 scale showed that 79 cases had mild depression and 82 cases had moderate and severe depression among 157 subjects. To reduce the error in the study of emotional state and OT level, this study compared the general data of patients in different emotional states, and the results showed that there was no difference in age, BMI, and educational level of patients. Through further comparison of OT levels in different groups, this study found that under different anxiety states, the mild anxiety group had higher OT levels than the moderate and severe anxiety group. Under different depression states, the mild depression group had higher OT levels than the moderate and severe depression group. Spearman correlation analysis showed that there was a moderate negative correlation of OT levels with anxiety and depression scores, which is consistent with the research results of some scholars [23]. Some positive effects of OT on puerpera have been widely recognized, such as uterine contraction, milk secretion, and postpartum maternal behavior. The impact of OT on maternal emotions is easily overlooked, but OT affects people's emotional states in various ways. OT can also affect the anxiety and depression of patients with PDD by interacting with the hypothalamic-pituitary-adrenal (HPA) axis [24]. One study has confirmed that OT can directly activate the oxytocin receptor expressed in the serotonergic neurons of the raphe nucleus to regulate the release of serotonin and play an anti-anxiety and anti-depression role [25]. Moreover, OT can act on the amygdala, insula, inferior frontal gyrus, and other brain regions closely related to

emotional expression, selectively reduce the reactivity of brain regions involved in stress and anxiety, and enhance the activity of dopamine and serotonin neurons, thereby affecting the emotional state of the human body [26]. Thus, multiple interventions should be implemented to improve the OT level of PDD patients and improve their anxiety and depression, such as proper exercise, stimulation of nipples, dietary conditioning, and drug treatment. The limitations of this study are as follows. First, the research results showed that OT level was correlated to anxiety and depression. Still, the occurrence and development of anxiety and depression are affected by multiple factors such as physiology, psychology, and society. This study does not consider the influence of social factors on emotions, such as family economic situation and an individual's desire for an infant's gender. Second, the sample size included in this study is relatively small, which may lead to biased results. Therefore, the shortcomings of this study should be considered when interpreting our results, and the sample size should be increased in future research to provide more scientific and accurate data for clinical practice.

Conclusion

In this study, we observed a difference in OT levels of PPD patients under different emotional states, and patients with severe anxiety and depression have lower OT levels. Additionally, we revealed a moderate negative correlation between the emotional states and OT levels. Therefore, clinical attention should be paid to postpartum emotions, reduce postpartum anxiety and depression, and improve maternal health of puerpera.

Availability of Data and Materials

The datasets used and/or analysed during the current study were available from the corresponding author on reasonable request.

Author Contributions

XY designed the research study. WPZ and YG performed the research. XY and WPZ provided help and advice on the ELISA experiments. YG analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study, conforming to the Declaration of Helsinki (2013), has been approved by the ethics committee of Cangzhou Central Hospital (approval No.: 2022-094-02(z)). This study was a retrospective analysis; all patients included had informed consent and signed relevant agreements.

Acknowledgment

Not applicable.

Funding

This research was funded by Research Plan Project of Hebei Provincial Administration of Traditional Chinese Medicine (The effect of self-formulated formula combined with acupoint therapy on postpartum lactation), Grant No. 2023452.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Stewart DE, Vigod SN. Postpartum Depression: Pathophysiology, Treatment, and Emerging Therapeutics. *Annual Review of Medicine*. 2019; 70: 183–196.
- [2] Tang J, Liu AM, Chen XY, Wang SW. Upregulation of Circulating MiR-211 and MiR-744 is Related to Postpartum Depression via Estrogen Receptor 1 Targeting. *Journal of Biological Regulators and Homeostatic Agents*. 2023; 37: 3173–3183.
- [3] Liu X, Wang S, Wang G. Prevalence and Risk Factors of Postpartum Depression in Women: A Systematic Review and Meta-analysis. *Journal of Clinical Nursing*. 2022; 31: 2665–2677.
- [4] Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. *Frontiers in Neuroendocrinology*. 2019; 52: 165–180.
- [5] Fawcett EJ, Fairbrother N, Cox ML, White IR, Fawcett JM. The Prevalence of Anxiety Disorders During Pregnancy and the Postpartum Period: A Multivariate Bayesian Meta-Analysis. *The Journal of Clinical Psychiatry*. 2019; 80: 18r12527.
- [6] Hübner-Liebermann B, Hausner H, Wittmann M. Recognizing and treating peripartum depression. *Deutsches Arzteblatt International*. 2012; 109: 419–424.
- [7] Marsh N, Marsh AA, Lee MR, Hurlmann R. Oxytocin and the Neurobiology of Prosocial Behavior. *The Neuroscientist: a Review Journal Bringing Neurobiology, Neurology and Psychiatry*. 2021; 27: 604–619.
- [8] Liu CM, Spaulding MO, Rea JJ, Noble EE, Kanoski SE. Oxytocin and Food Intake Control: Neural, Behavioral, and Signaling Mechanisms. *International Journal of Molecular Sciences*. 2021; 22: 10859.
- [9] Erickson EN, Lee CS, Emeis CL. Role of Prophylactic Oxytocin in the Third Stage of Labor: Physiologic Versus Pharmacologically Influenced Labor and Birth. *Journal of Midwifery & Women's Health*. 2017; 62: 418–424.
- [10] Feifel D, Shilling PD, MacDonald K. A Review of Oxytocin's Effects on the Positive, Negative, and Cognitive Domains of Schizophrenia. *Biological Psychiatry*. 2016; 79: 222–233.
- [11] Li XH, Matsuura T, Xue M, Chen QY, Liu RH, Lu JS, *et al.* Oxytocin in the anterior cingulate cortex attenuates neuropathic pain and emotional anxiety by inhibiting presynaptic long-term potentiation. *Cell Reports*. 2021; 36: 109411.
- [12] Yoon S, Kim YK. The Role of the Oxytocin System in Anxiety Disorders. *Advances in Experimental Medicine and Biology*. 2020; 1191: 103–120.
- [13] Carter CS, Kenkel WM, MacLean EL, Wilson SR, Perkeybile AM, Yee JR, *et al.* Is Oxytocin “Nature’s Medicine”? *Pharmacological Reviews*. 2020; 72: 829–861.
- [14] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013; 310: 2191–2194.
- [15] Chen YF. Chinese classification of mental disorders (CCMD-3): towards integration in international classification. *Psychopathology*. 2002; 35: 171–175.
- [16] Park SH, Kim JI. Predictive validity of the Edinburgh postnatal depression scale and other tools for screening depression in pregnant and postpartum women: a systematic review and meta-analysis. *Archives of Gynecology and Obstetrics*. 2023; 307: 1331–1345.
- [17] Luo W, Luo L, Wang Q, Li Y, Zhang Y, Hu Y, *et al.* Disorder-specific impaired neurocognitive function in major depression and generalized anxiety disorder. *Journal of Affective Disorders*. 2022; 318: 123–129.
- [18] Levis B, Benedetti A, Thombs BD. DEPRESSION Screening

- Data (DEPRESSD) Collaboration. Accuracy of Patient Health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis. *BMJ (Clinical Research Ed.)*. 2019; 365: 11476.
- [19] Liu L, Wang H, Chen X, Zhang Y, Zhang H, Xie P. Gut microbiota and its metabolites in depression: from pathogenesis to treatment. *EBioMedicine*. 2023; 90: 104527.
- [20] Swetlitz N. Depression's Problem with Men. *AMA Journal of Ethics*. 2021; 23: E586–E589.
- [21] Shorey S, Chee CYI, Ng ED, Chan YH, Tam WWS, Chong YS. Prevalence and incidence of postpartum depression among healthy mothers: A systematic review and meta-analysis. *Journal of Psychiatric Research*. 2018; 104: 235–248.
- [22] Cevik A, Alan S. Are pregnancy and postpartum oxytocin level a predictive biomarker for postpartum depression? *The Journal of Obstetrics and Gynaecology Research*. 2021; 47: 4280–4288.
- [23] Di TQ, Huang YJ, Gao J. The moderating effect of oxytocin on maternal behavior in patients with postpartum depression. *Advances in Psychological Science*. 2020; 28: 456–464. (In Chinese)
- [24] Thul TA, Corwin EJ, Carlson NS, Brennan PA, Young LJ. Oxytocin and postpartum depression: A systematic review. *Psychoneuroendocrinology*. 2020; 120: 104793.
- [25] Nagahashi-Araki M, Tasaka M, Takamura T, Eto H, Sasaki N, Fujita W, *et al.* Endogenous oxytocin levels in extracted saliva elevates during breastfeeding correlated with lower postpartum anxiety in primiparous mothers. *BMC Pregnancy and Childbirth*. 2022; 22: 711.
- [26] Whitley J, Wouk K, Bauer AE, Grewen K, Gottfredson NC, Meltzer-Brody S, *et al.* Oxytocin during breastfeeding and maternal mood symptoms. *Psychoneuroendocrinology*. 2020; 113: 104581.