Relationship between psychological state and urinary catecholamines and serotonin in 1-month postpartum mothers

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Abstract

Purpose

In postpartum mental health, postpartum depression is a serious disorder. In Japan, the Japanese version of Edinburgh Postnatal Depression Scale (EPDS) has been used to screen for postpartum depression, but it has not screened all mothers at risk. Therefore, we examined objective indicators that reflect the psychological state of the mother, which can be used in conjunction with the EPDS to accurately screen mothers at risk. This study examined the relationship between maternal psychological status and urinary catecholamines and serotonin at 1-month postpartum.

Methods

We used the EPDS and Profile of Mood States Second Edition (POMS-2) to measure mothers’ postpartum psychological state. Analysis was conducted on 94 women at their 1-month postpartum checkup in Ibaraki Prefecture, Japan. Psychological state and biological state and background factors were analyzed using logistic regression analysis and multiple regression analysis. Urinary catecholamines and serotonin were measured as stress response and depression indicators. Background factors were age, parity, delivery method, support, and lactation status.

Results

Higher urinary noradrenaline levels were associated with an EPDS score. Lack of husband support was associated with higher POMS-2 Total Mood Disturbance, Confusion-Bewilderment, and Depression-Dejection scores. In addition, first-time mothers had higher Tension-Anxiety scores on POMS-2, and mothers using formula milk or mixed feeding scored higher on Confusion-Bewilderment.

Conclusion

These results suggest that urinary noradrenaline reflects postpartum maternal depression. In addition, the husband’s support, being primipara, and breastfeeding were associated with better mental health for mothers.

Key words: postpartum psychological state, postpartum depression, urinary catecholamine, urinary serotonin, one month postpartum

Introduction

The perinatal period, women may lose their mental and physical stability due to increased physical load, changes in their psychosocial environment (for instance, assuming the new role as a mother), and endocrinological changes associated with pregnancy and childbirth (Yaginuma et al., 1984; Yokoo, 2018). Subsequently, postpartum depression may develop, leading to marital crisis, child abuse, and maternal suicide (Goodman, 2004; Ueshima, 2010; Wakamatsu et al., 2018). Postpartum depression occurs in 10-20% of mothers (Horwitz et al., 2007), which is relatively high.

In Japan, the Edinburgh Postpartum Depression Scale (EPDS) is widely used to screen for postpartum depression; screening at 1-month postpartum is recommended (Japan Society of Obstetrics and Gynecology, 2017). However, according to the EPDS score, the percentage of
mothers with postpartum depression according to the EPDS score is as low as 8.5% (Ministry of Health, Labour and Welfare [MHLW], 2018a), which is lower than the prevalence of postpartum depression. Therefore, the EPDS may not be able to adequately screen all mothers at risk of postpartum depression, as it is a subjective self-administered measure. Thus, mothers who are unaware of their psychological symptoms or hesitant to disclose them may not be identified as being at risk of postpartum depression. Therefore, there are limitations to screening based on the use of subjective information alone, and we believe that objective indicators used in conjunction with this information may help to accurately screen mothers at risk.

Although various objective indicators have been used to examine their relationship between psychological states and maternal psychological state, their validity as indicators of postpartum psychological state has not been investigated thus far. In this context, urinary catecholamines and serotonin have been implicated in depressive states and stress responses (Wallenstein, 2002); furthermore, these may be potential indicators for screening postpartum depression because they are easy to collect. However, to the best of our knowledge, thus far, there has been no study on the level of these substances in relation to depression in postpartum mothers.

Therefore, this study aimed to determine whether urinary catecholamines and serotonin were associated with maternal psychological status in the first month postpartum. We investigated the association between the scores on psychological scales EPDS and Profile of Mood States - Second Edition (POMS-2) and urinary catecholamines and urinary serotonin levels. The results of this study provide a basis for the investigation of biochemical indicators for simple and objective evaluation of psychological states.

Methods

Study design, setting, and participants.

We conducted a quantitative cross-sectional study using questionnaires. We also measured the level of urinary substances in 1-month postpartum mothers. The study was conducted in two maternity wards that mainly handle low-risk deliveries.

Of the 109 patients who attended the 1-month postpartum checkup from October to November 2019 responses were obtained from 100 patients (response rate 91.7%); nine patients who did not meet the eligibility criteria or did not consent were excluded. After data collection, questionnaires with missing data were excluded; thus, the final analysis included data from 94 individuals (valid response rate 94.0%) (Table 1).

Each participant was provided with a participant information sheet and signatures were obtained through an informed consent form. Questionnaires were handed out to the mothers during their visit for the 1-month postpartum checkup. A consent withdrawal form was distributed to the mothers along with a questionnaire so that they could withdraw at any time, even after providing consent. Urine samples were collected during postnatal checkups, and a professional analytical company was hired to analyze the level of catecholamines and serotonin.

The inclusion criteria were as follows: the participants should be 1) 1-month postpartum and 2) able to communicate in Japanese and answer the questionnaire. The exclusion criteria were 1) taking medication for psychiatric disorders at the time of the survey or for more than 6 months, 2) chronic diseases, and 3) cases of stillbirth.

Measures

Participant attributes: The demographic variables assessed were based on previous studies (Beck, 2001; Sato et al., 2002; Umezaki et al., 2015). Alongside the psychological scales, participants also completed a self-administered questionnaire including age, single/multiple...
birth, parity, marital status, mode of delivery (transvaginal, cesarean), health status of child, number of weeks of gestation, instances of hospitalization (Neonatal Intensive Care Unit or Growing Care Unit), presence or absence of disease, presence or absence of supporters, lactation status (breastfeeding, formula milk, or mixed feeding), history or complications, and presence or absence of long-term medication.

The EPDS developed by Cox et al., (1987), is a questionnaire designed to screen for postpartum depression. We used the version translated into Japanese by Okano et al., (1996), which indicates a high probability of postpartum depression if the score is 9 or higher.

The POMS-2, developed by Juvia et al., (2012) and translated into Japanese by Konuma et al., (2015), is a measure of mood state. The POMS-2 can quickly assess not only relatively long-lasting mood states but also fluctuating and transient mood states. Responses on the scale are combined to produce seven scores: a Total Mood Disturbance score (minimum-max, average=27-83) and scores on six mood clusters, namely “Anger-Hostility” (37-75), “Confusion-Bewilderment” (36-78), “Depression-Dejection” (39-79), “Fatigue-Inertia” (29-75), “Tension-Anxiety” (31-74), “Vigor-Activity” (34-74), and “Friendliness” (28-77), with higher scores for each indicating a higher level of the emotion. The average level of each score is between 40 and-59 points (Juvia et al., 2012; Konuma et al., 2015).

Urinary biomarkers

The urinary biomarkers examined in this study are adrenaline, noradrenaline, dopamine and serotonin. The normal values for each biomarker are 3.4 ~ 26.9µg/day for adrenaline, 48.6 ~ 168.4µg/day for noradrenaline, 365.0 ~ 961.5µg/day for dopamine and 1.0 ~ 6.0mg/day for serotonin.

The study used creatinine-corrected as-needed urine, collected for medical use at the 1-month physical examination. The high-performance liquid chromatography-1,2-diphenylethylenediamine method was used measure catecholamines, and the enzyme-linked immunosorbent assay method was used for serotonin.

Among the urinary catecholamines, adrenaline and noradrenaline have been described to have high intraday variability, with a circadian rhythm that decreases from night to early morning, rises after waking, and peaks at 13:00 (Turton, 1974). Dopamine has no intraday variation (Yoshimura et al., 1993). Therefore, in this study, urine samples were collected at all hours except early morning and night. The urine samples in this study were collected between 10:00am and 14:00 hours.

Previous studies have shown that concentrations of catecholamines and serotonin are similar in blood and urine (Kakeda, 2011; Katz et al., 1991); furthermore, transient stress at the time of blood collection also affects the measurements, we decided to measure urinary levels in the participating mothers.

Ethical considerations

The study was approved by the ethical review board of the University of Tsukuba Committee on Medical Ethics. (approval number 2651).

Data analysis

The statistical software IBM SPSS Statistics v. 24 was used to analyze the data. We performed binomial logistic and multiple regression analyses to determine the impact of maternal neurotransmitters and attributes on EPDS and POMS-2 scores at 1-month postpartum.

In addition, Pearson’s correlation analysis was performed for the relationship between EPDS and POMS-2 scores.

Since it is recommended that the EPDS score be added by even one point to determine that there is some psychological problem and that the questionnaire should be asked in detail (Japanese Society of Obstetricians and Gynecologists, 2017), a binomial logistic regression analysis was performed by dividing the EPDS score into two categories: “0” and “1 or higher.” Multiple regression analysis was performed to assess the association of maternal neurotransmitters and attributes with POMS-2 scores.

Results

For the psychological scale, the mean EPDS score was 2.9 (standard deviation [SD]=2.73). Three patients (3.2%) had an EPDS score of 9 or higher, indicating postpartum depression. Conversely, 56 patients (59.6%) had an EPDS score of 0 and 38 (40.4%) had an EPDS score of 1 or higher.
As for POMS-2 scores, the mean Total Mood Disturbance score was 42.9 (6.22), and the mean scores for sub-scales were as follows: Anger-Hostility 44.0 (5.98), Confusion-Bewilderment 44.2 (6.14), Depression-Dejection 44.6 (4.91), Fatigue-Inertia 44.1 (6.15), Tension-Anxiety 46.0 (8.22), Vigor-Activity 55.3 (8.12), and Friendliness 56.6 (7.34).

Regarding the urinary biomarkers, the mean concentrations of neurotransmitters in urine were 12.6 (8.80) µg/day of adrenaline, 121.3 (108.01) µg/day of noradrenaline, 1204.1 (1892.72) µg/day of dopamine, and 230.9 (153.96) µg/day of serotonin. As the neurotransmitter measurements were often outliers and normality was not guaranteed, they were log-transformed before analysis.

Correlation between EPDS and POMS-2 was found for TMD (.583**), Anger-Hostility (r=.574), Fatigue-Inertia (r=.501), Fatigue-Inertia (r=.406), and Tension-Anxiety (r=.453**) were the most highly correlated with EPDS (Table 2).

Regarding the effect of maternal neurotransmitters and attributes on EPDS scores, the analysis showed that only noradrenaline had a significant positive correlation with EPDS score (odds ratio [OR]=1.83, p=0.019) (Table 3).

Husband's parenting support had a significant effect on Total Mood Disturbance scores (p=0.038), husband's parenting support (p=0.039) and lactation status (p=0.016) affected Confusion-Bewilderment scores, husband's parenting support affected Depression-Dejection scores (p<0.001), and parity affected Tension-Anxiety scores (p=0.009) (Table 4).

### Discussion

#### Characteristics of the participants

The results of the EPDS in this study showed that 3.2%...
of the subjects had a score of 9 or higher which is indicative of postpartum depression as, compared to 13.7% in previous studies (Yamaguchi et al., 2017) and 8.5% in a survey by the Ministry of Health, Labour, and Welfare (MHLW, 2018a). This can be attributed to the fact that the study facilities provide psychological support to mothers, as they handle deliveries at other hospitals in cases of severe mental illness and conduct two-week postpartum checkups, which may contribute to the current low EPDS positivity rate.

The average of each item in the POMS score is between 40-59 (Juvia et al., 2012). The participants’ scores were average. Among them, the mean scores of “Vigor-Activity” scores (55.3) and “Friendliness” scores (56.6) were about 10 points higher than the other items, suggesting that the subjects in this study were a group that had a comparatively positive outlook. The reason for the stronger positive emotions is that the study facility handles low-risk deliveries, and the EPDS scores are also much lower than the national average, suggesting that this was a psychologically stable group.

Regarding the neurotransmitters, dopamine and serotonin showed slightly higher values than the standard values. For dopamine, the mean value was higher because there were more outliers than the standard deviation (±1892.73). A study by Nishiumi et al. (2012), which measured substances in urine during the first month after childbirth, also showed higher values than adult women, suggesting that neurotransmitters in mothers during the first month after childbirth are higher than in adult women. During the postpartum period, the anatomical and physiological changes that occurred during pregnancy and childbirth are restored to the pre-pregnancy state, and the mother is in the process of recovering from the invasion caused by childbirth. Therefore, assumed that the concentration of neurotransmitters in the subjects was high in this study.

**Relationship between EPDS and POMS-2 scores**

The results of the EPDS and POMS2 analyses revealed that mothers with higher EPDS scores had not only more depressive feelings, but also more feelings of “Confusion-Bewilderment,” “Fatigue-Inertia” and “Tension-Anxiety”. The symptoms of postpartum depression are similar to those of general depression, and include depression, loneliness, tension, agitation, anguish, and despondency (Kitamura, 2007). Previous studies have also revealed that women in the first month after childbirth show strong feelings of “Tension-Anxiety,” “Depression-Dejection,” “Anger-Hostility,” “Fatigue,” and “Confusion” (Kawano et al., 2012). This suggests that women are more likely to experience negative emotions in the first month after childbirth, which may result in the transition to depression. The first month after childbirth is a period when postpartum depression is likely to occur (Murray et al., 2000) and when mental health is reported to be low (Sakanashi et al., 2015). In order to prevent postpartum depression, it is important to recognize mothers’ psychological problems at an early stage and provide them with appropriate support. Even in the absence of depression, strong feelings of confusion, fatigue, and tension may serve as potential indicators of postpartum depression risk.

**Urinary biomarkers and psychological state.**

In the stress theory advocated by Selye (1978), there are three phases of stress response: the warning response phase, the resistance phase, and the exhaustion phase. During the warning and resistance phases after the stress response, the sympathetic nervous system becomes temporarily active due to the defense response, but during the exhaustion phase, the resistance decreases and mental disorders such as depression eventually develop (Selye, 1978). Depressed patients exposed to chronic stress conditions have been reported to have low noradrenaline levels (Ikuta, 2003), which may be due to a decline in the defense response caused by persistent stress and a decrease in secretion after the neurotransmitter’s regulatory function is disrupted.

In this study, an EPDS score of 1 or higher was associated with higher levels of adrenaline levels; therefore, an EPDS score of 1 or higher may be associated with a state of stress. The stress theory, postulates that depression can develop as a result of a persistent state of stress even if EPDS scores are low. If mothers’ EPDS score increases by even one point, it is necessary to check if they have any problems or concerns, and to intervene to prevent a situation of persisting stress.
Participant attributes related to mental status

Husband's childcare support. In recent years, the number of mothers without the support of biological or in-law parents has increased due to the increasing trend of nuclear families, and the participation of husbands in childcare has become important (Ministry of Health Labour and Welfare, 2018b). The higher the husband’s satisfaction with childcare cooperation, the lower the mother's sense of childcare difficulty (Fujioka et al., 2013), and lower the depression levels (Kobayashi, 2008); thus, the husband’s childcare support status influences the mother's psychological state. In the present study, it was also found that lack of husband's support was a factor that increased the mother's negative feelings. The fact that mothers have thoughts about “experience difficulties” in their daily child-rearing (Takeda et al., 2013) and seek emotional support from their husbands (Oka et al., 2019) suggests that mothers are reassured and feel supported when their husbands understand the difficulties of child-rearing and feel empowered to raise children together, rather than just mechanically cooperating with them.

Parity. In this study, first-time mothers had a higher score on Tension-Anxiety, a result similar to Kataoka et al., 2000. First-time mothers have a strong sympathetic activity index and are physically tense compared to non-first-time mothers (Izumi et al., 2015). Furthermore, they experience strong anticipatory anxiety about failing in childcare and lack confidence as mothers (Kitamura et al., 2017); moreover, in the first month after childbirth, they report significant symptoms of anxiety (Tokoro et al., 2019), suggesting that they spend the initial childcare period feeling nervous and anxious. In a previous study, baby massage in the third or fourth month after childbirth significantly lowered mothers’ own feelings of tension and anxiety (Nohmachi et al., 2013); therefore, baby massage in the first month after childbirth may lead to a reduction in mothers’ Tension-Anxiety feelings.

Lactation status. As many as 88% of mothers feel troubled by mixed feeding (e.g., using both formula and breastmilk; MHLW, 2015), and this study also found that mothers using formula milk or mixed feeding had higher scores on the Confusion-Bewilderment scale than breastfeeding mothers. This indicates that mothers using formula milk or mixed feeding experience more trouble and have stronger negative emotions than mothers that breastfeed. In Japan, support for breastfeeding is specifically offered, including providing information to families, referring them to places where they can consult, helping them build friendships (MHLW, 2019). Thus, strengthening these supports may help mothers resolve their confusion-bewilderment feelings and feel more positive about breastfeeding.

Conclusion

Urinary noradrenaline may reflect postpartum mother's psychological state. Mothers without childcare support from their husbands had higher total mood disturbance as well as Confusion-Bewilderment and Depression-Dejection scores than those with husband’s support. Mothers using formula milk or mixed feeding had higher Confusion-Bewilderment scores than breastfeeding mothers. First-time mothers had higher Tension-Anxiety scores than non-first-time mothers.

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Conflict of interest

The authors have no conflicts of interest to declare.

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産後1ヶ月の母親の心理状態と
尿中カテコールアミンおよびセロトニンとの関係

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抄録

目的
産後のメンタルヘルスにおいて、産後うつ病は重篤な有症疾患である。日本では、産後うつ病のスクリーニングにエジンバラ産後うつ病自己評価票（EPDS）の日本語版が用いられているが、リスクのあるすべての母親をスクリーニングするためにはまだ課題が残るとされている。そこで、EPDSと併用できる母親の心理状態を反映した客観的な指標を検討する必要があると考えた。本研究では、産後1ヶ月時点での母親の心理状態と尿中カテコールアミンおよびセロトニンとの関係を検討した。

方法
EPDSと日本語版POMS-2を用いて、母親の産後の心理状態を測定した。尿中カテコールアミンとセロトニンをストレス反応とつつ病の指標として測定した。背景因子は、年齢、分娩経験、分娩方法、支援状況、授乳状況であった。産後1ヶ月検診時に94人の女性からデータを収集した。

結果
尿中ノルアドレナリン値の高さは、EPDSスコアと関連していた。また、夫のサポート不足は、POMS-2の総合的気分状態【TMD】、混混乱-不安【CB】、抑うつ-不安【DD】スコアの上昇と関連していた。さらに、初産婦はPOMS-2の緊張-不安【TA】スコアが高く、混合栄養や人工栄養の母親は混乱-不安【CB】スコアが高かった。

結論
これらの結果は、尿中ノルアドレナリンが産後の母親のうつ病を反映していることを示唆している。さらに、夫のサポート、初産婦、授乳状況についての背景因子も母親の心理状態に関係することが明らかとなった。

キーワード：産後の心理状態、産後うつ病、尿中カテコールアミン、尿中セロトニン、産後1ヶ月