Journal of Affective Disorders 238 (2018) 526–533

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Involvement of prolactin in newborn infant irritability following maternal perinatal anxiety symptoms

Zhang Huiping[a], Shao Shuya[a], Su Qian[a], Yao Dan[a], Sun Hongli[b], Ding Ding[a], Dang Shaokang[a], Wang Shan[a], Zhu Zhongliang[c,*], Li Hui[a,*]

[a] Department of Neonatology, First Affiliated Hospital of Xi'an Jiaotong University, 277 West Yanta Road, Xi'an, Shaanxi 710061, China
[b] Shaanxi Institute of Pediatric Diseases, The Affiliated Children Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi 710003, China
[c] Shaanxi Province Biomedicine Key Laboratory, College of Life Sciences, Northwest University, 229 Taibai North Road, Xi'an, Shaanxi 710069, China

ARTICLE INFO

Keywords:
Newborn irritability
Maternal anxiety
Perinatal
Prolactin

ABSTRACT

Background: Newborn irritability could be an unique and special status and/or adverse neurobehavioral outcomes which was independent of serious disease. To determine whether maternal perinatal anxiety symptoms was associated with newborn irritability, and whether the alteration of serum prolactin in newborns were involved in newborn irritability.

Methods: 205 pregnant women were recruited: normal group (n = 100), and anxiety group (n = 105), which was randomly divided to Newborn Behavioral Observations (NBO) + anxiety group(n = 65) and control + anxiety group(n = 40). Newborn Irritability was assessed by Neonatal Behavioral Assessment Scale(NBAS). Serum prolactin, cortisol and 5-HT in mothers and infants were measured.

Results: 1. The scores of irritability items in the newborns of anxiety group were higher than that of the normal group ($p < 0.05$). 2. Lower serum PRL, 5-HT and higher serum cortisol were found in the newborns of anxiety group compared with that of the control group both postpartum 2d and 15 ($p < 0.05$). 3. The level of serum PRL in newborn infants were significantly and negatively correlated to the scores of irritability items ($p < 0.05$). 4. After 7 rounds of NBO interventions, the anxiety scores of mothers and the scores of irritability items of newborns in the NBO intervention group were all lower than those of the control group ($p < 0.05$) .

Limitations: In future experiments, we should explore the effect of PRL in the breast milk on newborn infant serum PRL.

Conclusions: Prolactin could be a potential mediator in newborn irritability following maternal perinatal anxiety symptoms.

1. Introduction

Newborn infant irritability was independent of serious disease and characterized by an increase in the amount and intensity of persistent and unexplained crying, diminished soothability, recurrent episodes of fussiness, and less synchrony in mother-infant interaction (Keefe et al., 1996). 15–30% of all newborns of physical health were affected by newborn infant irritability, regardless of sex, birth order, race, gestational maturity or socioeconomic status (Keefe et al., 2006). The adverse neurobehavioral outcomes of newborn infant irritability often were profoundly disturbing and suffering to the infant and parents who experience it. For example, in a longitudinal investigation, newborn irritability were related to insecure attachment in 12-month infants and less exploration and sociability in 18- and 24-month toddlers (Stupica et al., 2011). Meanwhile, irritability in little infant could result in increased parental stress because of lack of information about the cause and ineffective management strategies (Keefe et al., 2006).

The characteristics of newborn irritability may differ from that of adult irritability. Adult irritability may be a common psychiatric symptom associated with anxiety or depression. Newborn irritability could be an unique and special status and/or neurobehavioral disorders which are not associated with serious disease. It is well-known that the early neurobehavioral outcomes in infants was related to maternal emotional state (Van den Bergh et al., 2005). Maternal anxiety is generally believed to be responsible for neurobehavioral disorders in little infants. For example, it is found that maternal anxiety disorders appeared to be a robust predictor for excessive infant crying (Petzoldt et al., 2014). Studies have also demonstrated that maternal anxiety symptoms could contribute to difficulty in early regulatory ability of 3-month-old infants, decreased rates of self-comforting

* Corresponding authors.
E-mail addresses: zlzhu@xjtu.edu.cn (Z. Zhu), huili@mail.xjtu.edu.cn (H. Li).

https://doi.org/10.1016/j.jad.2018.05.080
Received 15 January 2018; Received in revised form 1 May 2018; Accepted 28 May 2018

behaviors, difficult temperament, more distress to novelty in infants, and anxiety disorders in newborns (Britton, 2011; Muller et al., 2016; Reck et al., 2013; Richter and Reck, 2013; Rifkin-Graboi et al., 2015). Given that the above behavioral disorders in little infants were risk factors for infant irritability, it seemed reasonable to assume that maternal perinatal anxiety symptoms was implicated in newborn irritability. However, little is known about the endocrine mechanism underlying newborn irritability.

Studies have shown that maternal perinatal anxiety symptoms impaired maternal care (Machado et al., 2016). In many species, the hormone prolactin (PRL) is an essential part of the neuronal and hormonal regulation of maternal care (Larsen and Grattan, 2012). The increased PRL was also essential for maintaining the pregnancy and survival of the fetus during pregnancy (Grattan and Kokay, 2008). The decreased maternal PRL was associated with low maternal care which were closely related to the adverse neurobehavioral outcomes in infants (Chokchaloemwong et al., 2015; Kaplan et al., 2008). Animal studies have demonstrated that increased anxiety in lactating female rats could be associated with reduced prolactin(PRL) level (Torner and Neumann, 2002), whereas increased PRL acting at brain level could result in the decrease of anxiety-like behavior in rodents (Torner et al., 2001). It is worth noting that the inhibition of maternal PRL level at the end of lactation could result in anxiety-like behaviors in the offspring (Fraga et al., 2011). Therefore, it is interesting to explore whether the change of maternal PRL resulting from maternal perinatal anxiety symptoms was involved in newborn irritability following lower maternal care.

One of the explanations for adult irritability were associated with excessive cortisol expression or abnormal serotonin [5-hydroxytryptamine (5-HT)] level (Melamed & Bruhis, 1996; Landen et al., 2009; Moses-Kolko et al., 2005; Salisbury et al., 2011). Meanwhile, the release and regulation of PRL was affected by cortisol or 5-HT. For example, increased PRL concentrations could contribute to ameliorate the excessive reactivity of the HPA axis and to further inhibit the overexpression of cortisol (Torner et al., 2002). Ashbury found that the drug of SSRI/ SNRIs could result in increased 5-HT accompanied by increased PRL (Ashbury et al., 2012). However, a different study showed negative correlation between plasma PRL and platelet 5-HT in women with mental disorder (Muck-Seler et al., 2004). It remains unclear how the change of PRL associated with cortisol and 5-HT in newborn was involved in newborn irritability.

There is a need to develop an effective, easily implemented intervention method to ameliorate newborn irritability resulting from maternal perinatal anxiety symptoms. The Newborn Behavioral Observations (NBO) was an infant-centered relationship-based intervention method, which has been successfully used to reduce symptoms of postpartum maternal depression (Nugent et al., 2014). Moreover, NBO would provide a excellent intervention opportunity for the professionals who are dedicated to giving newborn and parents the best possible start in life in newborn period which is an extremely sensitive stage in the transition to parenthood (Nugent, 2013).

The present study aimed to determine whether newborn irritability resulted from maternal perinatal anxiety symptoms, and whether the alteration of PRL associated with cortisol and 5-HT in infant were associated with newborn irritability; Further to explore the efficacy of the NBO in ameliorating newborn irritability following reducing maternal perinatal anxiety symptoms.

2. Method

2.1. Participants

The subjects were recruited from the hospitalized pregnant women (37–42 weeks of gestation)waiting for delivery from the department of obstetrics of the first affiliated hospital of Xi'an Jiao tong university between January 2015 and August 2017. Hamilton Anxiety Scale (HAMA) was applied to assess maternal anxiety symptoms. Normal group (n = 110) and anxiety group (n = 120) were recruited.

A total of 230 women were recruited, of whom 120 were diagnosed with anxiety group(n = 120). The number of normal group(healthy group) was 110(n = 110). Inclusion criteria were applied: 1. Mother aged 18–40 years; 2. First-time mother, full-term and singleton pregnancy; 3. The birth with no intrapartum complications; and 4. Apgar score >8 at the first, fifth, and tenth minutes after birth. Exclusion criteria were as follows: any maternal medical illness, hypertension, advanced liver disease, renal failure, cancer, valvular heart disease, heart failure, stroke, atrial fibrillation, peripheral arterial disease, and other severe diseases. Infants with congenital anomalies, signs of illness, or high-risk factors were excluded from the study. According to the willing and cooperation degree of the mother-infant dyads, the anxiety group were divided into two groups: the number of Control + anxiety group was 45(n = 45) and NBO + anxiety group (n = 75) was presented NBO video intervention before delivery, and NBO operation from 3 days to 42 days postpartum, once every week. Control + anxiety group was nonintervention. The number of women followed to 42 days postpartum was 205, for a retention rate of 89%; 15 of anxiety group and 10 of normal group were excluded because mothers did not wish to have a blood draw or their babies were bottle milk feeding. This sample of 205 women was used in the analyses reported here. There were no significant difference in demographic characteristics of pregnant women among the normal group, Control + anxiety group and NBO + anxiety group according to maternal age, gestational age, residence, education, family income, professional status and matrimonial status. (p > 0.05) (Table 1).

2.2. Procedures

The level of maternal anxiety symptoms was measured by the 14-item Hamilton Anxiety Scale(HAMA) at 4 time points: before delivery, and after 1,3,7 rounds of NBO interventions (within 3,15,42 days postpartum). Meanwhile, Neonatal Behavioral Assessment Scale (NBAS) was used to assess neonatal neurobehavioral development and newborn irritability. The investigation conformed to the Declaration of Helsinki and the protocol was approved by the Institutional Ethics Committee of the first affiliated hospital of Xi'an Jiao tong university and written informed consent was obtained from all the subjects.

2.3. Newborn behavioral observations

The NBO as a relationship-based intervention, designed to provide information and emotional support to parents, can enhance the social, cognitive and emotional development of the infant. NBO is a relationship-based, structured, neurobehavioral observation which enables infant specialists and family workers to describe and interpret newborn behavior for parents. The NBO is best done in a family context, which provides an opportunity to focus on the potential role of the infant in influencing mother, father, grandparents, neighbors or whoever makes up the informal network of relatives or friends that has an investment in the growth and well being of this new baby. The NBO operators had be trained and received a certificate from the brazelton institute of the harvard medical school. NBO operation were taken place in clinic, ward or home. During the NBO operation, mother-newborn pairs and fathers were present. Mother-newborn pairs were administered NBO operation once a week from 2 days postpartum.

2.4. Maternal and neonatal covariates

A total of 205 mother-newborn pairs were recruited, and there were normal group (n = 100), anxiety group (n = 105) randomly divided to Control + anxiety group (n = 40) and NBO + anxiety group (n = 65). Because the expression of serum PRL in newborn infant could be influenced by circadian rhythms and breastfeeding (Alvarez et al., 2006),