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REVIEW

The Role of Breast Milk in the Formation of the Newborn's Circadian Rhythm

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ABSTRACT

Circadian rhythm, also called the biological rhythm, refers to the repetition of an individual's 24-hour biochemical, physiological, and behavioral cycles. The sleep-wake cycle is the most basic circadian rhythm. The hormones that play a key role in regulating it are cortisol and melatonin. In the first years of life, breast milk plays an important role in the formation of the circadian rhythm and helps the newborn adapt to its new environment outside the womb. The composition of breast milk is quite variable, and this variability provides the baby with clues about the outside world. Breast milk secreted during the day has a high lactose content, which provides energy for the baby, improves learning ability, and quenches thirst. Breast milk secreted at night has a lower lactose concentration but higher fat and melatonin concentrations. In the case of feeding with expressed milk, the time of expression and the time of feeding should align to maintain the sleep-wake cycle.

Introduction

Breast milk is the ideal food for babies. The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) advise breastfeeding exclusively for the first 6 months. Breast milk protects babies from infectious diseases and also shortens the recovery period during illness. In addition to its short-term health benefits, it is also known to lower the incidence of chronic diseases such as diabetes, cardiovascular diseases and cancer in the long term (Italianer et al., 2020; WHO, 2023). Although the content of breast milk varies between individuals, it is influenced by pregnancy, birth, maternal and baby-related factors, chronic and environmental factors, and circadian rhythm (Moran-Lev et al., 2015; Fischer Fumeaux et al., 2019; Kiełbasa et al., 2021).

Breast Milk and Nutritional Composition

Breast milk is a unique food that meets all the energy and nutrient needs of the newborn. The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) recommend that newborns be breastfed within the first hour after birth and exclusively breastfed for the first 6 months. Breast milk meets all of the baby's energy and nutrient needs in the first 6 months of life, half or more in the second 6 months, and one-third in the second year of life. Breast milk is clean, reliable, and protects against many childhood diseases. It enhances cognitive development and reduces the risk of being overweight or obese (WHO, 2023). Breast milk contains both macronutrients and micronutrients, such as carbohydrates, proteins, lipids, vitamins, and minerals, as well as growth factors, hormones, antimicrobial

components, digestive enzymes, glucocorticoids, and many other bioactive components (Chiurazzi et al., 2021; Zielinska-Pukos et al., 2022). Breast milk contains 87-88% water. The energy value of breast milk is 65-70 kcal/100 mL. The main components that contribute to the energy value are carbohydrates, proteins, and lipids. The carbohydrate content is 60-70 g/L, protein content is 8-10 g/L, and fat content is 35-40 g/L. The main carbohydrate in breast milk is lactose. Oligosaccharides are also important components of the carbohydrate content. Casein and whey proteins (α-lactalbumin, secretory IgA and lactoferrin) are the main proteins in breast milk. The protein content is highest in the early stages of lactation and decreases as time passes. The fats in breast milk are important both for providing energy and for being integral to the structure of the cell membrane. Long-chain polyunsaturated fatty acids are essential fatty acids for babies (Stam et al., 2013; Kim and Yi, 2020). Although the content of breast milk varies between individuals, it also varies according to the time of lactation, maternal diet, and breastfeeding duration (Kiełbasa et al., 2021). Furthermore, the composition of breast milk can vary even within a 24-hour period (Mitoulas et al., 2002).

Circadian Rhythm

Circadian rhythm refers to the repetition of physiological, biochemical, and behavioral rhythms, including the individual's sleep-wake cycle, hunger and satiety, secretion of hormones such as cortisol, melatonin, and growth hormone, heat regulation, gene expression, and metabolic systems, all occurring within a 24-hour period. Circadian rhythm is controlled by the suprachiasmatic nucleus (SCN) located in the anterior hypothalamus. It can be affected by factors such as age, gender, hormones, light, sleep, and nutrition (Koçar and Elçioğlu, 2022). The sleep-wake cycle is the most basic circadian rhythm, with melatonin and cortisol playing major roles. The SCN contains melatonin receptors. Melatonin is the hormone that facilitates the transition to sleep. Melatonin concentrations are suppressed as light increases, increase as light decreases, and reach their highest levels in darkness. In contrast, cortisol is released in response to light and helps keep the body awake (Vasey et al., 2021; Koçar and Elçioğlu, 2022). The circadian rhythm begins with daylight. In the morning, cortisol is released, initiating the circadian rhythm. Approximately 30-40 minutes after waking up, cortisol levels peak, drop within a few hours, and are replaced by melatonin at nightfall. Thus, a daily cycle is completed. In adults, melatonin levels rise in the evening, peak in the middle of the night, and return to low levels in the morning, remaining low throughout the day (Adam et al., 2017; Wong et al., 2022).

The Role of Breast Milk in The Formation of The Newborn's Circadian Rhythm

The circadian rhythm begins in intrauterine life. The first report in the literature indicating that the fetus has a circadian rhythm was published in 1975 (Deguchi, 1975). Although it is believed that the sleep-wake circadian rhythm associated with cortisol develops during the first year of life, the exact timing of this development has not yet been determined (Ivars et al., 2016). It has been observed that the circadian rhythm in premature infants develops similarly to the process observed in term infants. Parallels have been found between the emergence of the circadian rhythm in premature infants and the onset of the sleep rhythm (Antonini et al., 2000).

After birth, the most important stimulating factor for the development of the newborn's circadian rhythm is daylight. However, breast milk and maternal factors also play a crucial role. The mother's activities, body temperature, and transplacental hormones such as cortisol and melatonin found in breast milk, as well as macro and micronutrients, stimulate the circadian rhythm (White, 2017). Glucocorticoids and melatonin pass from plasma into breast milk, and their concentrations in breast milk are the same as in plasma (Italianer et al., 2020). Melatonin is a transplacental hormone, and maternal melatonin production increases after the 32nd week of pregnancy. Premature babies born before this stage, without exposure to maternal melatonin, are a notable group in terms of melatonin deficiency. Circadian melatonin production begins a few months after birth, so melatonin deficiency can be seen in newborns. Some of the newborn's melatonin deficiency can be compensated by the melatonin they receive through breast milk. Melatonin concentrations in breast milk increase in the evening and decrease during the day, reflecting a regular maternal circadian rhythm. The circadian variation in melatonin concentrations in maternal plasma and breast milk influences the development and continuity of the newborn's circadian rhythm (Häusler et al., 2024).

Glucocorticoids in breast milk mainly include cortisol, cortisone (an inactive cortisol metabolite), and corticosterone (Zielinska-Pukos et al., 2022). These hormones play an important role in gluconeogenesis, lipolysis, and energy metabolism, and are produced by the adrenal glands in response to physiological and psychological stress (Pundir et al., 2019). Like melatonin, maternal cortisol levels increase in the third trimester. On the other hand, fetal adrenal cortisol and cortisone production gradually increase to prepare the fetal organs for the postpartum environment. To protect the fetus from excessive cortisol exposure, the placenta expresses the enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2), which converts cortisol to its inactive form, cortisone. In preterm infants, several factors—such as maternal obesity, postpartum stress, maternal depression, gestational age, infant head circumference, and body composition—have been associated with glucocorticoid concentrations in breast milk (Muelbert et al., 2022). Pundir et al. (2017) examined breast milk glucocorticoid concentrations over a 24-hour cycle by measuring them at four different time periods: morning, afternoon, evening, and night. According to the research, cortisol and cortisone concentrations were found to be highest in the morning and decreased throughout the day.

These findings support the circadian pattern (Pundir et al., 2017).

In addition to hormonal changes, the nutrient content of breast milk also varies between day and night. Breast milk secreted during the day has a high lactose content, which provides energy for the baby, improves learning ability, and quenches thirst. In contrast, the lactose concentration is lower in breast milk secreted at night, while fat and melatonin concentrations are higher (Sánchez et al., 2013). When the 24-hour circadian variation of breast milk was examined, it was found that the fat content was more variable compared to the carbohydrate and protein content (Moran-Lev et al., 2015; Suwaydi et al., 2023). Compared to formula feeding, the variable fat content in breast milk helps protect against obesity related to nutrition and supports healthy growth (Italianer et al., 2020). These changes in breast milk throughout the day and night also help babies develop the concepts of day and night (Aksoy and Bekar, 2023). In the expressed milk feeding method, it is emphasized that the time of milk expression and the time the baby is fed should align in order to maintain the sleep-wake cycle (Italianer et al., 2020).

Conclusion

Circadian rhythm is the regulation of biological processes that occur in a 24-hour cycle, driven by the body's biological clock. This rhythm begins to develop in the early years of life, with its foundational stages particularly established during intrauterine life. Breast milk plays a crucial role in regulating this rhythm because it helps babies adapt to the day-night cycle through the hormones, nutrients, and biological components it contains, thus supporting the healthy development of their circadian rhythms. Therefore, parents' awareness of these biological changes during breastfeeding offers a significant advantage for their babies' overall health and sleep patterns.

Declarations

Acknowledgments
Not applicable.

Conflict of Interest
Authors disclose no potential conflicts of interest.

Ethics Statement
Not applicable.

Informed Consent
Not applicable.

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Data Availability
The data used to support the findings of this study can be made available upon request to the corresponding author.

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