Breastfeeding may improve nocturnal sleep and reduce infantile colic: Potential role of breast milk melatonin

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Received: 13 October 2011 / Accepted: 13 December 2011 / Published online: 29 December 2011
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Abstract Melatonin is secreted during the night in adults but not in infants. It has a hypnotic effect as well as a relaxing effect on the smooth muscle of the gastrointestinal tract. It is plausible that breast milk, which consists of melatonin, may have an effect on improving infants' sleep and reducing infantile colic. Our first goal was to assess the differences in the prevalence and severity of infantile colic and nocturnal sleep between breast-fed infants and supplement-fed infants. The second was to characterize the profile of melatonin secretion in human breast milk compared to artificial formulas. Ninety-four mothers of healthy 2 to 4-month-old infants filled a questionnaire regarding irritability/potential infantile colic and sleep characteristics. For the second part, we measured melatonin levels in breast milk of five women every 2 h during 24 h and in three samples of commonly used artificial formulas. Exclusively breast-fed infants had a significantly lower incidence of colic attacks \((p=0.04)\), lower severity of irritability attacks \((p=0.03)\), and a trend for longer nocturnal sleep duration \((p=0.06)\). Melatonin in human milk showed a clear circadian curve and was unmeasurable in all artificial milks. Conclusions. Exclusive breastfeeding is associated with reduced irritability/colic and a tendency toward longer nocturnal sleep. Breast milk (nocturnal) consists of substantial melatonin levels, whereas artificial formulas do not. We speculate that melatonin which is supplied to the infant via breast milk plays a role in improving sleep and reducing colic in breast-fed infants compared to formula-fed ones.

Keywords Infants · Sleep · Melatonin · Infantile colic

Introduction

Infants during their first months of life may demonstrate two known nocturnal problems: infantile colic and fragmented nocturnal sleep. Infantile colic is a syndrome of excessive crying and paroxysmal irritability, usually worsening during the evening and night in infants. It is often defined by the "rule of three" crying for more than 2 h per day, for more than 3 days per week, and for longer than 3 weeks in an infant who is well fed and otherwise healthy [11]. The etiology of this syndrome is not well understood, but an acceptable theory is that the excessive crying results from hyperperistalsis and inability of the gastrointestinal system to handle gas, which leads to abdominal distention and pain [11]. Currently, there are no established risk factors or treatment and it resolves spontaneously between the ages of 4 to 6 months [11].

As for sleep, newborns sleep at random hours throughout the day and do not have an organized circadian rhythm upon their birth [8]. The consolidation of a continuous 6 h
nocturnal sleep is developed approximately between the ages of 4 to 6 months [8]. There is no consensus about the relation of breastfeeding to infantile colic or nocturnal sleep. This matter has been sparsely studied and revealed contradictory results [5, 8, 10].

An interesting fact is that the aforementioned phenomena resolve at the same age that synthesis of effective melatonin begins. An established day–night rhythm in melatonin production, as the hormone's level rise at night, can be detected around the age of 12 weeks [7].

Among the hormone's known effects are a relaxing effect on gastrointestinal smooth muscle [4] and a hypnotic effect [3]. It is plausible that maternal melatonin may pass through milk to the infant [6] and as a result the infant will have a better nocturnal sleep, earlier establishment of circadian rhythm, and decreased incidents of infantile colic.

We planned the current study in order to test this hypothesis. Utilizing questionnaires, we explored the influence of breastfeeding on infantile colic and sleep consolidation, in comparison with formula feeding. In addition, we sampled melatonin levels in breast milks and artificial formulas.

Methods

The questionnaire utilized was a one-page questionnaire, consistent of three parts: general/demographic information, questions regarding infantile colic, and questions regarding sleep. The latter two sections were quantitative questions, where the mothers were asked to rate any phenomenon on a visual analog scale. These included rating the severity and frequency of crying attacks, quantifying the total nocturnal sleep time, number of awakenings per night, and subjective estimation of wake time after sleep onset. The data were then compared between the groups using student's t test with statistical significance determined at p<0.05.

Participants were recruited in child’s health care clinics. Researchers approached mothers of 2 to 4-month-old infants. This was a convenience sample. Exclusion criteria were the usage of formula in addition to breastfeeding or mothers who switched from one method to the other and unhealthy infants (any chronic illness or disorder that could harm infants' nocturnal sleep).

The sample size was calculated based on a preliminary survey by which we expected a difference of 1.5 points in the questionnaire (in a scale of 0–10) and a standard deviation of 2 points. With a power of 0.8 and an alpha error of 0.05, the required sample size was 58 (29 in each group). In order to be on the safe side, we recruited at least ten participants over the minimum required for each group, and eventually 94 mothers answered the questionnaire. All the mothers who were approached agreed to participate and signed a written informed consent form.

For the second part of the research, we measured melatonin level in breast milk of five breastfeeding women, in samples taken every 2 h during 24 h, using ELISA. We then measured melatonin in five samples of three different commonly used artificial formulas.

Results

The most important results are presented in Table 1.

General data

Ninety-four mothers participated in the study, 54 (57%) were exclusively breastfeeding and 40 (43%) were exclusively formula feeding. The mean infant age, mean weight, and mean gestational age at birth were 2.7 months, 5.36 kg, and 39.2 in the breast-fed group and 2.8 months (NS), 5.79 kg (p<0.05), and 39.0 weeks (NS) in the formula-fed group, respectively.

Influence on infantile colic attacks

In the breastfeeding group, 56% of the mothers reported paroxysmal irritability. The mean severity, scaled on a visual analog scale from 1 to 10, in which 10 represented the most severe attacks, was 5.1, with a mean frequency of 4.8 times per week. In the formula feeding group, 72.5% of the mothers reported on paroxysmal irritability (p<0.05), mean severity was 6.4 (p<0.05), and a frequency of 5.9 per week (p<0.05).

Influence on sleeping patterns

Breast-fed infants slept for an average of 9.2 h per night compared to 8.5 h per night for the formula-fed infants (NS). The breast-fed infants aroused more times during the night (1.88 times vs. 1.49 times per night, p<0.05). However, there was no significant difference regarding the overall wake time after sleep onset.

Melatonin levels in human milk

Average melatonin concentration in the breast milk according to time of the day is presented in Fig. 1. As can be seen, there is a clear circadian rhythm of melatonin in breast milk, which was seen in all five women milks. The hormone levels in milk were undetectable during daytime hours, then elevated at night, peaking at 3:00 and then declined again. In all 15 samples of artificial formulas, there were undetectable levels of melatonin.
Discussion

Our results demonstrated a clear advantage for breastfeeding over artificial formula regarding crying attacks, suggestive of infantile colic. According to maternal reports, breast-fed infants had less crying episodes and a decreased severity when events existed.

The influence of feeding method on infants' nocturnal sleep was less dramatic. There was a trend toward longer

![Melatonin Level in Human Milk](image)

**Fig. 1** Average melatonin levels in breast milk per time of the day. A clear circadian pattern can be seen, similar to that seen in the blood, urine, or saliva

nocturnal sleep in the breast-fed group. The breast-fed infants had a more fragmented sleep as was also previously described [8, 12], but the overall duration of wakefulness at night was similar in both groups. One possible explanation is that the breast-fed infants fell back asleep faster each time they woke up, although this aspect was not assessed.

Another finding was that the formula-fed infants were heavier than the breastfed, even though age and birth weight were similar in both groups. This finding was expected based on previous reports [9]. Whether increased weight had an influence on our results remains an open question.

In addition, we found that breast milk contains melatonin in a circadian pattern, mimicking the melatonin levels in the blood or saliva [2]. The hormone levels rise at night, peak at 03:00 a.m. and undetectable during daytime, while artificial formulas do not contain melatonin.

There is a potential connection between the questionnaire results and the melatonin in breast milk. The nocturnal breast milk provides an exogenous source of melatonin which may be absorbed through the gastrointestinal tract of the infant. Based on the known properties of the hormone, hypnosis and relaxing GI smooth muscle, it is plausible that the nocturnal melatonin provided to the breast-fed infant results in reduced gastrointestinal activity and therefore less infantile colic as well as promoting nocturnal sleep. Obviously since melatonin levels in the current study were not quantified in the intestine or serum, this is a theoretical and speculative explanation. Previous studies found that melatonin is absorbed through the infant gastrointestinal tract [6] and few studies demonstrated that external melatonin added to infants' nutrition resulted in earlier development of circadian rhythm and in improved nocturnal sleep [1].
Our study has several limitations. First, there could be a selection bias. We attempted to diminish that by randomly approaching the mothers and explain the goal of the research only after they have agreed to cooperate. In addition, none of the mothers refused to participate. Another potential bias is psychosocial, such as socioeconomic status, the family unit composition etc. We have not controlled for that since we chose to minimize the length of the questionnaire. While indeed we had 100% compliance, we may have missed some worthy data. Nevertheless, all mothers were recruited at the same clinic, from the same neighborhood and we believe that this potential bias is random.

Third, our study is based on subjective reports and not on objective measurements. While there is no real objective assessment of colic, we could have studied sleep by actigraphy and believe this should be done in future studies.

Nevertheless, despite these limitations, we believe our results express a real difference and not an artifactual one and indicate that breastfeeding is associated with less colic, which may potentially result from melatonin supplied to the infant via the breast milk during the night.

More research is needed in order to fully understand the hormone's role in these nocturnal phenomena of the infant. If indeed melatonin has a meaningful role, it will encourage women to breastfeed and support the evolving concept of chrononutrition, which recognizes that the content of human breast milk is changing during the day and the artificial formulas should differ accordingly.

Conflict of interest None of the authors has any conflict of interest in this study, and there is no any commercial company involved in the current study.

References
