

Breastfeeding and Migraine: a brief review

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Abstract (Approx. 200 words)

Migraine is an important cause of disability that occurs in at least 14% of the world's population, including 212 million persons in East Asia. The aim of this review is to explore possible links between breastfeeding and reduced rates of migraine in mothers and children. Migraine episodes fluctuate with levels of sex hormones and are reduced in mothers in the post-partum period while they are lactating. The reduction may be as much as 60% in lactating mothers compared to those mothers who are feeding their infants formula. The reduction appears to be related to stabilization of estrogen levels. One large scale retrospective study (n=24011) found that there was a significant reduction in migraine episode's in children aged 3-17.

The evidence of a short-term reduction in migraine in breastfeeding mothers is of moderate strength. The link between breastfeeding and migraine in children is only suggestive. Further long-term cohort studies are required to test whether an association exists.

抄録

片頭痛は、少なくとも東アジアの2.12億人を含む世界人口の14%が抱える健康障害の原因である。本総説では、母乳育児と母親および子どもにおける片頭痛発生率の低下との可能性について探ることを目的とした。片頭痛症状の発現は性ホルモンの量で変動し、出産後に授乳を行っている母親で改善が報告されている。人工栄養を与えている母親と比較して、母乳を与えている母親における片頭痛の発生率は最大で60%まで減少する。この現象はエストロゲンの量が安定することに因るものと思われる。大規模な後ろ向き研究 (n=24,011) では、3-17歳の子どもの片頭痛症状の発現の有意な減少が報告されている。

母乳を与えている母親では、片頭痛の短期的な軽減効果を示す根拠が適度に示されていた。母乳と子どもの片

頭痛の関係は示唆できる程度であった。実際の関連性の有無を検証するためには、さらに長期的なコホート研究が必要である。

Introduction

The Drs Shozo and Aya Kagawa, founders of Kagawa Nutrition University (KNU) were pioneers in research and in the promotion of clinical and public health nutrition in Japan. They gained an international reputation for establishing nutrition as a discrete academic discipline in Japan where previously it was viewed as a part of home economics or medicine. Drs Kagawa conducted pioneering research into the B vitamins and their impact on health status as well as research from food science perspectives^{1, 2}. They established a research institute, currently known as the Institute of Nutrition Sciences (IoNS) and the KNU Nutrition Clinic to foster research activities and put research outcomes into practice. Today, KNU is taking a leading role in promotion of folate intake for the prevention of chronic health problems with understanding genetic polymorphisms of individuals³.

If Drs Kagawa had been living in the 21st century at the time of their work they would have been strong supporters of breastfeeding and its scientific value. Until the mid-20th century, breastfeeding was universal in Japan and during their lives breastfeeding, or not breastfeeding, would not have been a major issue - its importance was simply acknowledged as a matter of life or death⁴. In the last 50 years the importance of promoting breastfeeding has emerged as a major public health issue as the availability of commercial infant milk substitutes has had detrimental effects on infant health^{5, 6}. Breastfeeding substantially improves the health of infants and has beneficial effects on many long-term chronic diseases for infants and mothers, including postnatal depression and diabetes⁷. Recently there have been

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suggestions of benefits to mothers who breastfeed in reduced rates of migraine and dementia^{8,9}.

The Global Burden of Diseases (GBD) study has found that headache is a major global public health concern, one of the most important causes of disability. It is estimated that in 2016, 1.04 billion persons (95% Uncertainty Interval 1.00-1.09) or 14.4% (13.8-15.0%) of the world's population, experienced migraine headaches (GBD 2016 Headache Collaborators, 2018). Migraines affect women three times more than men^{10, 11} and are most common in women in the 15-49 year age group. The prevalence is estimated to be slightly greater in higher income societies and overall has decreased by 1.8% in the past 25 years¹². About 18% of women overall and 24% between 30 and 39 years of age suffers from migraine¹³.

Several research studies have suggested important roles for hormones in of the aetiology of migraines. Fluctuations in the levels of sex hormones are associated with the occurrence of migraine attacks. Withdrawal of oestrogen may trigger migraine pain, whereas levels of progesterone and testosterone function as suppressors as they are involved in a range of metabolic pathways that trigger inflammatory responses and the production of neurotransmitters^{10, 11, 14, 15}.

The aim of this commentary is to explore associations between:

1. Migraine prevalence in mothers who breastfeed their infants.
2. Migraine prevalence and in children who were breastfed, (or later in life in adults who were breastfed).

Methodology

A literature search was undertaken using the keywords 'migraine' and 'breastfeeding' in English, with no time restrictions, using the databases PubMed and Web of Science. A total of potential 171 references were identified after screening of abstracts for relevance, and the full texts of 74 papers were retrieved.

Migraine headaches are defined in lay terms as:

"Migraines are headaches that typically last from 4-72 hours and you may experience nausea and vomiting as well as sensitivity to light or sound. Migraine sufferers frequently report throbbing pain that worsens with normal activity." Migraines are associated with auras in some people. Auras are warning symptoms that may occur before you experience a migraine. These warning symptoms usually consist of visual disturbances such as flashing lights, or changes in smell or perception."¹⁶ The complete definitions of migraine headaches from the International Headache Society covers more than 40 pages of details¹⁷.

Breastfeeding Research -

The usual steps in understanding of causation of human conditions is to undertake observation studies, beginning with cross-sectional observations and moving into more complex cohort studies. Proposed mechanisms are usually explored in the laboratory to establish biological plausibility. After associations are proposed using the results of observational studies a randomised controlled trial is undertaken with double or triple blinding. Research into infant nutrition, especially involving breastfeeding, is more difficult because of the important ethical issues involved¹⁸. The known value of breastfeeding, and the risk of morbidity and mortality from use of artificial feeding substitutes, means that no options are available for a true control group¹⁸. Evidence must be accumulated from multiple cohort studies undertaken in different cultures and even then, it is also difficult to adjust for all potential confounding factors. The difficulties of understanding the effects of small differences in exposures in nutritional research are even more pronounced in infant feeding, as breastmilk is a living biological fluid that varies with infant age, maternal nutrition and health⁷. For these reasons the outcomes of breastfeeding research outcomes must be assessed differently to trials in clinical medicine and pharmacology. However, overestimating the benefit of increasing the prevalence or duration of breastfeeding would have no detrimental effects, compared to a new drug with potentially dangerous side effects. In the assessment of breastfeeding the large number of studies, large sample sizes and studies in many cultures increases the importance if the results of breastfeeding research and it should be ranked as a higher level of evidence.

Results and Discussion

Migraine headaches in East and South East Asia are estimated to affect 212 million persons, a significant cause of disability¹². Among females of the reproductive age, although it has been reported that migraines tend to improve during pregnancy and breastfeeding¹⁰, a minority actually worsened their symptoms^{10, 19}.

Recent studies report that migraines is a risk factor for pregnancy complications, including pregnancy-associated hypertension disorders and miscarriage, and also birth outcomes such as low birth weight, preterm birth and caesarean delivery¹⁹⁻²¹. However an earlier review suggested that there was no relationship²². Further studies are needed as the exploration of causes and the prevention of migraine may bring benefits to pregnancy outcomes.

Breastfeeding influences hormone levels and has been shown to reduce ovarian and breast cancers, which are also sensitive to hormonal changes⁶. Oestrogen secretion is stabilized during pregnancy and lactation. In addition, breastfeeding stimulates secretion of oxytocin that has been suggested to function as a potential analgesic agent for migraine²³. Consequently,

breastfeeding may be beneficial in minimizing the occurrence of migraines and associated pain. The first report in the literature summarised a series of case reports in the 1990s²⁴. There have since been several reports on associations between breastfeeding a reduction in the severity and frequency of migraine in mothers²⁵. In a cohort study of 686 mothers in Brazil, 266 were identified as migraine sufferers before pregnancy and after delivery those who were exclusively breastfeeding had a 60% reduction in episodes in the first 4 weeks after delivery²⁵. Of the mothers who were identified antenatally as migraine sufferers, of those who were exclusively breastfeeding (n=53), 32% had a migraine attack compared to 85% (n=40) in those using infant formula (n=40, $p<0.001$)²⁵.

A similar reduction was found in a cohort study of 208 mothers recruited antenatally and followed to 12 months postpartum in Japan²⁶. Of the 60 women who were identified as having migraine there was an 85% remission rate in the third trimester. In the first 6 months post-partum period the rates of migraine were 71% in breastfeeding mothers, significantly lower than the 95% in those using bottle feeding²⁶. A cohort of 96 mothers from Italy who had migraine found that at 4 weeks postpartum in the mothers breastfeeding 43% reported at least one episode of migraine compared to 100% in the mothers who were breastfeeding.

A comprehensive review of headaches, including migraine in pregnancy concluded that “most women notice their headache either go away or greatly improve in the second and third trimesters of pregnancy”²⁷. Although there is probably a reduction in migraine in women susceptible to headaches when breastfeeding it still means that many breastfeeding women will require medication and this can generally be given safely^{11, 28}.

Several studies have raised the possibility that infants who are breastfed have a reduction in migraine episodes later in life, an effect proportional to the duration of breastfeeding^{9, 29}. A large retrospective analysis of 24011 adolescents in Croatia found that 8.3% had experienced migraine headaches. There was a significant inverse correlation between the duration of breastfeeding and the prevalence of migraine^{9, 29}. However, in this study the history of breastfeeding was obtained retrospectively and as the control group was children with other types of headache there was the potential for misclassification.

Breastfeeding in infants results in changes in the microbiome which may be the mechanism for the association between breastfeeding and reduced rates of some chronic disease risk factors⁶. People who have migraine are more likely to be infected with *Helicobacter pylori* (*H. pylori*)^{30, 31}. Breastfeeding is associated with lower rates of *H. pylori* infection in infancy, but infection rates increase throughout childhood suggesting that the protective effect of breastfeeding is limited to the early years of life^{32, 33}.

Further research is required in this area, but it is possible that breastfeeding, a healthy microbiome, *H. pylori* infection and migraine in children could be associated in some way as a component of the hypothesised gut-brain axis. The relationship between *H. pylori* infection, other gastro intestinal tract (GIT) diseases (such as irritable bowel disease [IBS] and coeliac disease) and migraine, depression and other central nervous system diseases is termed the Gut-Brain axis³⁴⁻³⁶. Further research on associations may find that a possible unifying mechanism is the relationship between the composition of the microbiome and breastfeeding and central nervous system pathology.

Conclusion

Breastfeeding research is always difficult as there are many confounding factors that require adjustment. This review provides supportive evidence of a protective association between breastfeeding and migraine in mothers and the possibility that protective effects may be evident in children who are breastfed. There are several plausible biological models that support this suggestion which makes it worthy of further study. While there are many cohort studies focusing on long-term benefits of breastfeeding, few have included any neurological outcomes. As an initial step it would be useful to add questions on migraine to long-term cohort studies of breastfeeding, based on standard definitions. Strict adherence to definitions of exposure and outcome would be needed. In the meantime, there are many other good reasons to support the promotion of breastfeeding.

Conflict of Interest. The authors declare that they have no conflicts of interest to declare.

Contributions of the authors. Both authors contributed equally to this review and take joint responsibilities for the content.

Ethics. This is a literature review and no ethics approval was required.

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