Allergol Immunopathol (Madr). 2017;45(6):616–618

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

REVIEW

Is the evidence of breast feeding protection against coeliac disease real?

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Received 9 November 2016; accepted 24 January 2017
Available online 12 April 2017

KEYWORDS
Immunology;
Microbiology;
Coeliac disease

Abstract Many recent studies discredit breastfeeding protection against coeliac disease. We will try to answer the question: ''Is the evidence of breast feeding protection against coeliac disease real?''
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Introduction

Human milk is the gold standard for newborn feeding.[1] Recommendations on breastfeeding (BF) have been updated.[2] However, a recent study revealed no significant effect of BF vs. no BF on coeliac disease (CD) risk with substantial heterogeneity (I^2 = 92%) among studies.[3] Another recent study revealed that there are no BF evidence-based criteria in order to prevent CD.[4] Our aim was to approach the protective effects of BF on CD risk.

Clinical approach

Better long-term health after BF was observed in CD.[5] Two effects of BF were also observed: delaying the introduction of gluten and increasing the latency time between gluten introduction and onset of CD.[6] When gluten is introduced in small doses during the BF period, CD prevention was obtained.[7] Fewer studies investigated the impact of BF on CD.[8] Breastfeeding offered a degree of protection against the early development of CD, but without reducing the incidence of CD.[9] An interesting study about BF in mothers who smoked revealed that alimentation based only on breastfeeding among smoking-mothers lowered the odds-ratio for CD, however due to the small number of CD children, further studies are needed.[10] A meta-analysis showed that the risk of CD was significantly reduced in infants who were BF at the time of gluten introduction compared to infants who were not BF during this period.[11] Breastfeeding at the time of gluten introduction delayed the appearance of CD[12] and was the most significant variable in reducing the risk.[13] Gluten was recommended to be introduced while the infant is still being BF.[14] Therefore, the role of BF during the weaning practice was increased.[15] Finally, a recent study demonstrated that BF during gluten introduction had a protective effect.[16]

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http://dx.doi.org/10.1016/j.aller.2017.01.005
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Immunological approach

T and B lymphocytes, some anti-inflammatory factors, cytokines and growth factors found in milk might direct the immune system of the infants.[17] Therefore, the milk may actively stimulate the immune system of the offspring via transfer of anti-idiotypic antibodies and lymphocytes. This may explain why BF diminishes the risk of developing CD.[18] Furthermore, enhanced humoral response in CD emerging not only to gliadin, but also to other food antigens is associated with CD.[19] Breastfeeding might have a positive immunomodulatory effect on lymphocyte subsets in infants at risk of CD.[20] Analysis of human milk has described the presence of gliadin, as well as soluble maternal semi-allogeneic HLA molecules. These proteins are antigens involved in the pathogenesis of CD.[21]

Another interesting interaction was found between CD and intestinal microbiota. Intestinal dysbiosis could promote an abnormal response to gluten in predisposed individuals.[22] However specific bacteria could play a protective role in CD patients by modulating immune responses to gluten.[23] It was also demonstrated that probiotic administration reduced molecular mucosal inflammation by downregulating the cytokines involved in CD pathogenesis.[24]

Relation between HLA and microbiota

Breast milk has a variety of non-digestible oligosaccharides. That stimulates *Bifidobacterium* spp. and *Lactobacilus* spp. development, which are considered to be health-promoting bacteria.[25] Environmental factors such as early feeding practices, infections, and alterations in the intestinal microbiota composition other than gluten might play a role in CD development.[26,27] Infections and antibiotic intake in the first four months of life are the early environmental factors strongly and/or frequently associated to lymphocyte subpopulations and microbiota composition, respectively, in infants at risk of CD.[28] The type of milk feeding and the HLA-DQ genotype also influence the colonisation process of *Bacteroides species*, and possibly the CD risk.[29] The combination between HLA-DQ allele and the milk-feeding type in infants has an impact on the subsequent gut colonisation. Therefore, BF has a protective role in CD pathogenesis due to facilitation of the gut colonisation of *Clostridium leptum*, *Bifidobacterium longum* and *Bifidobacterium breve* in infants with HLA-DQ genotype. There was a strong relationship between the type of milk used in infants and the gut colonisation: in breast-fed children, a higher number of *Clostridium leptum* was found, while in the formula-milk fed children *Staphylococcus* spp. and *Bacteroides fragilis* spp. were more abundant.[30] The high-risk HLA genotype has the most influence on CD onset.[31] The breast milk of CD mothers has a reduced amount of protective factors such as: TGF-β1 and sIgA and bifidobacteria, resulting in a diminished protective role of BF in groups that are at risk of developing CD.[32] Furthermore, a strong correlation was found between the maternal coeliac disease and its development in offspring.[33]

Optimal management of milk-feeding in genetically susceptible infants is not known.[34] The optimal amounts of gluten to be introduced at weaning is also not known.[35]

Conclusion

Some evidence for the protective role of BF in CD was found. HLA screening in infants is required for high-risk HLA genotype detection in CD. Further studies on BF and CD in order to develop future intervention strategies are necessary.

Conflict of interest

None.

Ethical disclosures

Confidentiality of data. The authors declare that no patient data appears in this article.

Right to privacy and informed consent. The authors declare that no patient data appears in this article.

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this investigation.

Acknowledgements

The first author received a grant from the University of Medicine and Pharmacy ''Iuliu Hațieganu'' Cluj – Napoca 2016, project no. 4995/21/08.03.2016.

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