

DEHYDRATED INFANT FORMULAS - A SAFE WAY TO FEED? SCOPING REVIEW

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Abstract: Goal: To map the evidence/literature regarding the presence of microorganisms with pathogenic potential in cow's milk-based dehydrated infant formulas, **Methodology:** A Scoping Review was carried out to answer the question - "Can the correct preparation, handling and administration of dehydrated infant formulas contribute to reducing the risk of disease associated with these by contamination?" The research process took place in March and May 2021, using the b-On and EBSCO databases, having been used as Descriptors in Health Sciences [DeCS], 2019 edition, "infant formula", "cronobacter sakasakii" and "breast milk substitutes". As inclusion criteria we defined: articles from nursing disciplines, articles from auxiliary medicine, nutrition, dietetics, health and medicine. Articles with full text available, regardless of language, peer-reviewed, published from January 2016 to May 2021 and addressing the presence of Enterobacter Sakasakii. After the analysis process, 4 articles were selected. **Results:** From the analysis of the selected studies, we found that the presence of microorganisms of various types is a reality in FDL, and these products are not sterile. We also found that these microorganisms can be associated with different types of diseases, so the correct preparation, handling and administration is essential to reduce this type of occurrence. **Conclusion:** The application of correct measures and procedures to be adopted in the preparation, handling and administration of this type of food are recognized as determining factors in reducing the incidence of pathological situations associated with FDL. Thus, it is imperative that health professionals have this knowledge, in order to train and guide providers of care for infants fed with FDL, for correct preparation, handling and administration. This guidance must be given from the time an FDL is first administered. Research and health education

in the area of food and nutrition is therefore essential. This effort must be essential to promote specific training on infant feeding using FDL, thus increasing the safety of this form of feeding. It is expected that knowledge and the adoption of health education practice will contribute to health gains, reducing the incidence of pathological situations associated with FDL and, consequently, the health costs inherent to these situations.

Keywords: Infant formula, Cronobacter sakasakii, Breast milk substitute.

INTRODUCTION

The World Health Organization [WHO] recommends the initiation of breastfeeding in the first hour of life, and must be maintained exclusively until six months and extended until two years of age together with complementary feeding. According to the breastfeeding manual of the United Nations Children's Fund (UNICEF) "breast milk is a live, complete and natural food, suitable for almost all newborns, with rare exceptions." ⁽¹⁾.

Exceptional situations for breastfeeding require an adequate response aimed at satisfying this basic need for the infant's life, which may be temporary situations or definitive situations. In addition to these situations, the mother's refusal to breastfeed, not being a contraindication, expresses a desire and materializes in an impediment to the breastfeeding process. Levy & Bértolo safeguard this fact "We cannot and must not blame a mother who does not want or cannot breastfeed, providing in these cases the appropriate advice for the practice of feeding with artificial milk" ⁽¹⁾.

The use of dehydrated infant formulas (FDL) is presented as a solution, however the FDL are not sterile products, and their correct preparation, handling and conservation are crucial for the success of feeding using these products. The European Society of

Hepatology, Pediatric Gastroenterology and Nutrition (ESPGHAN, 2004), alerts to the fact that dairy products constitute an excellent medium for the multiplication of bacteria with pathogenic potential, noting that the preparation and handling of infant formulas can constitute a high risk for infants ⁽²⁾. The W.H.O. reinforces this idea by stating that, “even when present in dehydrated formulas at very low levels, the inadequate preparation and handling of reconstituted PDF provides ideal conditions for the multiplication of these pathogenic organisms, which substantially increases the risk of infection” ⁽³⁾.

Turck, (2012) states that “Safe infant feeding the production of microbiologically cleaner IF by industry, and both education and support for the caregivers in preparing and handling the formula” ⁽⁴⁾. Corroborating what the WHO, in collaboration with the Food and Agriculture Organization of the United Nations, defend when they elaborate a manual of good practices that aims to provide specific guidelines on the most appropriate practices in the different stages of preparation of the LDF, as well as the care of hygiene to have with the necessary utensils for the preparation of this type of food. This manual arises from the WHO finding that “(...) many people who prepare PDF (both the general public and healthcare professionals) are not aware of the risks associated with this product, nor are they familiar with the best practices for its reconstitution” ⁽³⁾.

The Royal College of Nursing (RCN) recognizes the importance of parents or caregivers receiving support and information for successful and safe FDL feeding. It emphasizes that nurses are the professionals who must help and support families in their decision-making regarding the feeding of their babies, for this “Nurses need to have knowledge and skill with regard to the safe preparation and storage of formula and

(...) have a good knowledge of the different formulas available and the different situations in which these may be used” ⁽⁵⁾. It reinforces that nurses have a duty to support parents in their decision regarding how to feed their baby “Parents have a right to choose how to feed their baby and nurses knowledge of different formulas can help families to make a suitable choice” ⁽⁵⁾.

It is our objective to map the evidence regarding the real presence of microorganisms with pathogenic potential in PDF, namely *Enterobacter Sakasakii* also called *Cronobacter* spp, and to alert to the central importance of the correct preparation, manipulation and conservation of this form of feeding with the objective of contributing to the decrease in complications associated with this type of food in infants. The search for this information aims at the inclusion of a safe and responsible clinical practice, to adequately respond to situations of infants fed using PSE, transmitting to care providers the necessary information for the safe preparation and administration of this form of feeding, as recommended. by the WHO.

METHODOLOGY

In order to obtain an answer to our research question, we developed the research strategy. As the objective of Scoping Review, we defined to map the evidence/literature concerning the real presence of the microorganism with pathogenic potential. We define the research question using the PICO method:

P- Population (infants); I- Intervention (strategies to be adopted in the preparation, handling and administration of dehydrated formulas for infants) C-Concept (decreased risk of disease); O-Outcome (reduction of contamination). Therefore, the following Review question came to us: “Can the correct preparation, handling and administration of dehydrated infant formulas contribute to

reducing the risk of disease associated with these by contamination?”

As inclusion criteria, we selected articles with full text available and publication date from January 2016 to May 2021, in order to maintain the rigor and scientific updating of this Scoping Review. Articles whose theme was not relevant to the review in question, articles without scientific methodology and Systematic Literature Reviews were excluded. In order to answer the research question, we carried out an electronic search in two recognized databases: EBSCO and B-On, using the DeCS, we selected as keywords: “infant formulas”, “cronobacter sakazakii” and “milk substitutes”. maternal”, using the Boolean operator “AND” to combine the search terms. The search was carried out applying inclusion and exclusion criteria from March to May 2021. We obtained a total of 4 articles, in English.

We excluded repeated articles in both databases as well as articles that addressed FDL that were not based on cow's milk and proceeded to the analysis of their relevance, by reading the title, abstract and, whenever necessary, reading the full text. After applying the defined exclusion/inclusion criteria, we selected 4 articles for this Scoping Review.

RESULTS

In the research we obtained the following sources of evidence, the first article selected, is from 2020 and is authored by Elkhawaga, A. ; Fetta, H.; Osman, N.; Hosni, A. & El-Mokhtar, M., has a category of Q8, The objective is to analyze the relationship between cases of neonatal sepsis caused by cronobacter spp and its presence in water, food and PDF and medicinal herbs collected in the city of Assiut,. In this study, the phenomenon of interest was the search for cronobacter spp in blood samples collected from hospitalized neonates with confirmed sepsis and the relationship

with the presence of cronobacter spp in 12% of the analyzed FDL. As a final result Cronobacter spp was detected in 12 out of 100 cases of neonatal sepsis. The organism was also isolated in FDL, herbs and water in the following percentages of 17.5, 9.2 and 7.5%. Regarding antimicrobial sensitivity, all strains were resistant to ampicillin, amoxicillin, ampicillin/sulbactam, clindamycin, cephalothin and cephalixin. In addition, they showed the ability to form biofilms, but with varying degrees of cell density. This study proved to be important for research as cases of neonatal sepsis caused by the emerging pathogen cronobacter spp were reported for the first time in Egypt. The organism has also been detected in contaminated PDF, herbs and water, which can be sources of infection for neonates, especially in countries where natural herbs are widely used as alternative medicine.

The second article selected from 2018 and authored by El-Zamkan, M.& Mohamed, H., presents a category of Q8, Its objective is to analyze in the laboratory the presence of Cronobacter spp and other closely related species in PDF and powdered milk. In this study, the phenomenon of interest was that formulas acquired in local markets in Qena, Egypt and transported to the laboratory in the original packaging for further analysis. As a result, 10 isolates were obtained from 60 PDF samples and milk powder samples (30 samples each). According to phenotypic identification, these isolates were classified into six genera-related A – F biogroups: Enterobacter spp., Klebsiella spp., Citrobacter spp. And Escherichia spp. Five groups of them (A – E) obtained from samples of PDF and the last one (group F) obtained from samples of powdered milk. This study proves that PDF samples can be contaminated with opportunistic pathogens and that when reconstituted they are nutritious and become fast growing media

when water, temperature and growth time are favorable. It refers to the need not to focus only on salmonella and cronobacter spp, although they are the agents with the greatest pathogenic potential, especially for newborns and preterm infants.

The third study from 2016 is by Silano, M.; Paganin, P.& Davanzo, R. and presents category Q6. Its objective is to reinforce the use of water at a temperature of “70 °C” in the PDF dilution, in order to prevent contamination and growth of cronobacter spp. The phenomenon of interest in this study was Reinforcement of the importance of good hygiene practices when preparing PDF and benefit of using water at 70°C.

It is concluded that cronobacter spp. It is relatively heat resistant and can survive after pasteurization. There is broad consensus in the WHO/FAO guidelines on the need for immediate use after PDF preparation or storage at a temperature below 5°C. Despite current controversies over FDL dilution, current scientific evidence suggests a precautionary approach. Therefore, it is advisable to use warm water at “70 ° C” for the dilution of PDF, especially in the feeding of premature and low birth weight babies.

Finally, the fourth article of 2020 by Parra-Flores, J.; Maury-Sintjago, E.; Rodriguez-Fernandez, A.; Acuna, S.; Cerda, F; Aguirre, J. & Holy, O. Presents category Q8. Its objective is to evaluate the presence of Cronobacter spp, determining the microbiological quality of PDF for infant consumption and the resistance of this microorganism to antibiotic therapy. His phenomenon of interest was the samples of formulas for preterm infants, infant formulas and follow-up formulas from brands sold in Chile from 4 countries (Chile, Mexico, Holland and Brazil). All analyzes were triplicate. The authors concluded that the rehydration of this product makes it an excellent medium for the growth of pathogenic

agents, and contamination may occur during its preparation, storage and refrigeration, or permanence in bottles for a period longer than two hours. Risk reduction mainly depends on temperature and preparation time, very important factors to consider when rehydrating PDF for hypersensitive children to prevent future disease incidents.

DISCUSSION

The three studies included in this Scoping Review took place between 2016 and 2019 and were published between 2016 and 2020 as well as the expert opinion article, making a careful presentation of their objectives, methodology used and study participants. Regarding the place where the studies were carried out, its incidence in South America was notorious (two studies), of which only one was carried out in Egypt. Although they can also focus on other dairy products, all studies analyze the presence of microorganisms with pathogenic potential in PDF.

The expert opinion article, published in the Italian Journal of Pediatrics, provides an overview of the situation regarding cronobacter spp in Europe and the United States of America (USA), also referring to the importance of adopting the recommended measures. by the WHO. It is known that infections by cronobacter spp. are underreported, and it is estimated that the real number is much higher than the known. According to Silano et al. (2016), most reported cases are from five countries, USA, UK, France, Belgium and Philippines. As the production of this food is industrially manufactured and exported internationally, it is clear that there will be countries where these infections occur, as in the aforementioned countries, but these are not properly associated as a consequence of cronobacter spp. or are not notified⁽⁶⁾. According to Lepuschitz et al. (2019), cited by Elkhawaga et al. (2020) “ (...) a low *C. sakasakii*

frequency, where only 11 of the 24 (45,8%) participating countries in Europe submitted *C. sakazakii* isolates, which was attributed to the imperfect detection system”⁽⁷⁾

Thus, taking into account the results of the included studies, we can see that the presence of microorganisms with pathogenic potential is a reality in LDF, and is often devalued through the adoption of procedures that do not safeguard this issue. It is also verified through them that the sterile production of these products would be the ideal solution, however the same is not possible industrially.

Although two of the three studies included directly focused on the microbiological quality of PDF, the third on the relationship between newborns with sepsis and the presence of *cronobacter* spp. in FDL and other products, the three concluded that the adoption of measures that aim to reduce contamination during the preparation, handling and administration process are the best way to reduce the risk of infection by *cronobacter* spp. and other microorganisms with pathogenic potential, as well as the preparation with water at about 70° C, the expert article reinforcing this WHO recommendation.

For Elkhawaga et al. (2020), it is clear that *cronobacter* spp. it is an opportunistic pathogen and a cause of great concern, especially for preterm infants, not only in developing countries, but throughout the world. According to the results obtained in this study, of the 100 blood samples collected, 12 were positive for *cronobacter* spp, which translates into a total of 12% of the samples.

⁽⁷⁾. Parra et al. (2020) reinforce that the mortality associated with this microorganism can range from 15% to 25%, in the case of preterm newborns, due to sepsis and neonatal meningitis, and it is known that the consumption of contaminated PDF is the main form of contamination.. They also warn that the WHO recommendations on the temperature

of water preparation and the storage of PDF at less than 4° C when already prepared are undervalued, representing an increase in risk⁽⁸⁾. The US Center for Disease Control (CDC) also warns of the harmful effects that *cronobacter* spp. may have in newborns and preterm infants, “*Cronobacter* bacteria can cause severe blood infections or meningitis. Infants of 2 months of age and younger are most likely to develop meningitis if they are infected with *cronobacter* bacteria. Infants born prematurely and those with weakened immune systems are also at increased risk for serious *cronobacter* infections”⁽⁹⁾.

Parra et al. (2020) also draw attention to the absence of this information on the label of FDL in Europe, which is also mentioned by other authors. For the authors of this study, there is no doubt that the reduction in the risk associated with this food is dependent on the temperature of the water when preparing the PDF, the preparation time and the storage temperature of this food after rehydration. Elkhawaga et al (2020) also point out that a collective effort by parents, health professionals and PDF production plants is necessary to prevent serious infections caused by *cronobacter* spp.

Also in the study carried out by El-Zamkan & Mohamed (2018), the presence of *cronobacter* spp. in FDL and other opportunistic pathogens, alerting the authors to the fact that in addition to *cronobacter* spp. and salmonella, the most dangerous pathogens in FDL according to the W.H.O., other agents also represent a danger essentially for newborns and preterm infants. They thus argue that more than focusing solely on reducing contamination during production, it is necessary to reinforce sanitary measures throughout the entire manufacturing process and reconstitution of PDFs before their administration.⁽¹⁰⁾. The authors caution that these are processes of complementary

importance, their importance not being superimposed on each other, and the WHO guidelines on this issue must be followed.

CONCLUSION

The W.H.O. (World Health Organization) recommendations are assumed as well as the best practices to be adopted. The RCN points out that inappropriate practices pose serious risks to infants “(...) unhygienic preparation of equipment, reconstitution, storage and administration of feeds may result in a risk of infection, dehydration, malnutrition and hypernatraemia.” (RCN 2016, p. 9).

Even so, the WHO recommendation regarding the water temperature for the preparation of PDF, around 70°C, is contested by ESPGHAN considering that a temperature close to the boiling point can have adverse effects on some nutrients present in the formulas, such as vitamins.

However, in addition to correct hand hygiene, of all materials, and of the formula preparation surface, this procedure is proven to be extremely important in the prevention of infections by *Cronobacter* spp. The Centers for Disease Control and Prevention (CDC) points out that “*Cronobacter* infections are rare, but they can be deadly in newborns. (...) Infants 2 months of age and younger are most likely to develop meningitis (...) Other infants more likely to get sick are those born prematurely and those less able to fight germs and sickness...⁽⁹⁾”. Thus, in order to prevent infection by this microorganism, the CDC also recommends that the formula be prepared with water at about 70°C, which is expected to be the temperature 30 minutes after the boiling point, which is also recommended by the WHO. and by the RCN Allow the boiled water to cool to no less than 70°C. (...) this means using water tha has been left covered for less than 30 minutes after boiling...⁽⁹⁾.

As PSFs are not sterile products, and are subject to contamination that can occur from the production process to the moment of administration, nurses play a decisive role in the success of feeding using this food, through teaching and safe practices. according to WHO recommendations. We conclude that only through raising awareness of the adoption of these measures and their correct implementation is it possible to reduce the risk of infection associated with these foods. Bearing in mind that there are several contaminating agents, these measures act not only to prevent contamination by *Cronobacter* spp., but also to prevent contamination by other agents with pathogenic potential.

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