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Breastfeeding Situation in Saudi Arabia and Recent Approaches in The Development of Follow-on Formula for Facing Breastfeeding Difficulties

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ABSTRACT

Infant formulae are an alternative to breastfeeding for many parents, despite breastfeeding providing all of the benefits for an infant. In cases where breastfeeding is not possible, infant and follow-on formulas should be recommended. It is well known that the compositions of cow milk proteins are very different from human milk and infants do not tolerate it.Unfortunately,the majority of follow-on formulae are formulated on the basis of using cow milk whey in their composition. So, many researchers suggested the use of goat or camel milk fractions as a base for making infant formulae.On the other hand, efforts made by researchers for the valorization of milk whey revealed that using camel or goat whey in infant feeding has great benefits for increasing the nutritional and biological values and digestibility of milk proteins. Also, fermented formulae are recommended for infants since they promote digestibility and tolerance and are considered safe for infants. Therefore, using lactic acid bacteria to produce fermented and/or acidified infant milk formulae has been recommended by many researchers.This review is mainly focused on the importance of using follow-on formulae for feeding newborns when breastfeeding is not an option. As well, the review presents the approaches that have been used to prepare different follow-on formulae based on the use of different milk types to provide nutritional and functional properties as close as possible to human milk. Also, proposed recent trends for improving the nutritional value of formulae to narrow the gap between using regular formulae and infant's needs are shown.

Keywords: breastfeeding, follow-on formulae, Whey, cow milk, camel milk, goat milk

INTRODUCTION

Mother's milk is known to be the best nutritional choice for a newborn. As the infant's digestive system is compatible with human milk as it contains bioactive components important for gut microbial colonization and immune maturation, it reduces the risk of gastrointestinal and respiratory infections. Human milk also has numerous factors that protect the infant against atopic disease. Nevertheless, breastfeeding cannot always be accomplished (Drapala *et al.*, 2016 and Huet *et al.*, 2016).

For children who have not received breast milk for more than six months, the follow-on formula becomes the only option for infant feeding. This was the major problem in urban areas worldwide and in Saudi Arabia as well. Consequently, in those situations there is always a strong need to develop alternative sources of mother's milk (Alyousefi *et al.*, 2017; Khresheh and Ahmed, 2018 and Alsulaimani, 2019).

Human milk has been substituted with cow milk formulas for infants and toddlers. The use of it for infant feeding has however caused many nutritional issues, especially in the form of cows' milk protein allergies and symptoms of gastrointestinal discomfort in infants. (Pescuma *et al.*, 2012; Martin *et al.*, 2016; Talarico *et al.*, 2019 and Ye *et al.*, 2019). The hydrolyzed and fermented cow milk-based infant formulae that contain live probiotic bacteria or those that do not contain live bacteria have become a good option to overcome the health problems associated with regular formula feeding (Martin *et al.*, 2016 and Szajewsk *et al.*, 2015).

Camel and goat milk is more similar to human milk in composition than cow milk, thus infant formulas that use these protein sources are healthier and more digestible for infants as they provide a suitable source of protein. (Biadała *et al*, 2020; Galdino *et al.*, 2020; Jrad *et al.*, 2020; and Oussaief *et al.*, 2020).

Recently, cheese whey has attracted consumers as well as nutritionists because of its health benefits. Thus, the value of this highly nutritious and immune-boosting by-product was realized by using it as a base for infant feeding, helping to solve problems associated with the use of cow milk-based formulas (Galdino *et al.*, 2020 and Osman *et al.*, 2015).

Due to this, the focus of this review is on the use of infant and follow-on formula to feed newborns when breastfeeding is neither possible nor feasible. As well, the review presents the approaches that have been used to prepare different follow-on formulae that are based on the use of cow milk and other species existing in the Kingdom of Saudi Arabia (goat and camel) to provide nutritional and functional properties as close as possible to human milk. Furthermore, recent trends for improving the nutritional and biological value of formulas have been reported to narrow the gap between regular infant formulas and infant needs.

Breastfeeding

Breastfeeding in Saudi Arabia

It was reported that only 13.7 % of infants were exclusively breastfed in a study on 322 Saudi mothers that

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have been done by Alyousefi *et al*. (2017) who examined the possibility of exclusive breastfeeding for the first six months of life. Previously, data collected from some Saudi mothers by Al Juaid *et al.* (2014) showed that Insufficient breast milk, maternal or child diseases, pregnancy or lactation problems are the main reasons for the decline in breastfeeding and the use of compound formulas. In addition, it has been reported that stopping breastfeeding is a reason for low breastfeeding self-efficacy among Saudi mothers. (Khresheh and Ahmed, 2018). In addition, lack of support was cited as one of the most important reasons for low rates of exclusive breastfeeding, alongside a variety of biological (e.g., chronic disease and obesity) and cultural factors (Alsulaimani, 2019).

Importance of breastfeeding

Suboptimal nutrition or inadequate nutrition during an infant's early life has serious consequences (Martin *et al*., 2016). Breast milk is the exclusive natural fluid that provides the newborn with the essential nutrients and requirements for development and growth, protecting it from disease while its own immune system matures. (Zou *et al*., 2017). In the same regard, the World Health Organization (WHO) has recommended that the exclusive breastfeeding should be applied throughout the first six months of newborns (Owens *et al*., 2013 and Gallier *et al*., 2015). The beneficial results of breastfeeding are limitless for both infants and nursing mothers (Alyousefi *et. al.*, 2017), the environment, economy and the entire society (Al Juaid *et al*., 2014) and certainly accounts for developing strong bond between the mother and her baby (Khresheh and Ahmed, 2018). The composition of breast milk is the perfect reason for minimizing the risk of gastrointestinal and respiratory infections (Drapala *et al*., 2016) and is compatible with the infant's digestive system as it contains bioactive components necessary for microbial colonization of the intestine are important. and immune maturation (Huet *et al.*, 2016). In addition, gut health at a young age has been shown to have fundamental aspects of psychosocial, physical and mental well-being (Vandenplas *et al*., 2017) and the protective role in hypertension (Sharmin *et al*., 2016) in later life. Reduced risk of obesity and metabolic diseases has also been observed in children who were exclusively breastfed for the first few years of life (Gallier *et al*., 2015).

Difficulties facing breastfeeding

Although it is well known that breastfeeding is the preferred food source that provides essential nutrients for growing babies (Owens *et al*., 2013), global breastfeeding rates are not only declining in Middle Eastern countries (Alyousefi *et al*., 2017) and the Arab world (Alsulaiman, 2019), but also in urban areas around the world (Sulaiman *et al*., 2016). Only 39% of infants under 6 months worldwide are exclusively breastfed (Mosquera *et al*., 2019), while no more than 15% can be continuously breastfed with complementary foods for up to two years, according to WHO recommendations (Saffari *et al*., 2017). Delivery mode, socioeconomic level, primiparity, early pregnancy, insufficient inter-pregnancy gaps, and lower maternal education have been reported to be the major contributors to changes in breastfeeding before the baby is six months old (Saffari *et al*., 2017). The same trend is also found in Arab countries and Saudi Arabia (Alsulaimani, 2019). Regarding working women in urban areas, Sulaiman *et al*. (2016) reported that women without the support of their families and husbands were less likely to exclusively breastfeed after returning to work than women with supportive families.

Infant and follow-on formulae

If a mother is unable to breastfeed her baby for one or more of the above reasons, a formula should be used instead (Zou *et al*., 2017). As seen in Table (1), if infant formula becomes an option to replace breastfeeding, much effort must be made to closely mimic the nutritional profile of human breast milk for normal infant growth and development (Martin *et al*., 2016). According to Codex Alimentarius and European Commission regulations, the levels of macronutrients and micronutrients in infant formula must be specified to simulate the composition of breast milk (Oussaief *et al*., 2020). Formula composition and functionality must include and balance protein content and profile, i.e., predominant whey protein profile and α-lactalbumin fortification; the profile of fatty acids, the content of carbohydrates, vitamins and minerals with those in breast milk (Drapala *et al*., 2016). Martin *et al*. (2016) reported that cow's milk-based formula; soy-based formulas and speciality formulas are the three main classes of infant formula, which differ in nutritional value, taste, calories, digestion, and cost.

Table 1. Chemical composition of different based infant formulas

Different based infant formulas	Purpose	Energy (kcal)	Intact protein (g)	Whey protein hydrolysate (g)	Fat (g)	Lactose (g)	References
Normal-infant formulas	when exclusively breastfeeding is not possible and for protein allergy management						
Cow milk based infant formulas		66	1.4	-	3.5	7.0	Karaglani *et al*., 2020
Goat milk based infant formulas		66.5	1.3	-	3.5	7.5	Wood *et al*., 2022
Cow-whey based infant formulas	To reflect the 60:40 ratio of human milk instead of 20:80 in cow's milk	65.5	1.4	-	3.4	7.2	Wood *et al*., 2022
Cow-fermented infant formulas	To prevent or relieve gastrointestinal symptoms	68	1.4	-	3.1	6.5	Beghin *et al*., 2020
Cow-hydrolyzed infant formulas	Protein allergy management	66	-	1.6	3.5	7.0	Karaglani *et al*., 2020

Cow milk as a base of infant formula

Most commercial infant formulas are made from cow's milk after it has been modified to provide quality nutrition for newborns. However, milk derived from cow's milk has a higher protein content, a different ratio of whey protein to casein than human milk, and different proportions of casein and whey protein (Ye *et al*., 2019). Due to the early introduction of cow's milk into infant diets, allergic reactions begin very early in infants' lives, as cow's milk is considered one of the most common causes of food allergies

(Martin *et al*., 2016). The cause of allergy problems, especially when infants are fed cow's milk, is that pepsin does not break down the protein (Pescuma *et al*., 2012 and Talarico *et al*., 2019).

Hydrolyzed infant formula from cow milk

Milk hydrolysates have received particular attention due to the antioxidant activity of milk protein hydrolysates and their released peptides after hydrolysis which was known for its benefits to promote human health (Virtanen *et al*., 2007). The use of enzymes in preparing pre-hydrolyzed milk has been applied as one of the important strategies to prepare protein hydrolysate formulae for infants who are unable to tolerate cow milk formulae (Martin *et al*., 2016).

Fermented infant formula from cow milk

The definition of fermented Infant and follow-on formulae means the formula fermented with lactic acid bacteria during the production process, with no significant amounts of viable bacteria in the final product (Heijning *et al*., 2014). While the remaining bacterial components and the effects of bacterial metabolites after fermentation are the sources of additional benefits of such formulas (Szajewsk *et al*., 2015). In this concern, the bacterial metabolites which have been revealed after fermintation are considered to have probiotic effects on infant health although the bacteria itself is no more available (Labuschagne *et al*., 2013). The fermented infant formulae have been used successfully to prevent or relieve gastrointestinal symptoms in infants (Heijning *et al*., 2014).

Infancy is a crucial time for gut development. The digestive system enables the body to absorb nutrients and fluids, encouraging growth and development. As a barrier against infectious agents as well as stimulating the immune system to establish mucosal and systemic tolerance, the gut plays a crucial role in the initiation of immunity. Also, the gut acts as a sensor for the brain to maintain its balance. The healthy development of the gut is related to the intestinal microbiota formed in the early years of human life especially when breast milk is exclusively offered as a sole source for feeding babies in the first 3 months of life. In contrast, the increase in allergy prevalence can be attributed to the early intestinal dysbiosis related to the imbalance of healthy gut microbiota. Therefore, breast milk has the potential to act as a natural synbiotic, as the bacteria in breast milk contain both prebiotics and probiotics that support the intestinal flora, intestinal barrier, and immune system. Infant formulas must offer nutritional solutions to infants unable to receive enough mother's milk, so it is without a doubt breast milk is the only acceptable model to be simulated when infant formulas are reformulation. So, infant formulas that mimic human milk must contain an array of ingredients reflecting recent developments, such as oligosaccharides, bacteria, and bacterial metabolites. Thus, scientists don't stop trying to promote the development of beneficial microbiota in infant formulas by using probiotics, prebiotics, synbiotics, and the so-called postbiotics (Fig. 1). So, to promote intestinal microflora similar to breastfeeding, probiotics related to the genera Lactobacillus and Bifidobacteria those normally found in infants' gut when breastfeeding are exclusively applied as well as prebiotics addition is added in fermented infant formulas which provide beneficial effects to the gastrointestinal system (Mugambi *et al*., 2012; Cukrowska *et al*., 2020 and Salminen *et al*., 2020)

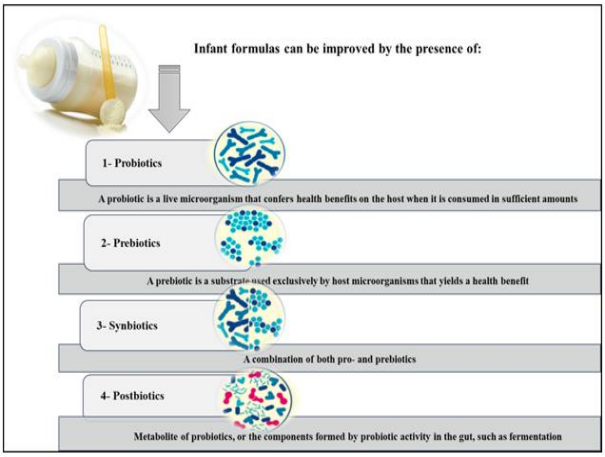

Figure 1. The meaning of using probiotics, prebiotics, synbiotics, and postbiotics in the development of beneficial microbiota in infant formulas (adapted from Salminen *et al*., 2020)

Whey as a base of infant formula

More than 180 to 190 million tons of whey are produced worldwide every year (Hausjell *et al*., 2019). Whey is a greenish-yellow liquid produced as a by-product produced during cheese processing in dairy and cheese processing plants. Whey is rich in valuable components like proteins, lactose or minerals (calcium, magnesium or phosphorous) which makes that the valorization and reuse of this by-product acquires a paramount importance. Whey proteins are highly functional food that shows a high protein quality and contains relatively high proportions of essential amino acids (Salami *et al*., 2010; Mirabella *et al*., 2014 and Lievore *et al*, 2015). Because of its nutritional value, whey became an interesting substrate for the development of fermented foods. It is a source of vitamins, minerals and high-quality proteins compared with caseins, egg and soy proteins but its proteins are differed among different human and/or animal species (Pescuma *et al*., 2012). Beta-lactoglobulin (β-Lg) is found in the whey fraction of cow milk but is absent in human milk which increases its allergenicity in infants when it used without modification in infant formula. Denaturation and proteolysis represent powerful tools for enhancing protein digestibility. Whey protein hydrolysates are physiologically better than intact proteins because their intestinal absorption appears to be more effective. Whey protein peptides released by enzyme hydrolysis or bacterial fermentation represent more important biological activities, such as antimicrobial, immunomodulatory, antioxidant, and antihypertensive activities, have been released (Osman *et al*., 2015).

Non-bovine milk as a base of infant formula

Camel milk and its whey

Camels are raised in areas with low rainfall and long dry periods (Brezovečki *et al*, 2015). Camel milk has been used for centuries as a medicinal drink in Middle Eastern, Asian and African cultures. Its popularity is because it has become one of the most promising foods regards to its potential antioxidant and antimicrobial activities derived from caseins and whey proteins (Osman *et al*., 2015 and Jrad *et al*., 2020). Camel milk differs from the milk of other species and is closest to human milk, especially in terms of its lack of β-lactoglobulin and the low amounts of κ-casein, which makes it a suitable diet for people with cow's milk protein allergy (Hochwallner *et al*., 2014; zibaee *et al*.,

2015; Jrad *et al*., 2020 and Oussaief *et al*., 2020). Furthermore, it was reported that camel milk is rich in vitamin C, iron and potassium contents and low in fat and lactose contents (Gopal *et al*., 2017). It has unique bioactive peptides released during the gastrointestinal digestion of milk proteins (Oussaief *et al*., 2020). Nevertheless, it was reported that camel whey protein is considered a strong natural antioxidant because it decreases oxidative stress, enhances immune system function, and increases glutathione levels and it is rich in lactoferrin, lactalbumin, lactoglobulins, lactoperoxidase, and lysozyme, and is rich in immunoglobulins (Badr *et al*., 2017).

Goat milk and its whey

Goat milk is recommended as an alternative to cow milk for infants and patients who are allergic to cow milk (Hochwallner *et al*., 2014). Goat milk is an attractive food because of its higher nutritional values and digestibility compared to cow milk due to the formation of softer curd (Biadała *et al.*, 2020). It has a lower level of α_{s1}-casein and its fat has higher levels of medium chain fatty acids and smaller fat globules than cow milk (Ye *et al*., 2019). Whey from goat milk contains approximately 55% of milk nutrients: soluble proteins, lactose, vitamins, minerals and a minimum amount of fat (Galdino *et al*., 2020). Previously, Zhou *et al*. (2014) reported that consumer demand for goat milk infant formulae is increasing. They found that goat milk formulae provide growth and nutritional outcomes in infants that did not differ from those provided by a standard whey-based cow milk formula.

CONCLUSION

Although exclusive breastfeeding is preferred for all term newborn and their mothers, human milk feeding may not always be possible. The decline in breastfeeding for infants under six months of age is in increase, especially in urban areas worldwide and in Saudi Arabia as well. Consequently, the human milk substitute is the option either as a sole feeding source or in mixed feeding systems. Therefore, the importance of developing infant's formula and follow-on formula has long been recognized by researchers a long time ago. Efforts for improving cow-milk-based formulae have no end (i.e., cow milk protein modification, hydrolyzed cow-milk based formula, prebiotic and probiotic formula and fermented formula). Latterly, involving camel and/or goat milk and their whey in the preparation of follow-on formulae as well as developing fermented follow-on formulae without live bacteria are attracted researcher's interest. In summary, there is a contentious need for evaluate and develop follow-on formulae that mimic mother's milk to be more compatible with infant digestive system, enhance immunity and reduce allergenicity.

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وضع الرضاعة الطبيعية في المملكة العربية السعودية والأساليب الحديثة في تطوير تركيبات المتابعة لمواجهة صعوبات الرضاعة الطبيعية

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على الرغم من أن الرضاعة الطبيعية توفر جميع الفوائد للأطفال ، فإن العديد من الآباء يختارون تركيبات الرضع كبديل لأطفالهم. فعندما تكون الرضاعة الطبيعية غير ممكنة ، يجب التوصية بتركيبات المتابعة، و من المعروف أن تكوينات بروتينات حليب البقر تختلف اختلافًا كبيرًا عن حليب الأم ولا يتحملها الرضع، و لسوء الحظ ، تتم صياغة غالبية تركيبات المتابعة على أساس استخدام شرش اللبن البقري في التركيبته، لذلك ، اقترح العديد من الباحثين استخدام مشتقات حليب الماعز أو الإبل كأساس لصنع تركيبات الرضع، و من ناحية أخرى، كشفت الجهود التي بذلها الباحثون لتثمين شرش اللبن أن استخدام شرش لبن الإبل أو الماعز في تغذية الرضع له فوائد كبيرة في زيادة القيم الغذائية والبيولوجية وهضم بروتينات اللبن، أيضًا، يوصى باستخدام التركيبات المتخمرة للرضع لأنها تعزز قابلية الهضم وتعتبر آمنة للرضع، لذلك أوصى العديد من الباحثين باستخدام بكتيريا حمض اللاكتيك لإنتاج تركيبات لبنالأطفال المتخمر، و تركز الدراسه المرجعيه بشكل أساسي على أهمية استخدام تركيبات المتابعة لتغذية الأطفال حديثي الولادة عندما لا تكون الرضاعه الطبيعيه خيارا متاحا، بالإضافة إلى ذلك، تعرض الدراسه المرجعيه الأساليب التي تم استخدامها لإعداد تركيبات متابعة مختلفة بناءً على استخدام أنواع البان مختلفه مختلفة لتوفير خصائص وظيفية وغذائية أقرب ما يمكن إلى لبن الأم، كما عرضت الاتجاهات الحديثة المقترحة لتحسين القيمة الغذائية لتركيبات الأطفال لتضييق الفجوة بين استخدام التركيبات العادية واحتياجات الرضع.