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scFOS supplemented follow-on formula in healthy infants: Impact on vaccine specific faecal secretory IGA response, faecal bifidobacteria, growth and digestive tolerance[☆]

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ABSTRACT

Objectives: Few studies have assessed efficacy and safety of prebiotics in infants at the time of diversification. We investigated the beneficial effects of a follow-on milk formula supplemented with short-chain fructo-oligosaccharides (scFOS) in healthy infants after 4 months of age.

Subjects/methods: 75 formula-fed healthy infants were included at the age of 4 months in a randomized, controlled, double blind study and received either a placebo or scFOS supplemented formula for six months. Faecal poliovirus sIgA after vaccination and bifidobacteria concentration, height, weight and digestive tolerance were monitored.

Results: After 1 and 2 months of supplementation, no significant difference was observed between the groups for the evolution of poliovirus sIgA concentration compared to baseline. A significant increase in bifidobacteria count was observed after 1 month of ScFOS supplementation, but this difference was no longer significant after 2 months. Breastfeeding history of infants was shown to have an impact on faecal bifidobacteria evolution. Tolerance and growth parameters were similar in the 2 groups.

Conclusions: A follow-on milk formula supplemented with scFOS modulates intestinal microbiota via an increase of faecal bifidobacteria concentration, while no effect on sIgA concentrations could be demonstrated. scFOS addition elicited normal digestive tolerance and normal growth suggesting it can be used safely at 5 g/L in infants after 4 months of age.

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1. Introduction

The development of the intestinal microbiota during the first months of life plays a crucial role towards a normal growth and an optimal protection against infections. It is now well established that the microbiota gut colonization in infants is influenced by several parameters such as mode of delivery, duration of gestation, antibiotic use, country of birth and type of feeding (Fallani et al., 2010, 2011; Penders et al., 2006). Breastfed neonates microbiota is mainly dominated by bifidobacteria and lactic acid bacteria whereas in formula fed babies the predominant organisms are enterococci (Balmer & Wharton, 1989). Mode of feeding also modulates the immune system (Holt, 1995), and it has been shown that the faecal sIgA levels in formula-fed infants are lower than those observed in breastfed infants (Koutras & Vigorita, 1989; Kuitunen & Savilahti, 1995; Maruyama, Hida, Kohgo, & Fukunaga, 2009). These data clearly indicate a positive impact of breast milk components on the gut microbiota and immune status of infants.

More than 130 different oligosaccharides have been identified in human milk and they are its 3rd most abundant component. Several studies have suggested they may be able to modulate the microbiota and immune system development (Arslanoglu, Moro, & Boehm, 2007; Stepans et al., 2006).

Based on these results, several infant formulas supplemented with different types of oligosaccharides have been marketed (Arslanoglu et al., 2007; Bruzzese et al., 2009; Campeotto et al., 2011; Chen, Alarcon, Comer, & Tressler, 2002; Stam, van Stuijvenberg, Garssen, Knipping, & Sauer, 2011; Veereman-Wauters et al., 2011). Most of the studies available have focused on a commercially available mixture containing short chain galacto-oligosaccharides (scGOS) and a high molecular weight fraction of inulin in a ratio 9:1 (Agostoni et al., 2010). This mixture has been shown to reduce stool pH and stool viscosity (Kapiki et al., 2007; Mihatsch, Hoegel, & Pohlandt, 2006), to modify gut microbiota in preterm and term infants (Bruzzese et al., 2009; Knol et al., 2005; Salvini et al., 2011) and to modulate the immune response (Arslanoglu et al., 2007; Bakker-Zierikzee et al., 2006; Bruzzese et al., 2009; Scholtens et al., 2008). Other studies reported that infant formula supplemented with

fructo-oligosaccharides (FOS) alone influenced the gut microbiota colonization (Brunser et al., 2006; Euler, Mitchell, Kline, & Pickering, 2005; Paineau et al., 2014; Veereman-Wauters et al., 2011).

However, while the vast majority of the studies point out the benefit of FOS in combination with other oligosaccharide or alone for newborns or in early infancy, the impact of the supplementation of follow-on formula on growth parameters, tolerance, bifidogenic or immune effects in infants above 4 months of age is not known (Brunser et al., 2006; Salvini et al., 2011; Stam et al., 2011). Vaccine-specific sIgA collected in saliva or in faeces are considered as highly suitable markers of immune response as they correlate with clinical endpoints (Albers et al., 2013) and poliovirus is a typical vaccine of early infancy with high coverage (Moturi et al., 2014) that stimulates mucosal and intestinal immunity and induces detectable level of faecal sIgA (Pasetti, Simon, Szein, & Levine, 2011). Moreover fructo-oligosaccharides (FOS) elicit immune stimulation through the intestinal mucosa as shown in animal models (Hosono et al., 2003; Nakamura et al., 2004) and stimulate the growth of intestinal bifidobacteria (Paineau et al., 2014) while bifidobacteria might have an implication for improving response to poliovirus vaccine (Mullie et al., 2004).

In order to investigate if a short-chain FOS (scFOS) supplementation in follow-on milk formula would achieve beneficial effects and would be well tolerated, we designed a randomized, double-blind study against placebo in 4 months old infants. We investigated the effect of 5 g/L scFOS on faecal specific poliovirus secretory IgA (sIgA) level following vaccination and on bifidobacteria faecal concentration after one and two months of supplementation. The effect of scFOS on digestive tolerance and growth parameters was also monitored during the study in infants up to 10 months of age.

2. Methods

2.1. Ethical considerations

The study was performed according to the Declaration of Helsinki II Principles and was approved by the Ethics Committee of the Fundació Unió Catalana D'Hospitals on 12th January 2009. All parents or caregivers of the participating infants

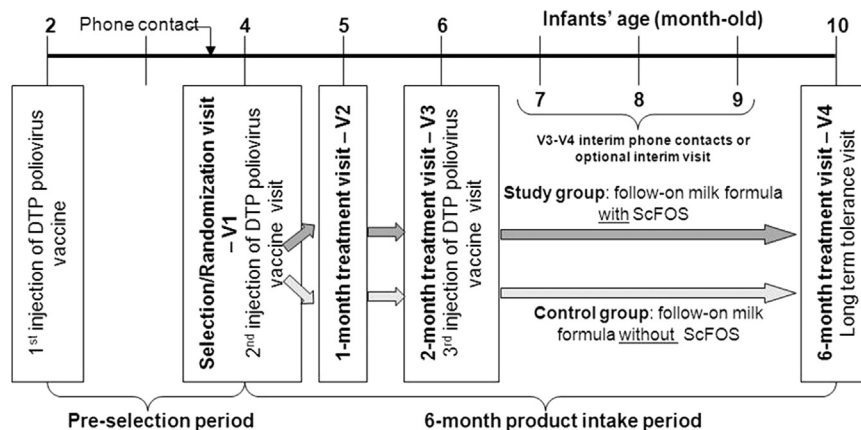


Fig. 1 – Study timeline.

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