**Supplementary Table 6.** Intestinal effects ofGOS/FOS in preterm infants.

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| **Reference** | **Prebiotics** | **Dose** | **Objectives** | **Subjects and main features of the trial** | **Outcomes** |
| Boehm et al., 2002 [55] | GOS/FOS  (ratio 9:1) | 1 g/100 mL | To investigate the effect of a preterm formula milk supplement consisting of oligosaccharides in similar proportions to human milk on the fecal flora and stool characteristics of preterm infants | Fifteen preterm infants were administered the formula supplemented with the prebiotics and 15 infants fed a formula supplemented with maltodextrin as placebo. A group fed fortified mother’s milk was investigated as a reference group (n = 12). On four days during a 28 day feeding period (1, 7, 14, and 28), the fecal flora was investigated, and stool characteristics, growth, and possible side effects were recorded | During the study period, the number of bifidobacteria in the group fed the GOS/FOS supplemented formula increased to the upper range of bifidobacteria counts in the reference group. The difference between the supplemented and non-supplemented groups was highly significant. The stool frequency after 28 days was significantly lower in the control group than in the GOS/FOS supplemented group and the reference group |
| Mihatsch et al., 2006 [56] | GOS/FOS | 1 g/100 mL | To assess if prebiotics can improve feeding tolerance in preterm infants on full enteral formula feeding | Placebo-controlled double-blind trial. Twenty preterm infants on full enteral nutrition were given prebiotics or placebo for 14 days. Tool viscosity was measured by high-pressure capillary rheometry. Gastrointestinal transport time was assessed as the time from feeding carmine red to its appearance in the diaper | Preterm infant formula supplementation with GOS/FOS reduced stool viscosity and accelerated gastrointestinal transport. No adverse effects were observed |
| Indrio et al., 2009 [52] | GOS/FOS  (ratio 9:1) | 0.8 g/100 mL | To evaluate the effect of a prebiotic mixture on gastric motility in preterm newborns | Double-blind, randomized, placebo-controlled study Twenty healthy preterm infants were fed pre-biotic supplemented standard preterm formula or the same formula with maltodextrin. After a feeding period of 15 days, gastric electrical activity was measured by electrogastrography, and the gastric emptying time was studied by ultrasound technique | The prebiotic group showed a higher percentage of propagation with respect to placebo group. The half-emptying time recorded after the intervention period was about 30% faster in the prebiotic group compared with the placebo. Only the prebiotic group showed a significant faster half-emptying time at day 15 than baseline |
| Indrio et al., 2009 [51] | GOS/FOS  (ratio 9:1) | 0.8 g/100 mL | To evaluate the effects of prebiotic, probiotic added to a standard formula on gastrointestinal motility respect to placebo-formula in preterm infants | Healthy preterm, appropriate for gestational age and with normal Apgar score were enrolled in a double-blind placebo controlled study within the first week of life. Forty-nine preterm newborns completed the study:17 newborns were exclusively breast-fed; the remaining 32 newborns randomly received: prebiotic-added formula (10) probiotic-added formula (10) and 12 newborns were fed with an indistinguishable placebo formulation for 30 days. Cutaneous electrogastrography (EGG) and ultrasound gastric emptying (GE) were performed | After the intervention period, the prebiotic group showed a higher percentage of EGG slow wave propagation and faster gastric half emptying time respect to placebo group |
| Modi et al., 2010 [57] | GOS/FOS (9:1 ratio) | 0.8 g/100 mL | To test if a preterm formula containing the prebiotic mixture, improves enteral tolerance in preterm babies when used to supplement insufficient maternal milk | Prospective, double-blind, randomized, controlled study. We recruited 160 infants. Infants were randomized within 24 h of birth to receive maternal milk with either a standard preterm formula or an identical formula supplemented with the prebiotic. Enteral feeds were commenced within the first 24 h of birth. The rate of increase in milk volume was based on a predefined protocol taking into account the clinical status of the infant and the volume of gastric residuals | The median time to achieve a daily enteral intake of 150 mL/kg was not statistically significant. There was no significant difference in the proportion of time from trial entry to 28 d/discharge during which a daily enteral intake of 150 mL/kg or greater was tolerated. A significant improvement in enteral tolerance with increasing immaturity in the group randomized to the prebiotic formula was found, with no benefit in babies >31-wk gestation |
| Armanian et al., 2016 [58] | GOS/FOS  (ratio 9:1) | 0.5-1.5 g/kg/d | To evaluate the effects of prebiotics in the management of hyperbilirubinemia in preterm neonates on enteral feeding | Randomized, placebo controlled trial. Of the 66 neonates enrolled, 50 completed the study. They were administered either the prebiotic mixture (n=25) or milk supplemented with distilled water (placebo, n=25). The study primary outcomes were bilirubin level after and during the intervention; secondary outcomes were stool frequency and meeting full enteral feeding | Bilirubin was decreased in the prebiotic group but not in the placebo group;the prebiotic group had also a lower peak bilirubin level than the placebo group over the study period. Stool frequency and frequently of meeting full enteral feeding were higher with the prebiotic than the placebo |