Stool Pattern Changes in Toddlers Consuming a Follow-on Formula Supplemented With Polydextrose and Galactooligosaccharides

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ABSTRACT

Healthy 9- to 48-month-old children (n = 133) were randomized to receive a cow's-milk–based follow-on formula (control) or the same formula with polydextrose and galactooligosaccharides (PDX/GOS) for 108 days. Pediatricians assessed diarrheal disease, stool pattern, acute respiratory infection, systemic antibiotic use, and growth. The 2 groups had similar weight-for-length/height *z* score and similar odds of having diarrheal disease, acute respiratory infection, and systemic antibiotic use; however, PDX/GOS had greater odds of increased defecation than control ($P \leq 0.01$). Addition of PDX and GOS to a follow-on formula was well tolerated and induced a pattern of more frequent and softer stools in toddlers.

Key Words: children, follow-on formula, galactooligosaccharides, polydextrose, prebiotics, stool pattern

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Constipation affects up to 30% of children, especially those younger than 5 years (1–3). Up to 95% of constipated children have functional constipation (4), which is commonly associated with change from breast milk to formula, start of solid foods, or painful defecation (1,3). Insufficient fiber intake, lower than the recommended minimum equal to age of the child in years plus 5 g/day (5), is frequently associated with constipation in children (1,2). Short-chain fatty acids produced from fermentation of fiber by colonic bacteria promote osmotic stimulation, which, along with the water-holding capacity of undigested fiber, contributes to soften stools (6). Additionally, fiber promotes faster colonic time (7), and the fiber-stimulated bacteria themselves may increase fecal mass (6). Prebiotic fibers can selectively stimulate beneficial bacteria in the colon and promote health benefits, including lower incidence of diarrhea and acute respiratory infection (ARI) (8–10). The present study assessed the effects of a formula supplemented with the prebiotics PDX and GOS on diarrhea, stool pattern, and ARI in toddlers attending a day care center in Salvador, Brazil.

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METHODS

Healthy 9- to 48-month-old children who had previously tolerated a cow's-milk–based beverage were eligible. Exclusion criteria included breast-feeding >50% of the child's number of milk feedings, diarrhea, or ARI in the previous 48 hours, or a history of underlying disease, which would interfere with normal growth, development, or evaluation of the child. The study was approved by the institutional review board and parents provided written informed consent.

In this randomized, double-blind, prospective study, participants received a cow's-milk–based follow-on formula (Enfagrow, Mead Johnson Nutrition, Evansville, IN) (control), or the same formula supplemented with a prebiotic blend of PDX and GOS, 0.5 g of each per serving (PDX/GOS). A nutritionist (M.V.P.) ensured that the participants received the randomized formula, and the pediatricians (P.S.A., T.C.M.R.) who assessed all of the medical events were kept blinded. Participants stayed at the day care center from 7 AM to 5 PM Monday through Friday and were offered a 245-mL serving of formula at breakfast and afternoon snack during a 108-day period. Apart from the study formulas, the diet offered to all of the participants at the day care center had the same composition. Formula was provided to participants to be consumed at home on weekends and holidays. Formula intake was calculated based on recorded volume not consumed. Trained personnel recorded daily stool consistency and frequency at the day care center. Stool consistency was assessed according to a visual gradient system in which pictures of stool representing consistency ranging from 1 to 5 (1 = hard, 2 = formed, 3 = soft, 4 = semiliquid, 5 = liquid) were used. Diarrheal disease (DD) was defined as ≥3 liquid/semiliquid stools per day with fever, vomiting, and/or dehydration and compromised general status. Increased defecation was defined as a stool consistency grade ≥3 occurring ≥3 times per day without any other symptoms. Body weight and length/height were recorded at enrollment and after 30, 60, 90, and 108 days of feeding and converted into *z* scores.

Statistical Analysis

A sample size of 60/group was chosen to detect a 30% reduction in incidence of DD and ARI ($\alpha = 0.05$, 88% power),

assuming a combined incidence of 40% in the control group. For categorical variables, Fisher exact test or χ^2 test was used, and for continuous variables, either analysis of variance or Kruskal-Wallis test was used depending on normality. For duration of DD, ARI, increased defecation, and systemic antibiotic use (SAU), the Cox proportional hazards model was used. Covariates were age (9–24 or 24–48 months) and sex. The counting process approach or the intensity model of Andersen and Gill was chosen, with the primary assumption that an event that occurred for the first time was the same type of event that occurred a second time. An event may last >1 day, and a new event was not counted until at least 1 event-free day was observed. SAS version 9.1.3 (SAS Institute, Cary, NC) was used for analysis.

RESULTS

A total of 133 children were enrolled and 129 children completed the study (PDX/GOS, n = 62; control, n = 67). The PDX/GOS and control groups were similar at study entry in sex, age, type of delivery, and nutritional parameters (Table 1). There were no statistically significant differences between the PDX/GOS and control groups for duration of breast-feeding since birth (median [interquartiles]: 152 [91–730] vs 198 [91–697] days; $P = 0.40$). Although a trend was observed for higher number of children who consumed milk beverages in addition to study formula in the control versus the PDX/GOS groups (65 [97%] vs 57 [88%], $P = 0.053$), the daily intake of other milk beverages during the study period in the control versus the PDX/GOS group was similar (mean ± standard deviation: 211 ± 41 vs 203 ± 47 mL/day, $P = 0.33$). The estimated daily consumption of dietary fiber (excluding the prebiotics in the PDX/GOS formula) was 9.2 g in the PDX/GOS and 8.9 g in the control group. Daily study formula consumption was similar in the PDX/GOS and control groups (median [interquartiles]: 362 [266–475] vs 372 [261–490] mL/day; $P = 0.60$]. For both groups combined, the median intake of formula was significantly higher in the 9- to 24-month-old (31 mL/kg) than in the 24- to 48-month-old children (25 mL/kg) ($P < 0.001$). Body weight-for-length/height z scores were similar in the 2 groups at all of the measured time points ($P > 0.27$).

There were no differences between groups in number of participants with 1 or more episodes, or in total number of episodes of DD, increased defecation, ARI, or SAU during the study. There were similar odds of having DD, ARI, and SAU in the 2 groups, both unadjusted and adjusted for age and sex. Conversely, the PDX/GOS group had significantly higher odds of having increased defecation compared with the control group (Fig. 1). The mean duration of the first and second episodes of DD and increased defecation were similar in the 2 formula groups. Both the PDX/GOS and control formulas were well tolerated, and there was no difference between groups in the incidence of adverse events.

DISCUSSION

In the present study, we observed significantly higher odds of increased defecation in the PDX/GOS group and no differences in the incidence of DD or ARI compared with the control group. It was demonstrated that the PDX/GOS blend used in the present study elicits a bifidogenic effect in the gut microbiota of infants (11). Modification of the gut microbiota can have an immune-modulating effect resulting in protection against DD and ARI (8–10). In the present study, however, the daily amount of PDX/GOS ingested by toddlers, 2 g/day, may have been insufficient to promote a detectable effect on incidence of DD and ARI. One possible explanation is that the estimated daily consumption of fiber in the PDX/GOS and control groups may have contributed greatly to the overall fiber intake and therefore overshadowed the supplemented prebiotic effect. Similar to our findings, no effect on incidence of diarrhea or infection was reported when cereal supplemented with fructooligosaccharides (FOS) was ingested in an average amount of 0.6 g/day by 6- to 36-month-olds (12) or 1.1 g/day by 4- to 24-month-old children (13). A larger amount of prebiotics, 8 g/L of GOS/FOS added to infant formula, elicited protection against ARI in infants (8). Parents/caregivers reported a protection against DD when 7- to 19-month-old children were supplemented with 2 g/day of FOS (10). In our study, DD was confirmed by a pediatrician following strict pre-established criteria, which may explain the differing results in the incidence of DD in the 2 studies. Another study showing protection against DD by GOS/FOS-supplemented

TABLE 1. Characteristics of the PDX/GOS and control groups at study entry

Characteristic	PDX/GOS	Control	P
n	65	68	
Sex, male/female*	34/31	40/28	0.488
Age, mo, n (%)†			0.728
9–24	28 (44)	32 (47)	
24–48	37 (56)	36 (53)	
Type of delivery, n (%)‡			0.854
Vaginal	45 (69)	46 (68)	
Cesarean	20 (31)	22 (32)	
Weight-for-length/height z score, mean (±SE)†	−0.14 (±0.12)	0.01 (±0.11)	0.239
Nutritional status‡, n (%)†			0.950
Obese	0	1 (2)	
Overweight	2 (3)	1 (2)	
Risk of overweight	5 (8)	5 (7)	
Normal growth	58 (89)	61 (90)	

GOS = galactooligosaccharides; PDX = polydextrose; SE = standard error.
* χ^2 test used to compare study groups.
† Fisher exact test used to compare study groups.
‡ Nutritional status was classified according to the weight-for-length/height z score: obese >3, overweight >2 to 3, risk of overweight >1 to 2, normal growth 1 to −2, wasted <−2 to −3, severely wasted <−3 (World Health Organization, present criteria).

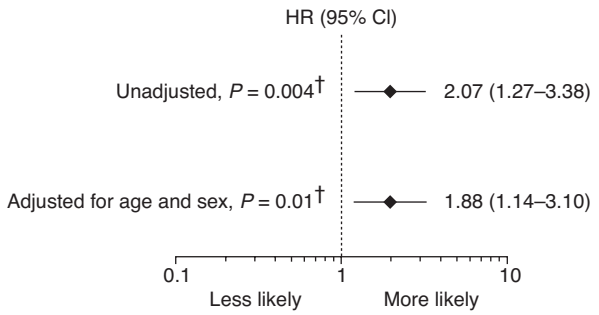

FIGURE 1. Odds of having increased defecation in the polydextrose and galactooligosaccharides group compared with the control group. †Unadjusted and adjusted (age and sex) hazard ratio with 95% confidence interval; Cox proportional hazards model, taking into account that some participants had multiple episodes of each outcome. Increased defecation defined as a stool pattern of more than or equal to 3 soft/loose stools per day without any other symptoms.

formula in infants had the limitation of not being blinded (9). Our study was powered to detect a difference in DD and ARI between groups assuming a 40% combined incidence of these diseases in the control group, which was higher than the actual incidence observed. This may be one potential reason for not finding a significant difference. Children in the 2 groups had appropriate growth during the study, consistent with previous studies in infants receiving this prebiotic blend (11,14). The amount of PDX/GOS did not provoke excessive gas production or adverse events, supporting the safety of this prebiotic blend, also demonstrated in previous studies (11,14).

The increased defecation without diarrhea observed in the PDX/GOS group is comparable with findings in other studies using PDX and GOS combined or alone in different populations (11,14–16), and neither age nor sex contributed to the differences between groups. Our criterion for increased defecation ($\geq$3 soft/loose stools per day without any other symptoms) made it distinguishable from the norm of $\leq$2 bowel movements per day, typical for this age group (1), and was clearly distinct from DD. The estimated daily consumption of dietary fiber other than PDX and GOS in the study formula was high but similar in the 2 groups. This allows us to hypothesize that the fiber-like effect seen in the stool pattern can be attributed to the prebiotic content of the formula supplemented with PDX/GOS. Despite the known benefit of increasing fiber content in the diet (5), this practice was difficult to implement, especially in young children (17). The high prevalence of constipation in early childhood justifies preventive measures, including the laxative effect of prebiotics (4,5). Whether there is an optimal amount of PDX/GOS to promote protection against diarrhea and respiratory infection in toddlers needs to be investigated further. The present study demonstrates that the addition of PDX/GOS to a follow-on formula can soften stools and increase stool frequency, which may have an important application in the management and prevention of functional constipation.

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