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Galacto-oligosaccharides and bowel function

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Abstract

Constipation is a common problem and its prevalence increases with age. Severe constipation requires treatment with laxatives, but nutritional therapy, especially increased dietary fibre intake, is recommended primarily for the prevention and treatment of mild constipation. One alternative may be the use of oligosaccharides, which act as soluble fibre and have a bifidogenic effect. Galacto-oligosaccharides (GOS) resembling oligosaccharides occurring naturally in human milk can be produced from lactose. Several clinical studies reviewed in this paper have shown that the use of GOS (5–15 g per day) may relieve the symptoms of constipation in adults and elderly people. In infants, the supplementation of formula with a mixture of GOS and fructo-oligosaccharides can modulate bowel function and stool characters in the same direction as does breast-feeding. Gastrointestinal symptoms may occur as side-effects of oligosaccharides, but 12 g GOS per day or less is usually well tolerated.

Keywords: *bifidogenic effect; constipation; defecation; fibre; prebiotics; stools*

Introduction

Constipation is a common problem that reduces the quality of life. The estimated prevalence of constipation varies from 2 to 27% (1), and the number of people reporting constipation increases with age (2). Diet and lifestyle are factors that affect bowel function, and adequate intakes of dietary fibre and fluid are usually recommended for the prevention of constipation. Serious constipation requires treatment with laxatives. Bulk laxatives, which absorb water from the intestinal lumen and soften stool, are generally well tolerated, but gas production and bloating may occur. Stimulant laxatives, which increase intestinal motility and secretion of water to the lumen, are more effective than bulk laxatives. However, unwanted effects such as abdominal cramps and, in chronic treatment, the development of gastrointestinal tolerance may result from the use of stimulant laxatives (3).

An alternative among nutritional therapies for constipation is the use of prebiotics, including galacto-oligosaccharides (GOS) and fructo-oligosaccharides (FOS). The latter occur naturally

in vegetables and can be commercially produced from sucrose or through hydrolysis of chicory roots. GOS is a collective term for a group of carbohydrates composed of oligo-galactose with some lactose and glucose. They are produced commercially from lactose by β -galactosidase (4). Oligosaccharides resembling GOS occur naturally in human milk and may be one of the factors that protect human infants from gastrointestinal pathogenic bacteria (5). In the literature the terms *trans*-oligosaccharide (TOS) and *trans*-galacto-oligosaccharide (TGOS) occur as synonyms for GOS. In this paper, the term GOS is used since it appears to be the most frequently used term.

The laxative effects of prebiotics such as GOS and FOS are attributed to their action as soluble fibres. They pass undigested into the colon where bacteria hydrolyse and ferment them (6). In addition, several studies on both infants (5, 7, 8) and adults (9–11) have shown the prebiotic, bifidogenic effect of GOS or a mixture of GOS and FOS on colonic flora. Some researchers have suggested that a reduction in the number of bifidobacteria has been related to constipation, and treatment to

correct this could therefore benefit bowel function (12).

This review summarizes clinical data concerning the effect of GOS on bowel function. To identify human clinical trials eligible for the review a Medline search was conducted, and publications on GOS and bowel function were included. Additional studies were obtained from the references of the selected articles, and from other databases and sources, and they were included if they were written in English or had an English abstract.

Effects of galacto-oligosaccharides on bowel function

Several studies performed in the elderly (13–15) and in adults (9, 16–19) have examined the laxative effect of GOS. In addition, several clinical trials have examined the effects of a mixture of GOS and FOS on bowel function in infants (5).

Studies in the elderly

Constipation is not a physiological consequence of ageing. However, age-related changes, such as increased use of medications, dietary changes and decreased mobility, may contribute to the increased prevalence of constipation in older adults. When the intake of food decreases with age, the intake of fibre may be inadequate to prevent constipation (20). The use of GOS offers an alternative to increase the amount of indigestible carbohydrates, i.e. dietary fibre, in the diet.

The composition of faecal flora changes with age, and in comparison to young adults, the number of bifidobacteria may decline in healthy elderly people (21, 22). These changes may alter intestinal motility, and thus treatment increasing bifidobacteria may relieve symptoms of constipation (12). Narimiya et al. (13) studied the effects of GOS (18.5 g per day), used as a substitute for sugar, on bowel function and faecal flora in 12 elderly subjects (mean age 66 years) suffering from type 2 (non-insulin-dependent) diabetes. Nine subjects were constipated and three had normal bowel function. In 11 subjects faeces were softer during the 1 month GOS period than during the baseline. In five subjects the laxative effect of GOS was statistically significant and accompanied by an increase in the ratio of bifidobacteria to total bacteria.

Teuri and Korpela (14) investigated the laxative effects of GOS in 14 elderly subjects (mean age 80 years) suffering from constipation. The study

was a double-blind, two-period cross-over study lasting for 6 weeks. After a 1 week run-in period, the subjects ingested, in random order, either a GOS yoghurt (9 g of GOS per day) or a placebo yoghurt twice daily for 2 weeks. Faecal samples were collected from nine volunteers during the run-in period and at the end of the study periods. The weekly defecation frequency was higher during the GOS period (mean 7.1, range 3–15) than during the control period (mean 5.9, range 1–14).

Recently, Sairanen et al. (15) examined the effect of yoghurt containing GOS (12 g per day), prunes (12 g per day) and linseed (6 g per day) on bowel function in 43 constipated, free-living elderly subjects (mean age 76 years). In this double-blind cross-over study, the subjects consumed, in random order, 260 g per day of either test yoghurt or control yoghurt for 3 weeks. This study showed the effects of the yoghurt containing GOS, prunes and linseed. The defecation frequency was higher (8.0 versus 7.1 times per week, $p=0.01$) and defecation easier ($p=0.01$). However, effects of the different fibre sources could not be separated in this study.

It has been reported that 65% of elderly people reporting constipation defecate at least once daily, and constipation among the elderly usually means difficulty in evacuation and hard stools (23). The results of the studies investigating the laxative effect of GOS in elderly people indicate that GOS reduce the most common symptoms of constipation in the elderly. The use of GOS could not, however, totally replace other laxatives (14, 15).

Studies in adults

The laxative effect of GOS varies from patient to patient (15, 16), as does the effect of any other fibre (24). Deguchi et al. (16) examined the laxative effect of GOS in 128 healthy adults with constipation tendency in two single-blind, placebo-controlled trials. In the first study, 76 women ingested a beverage supplemented with GOS (2.5 or 5 g per day) or a placebo beverage for 1 week. After a 1 week washout period, the subjects were inverted for the second 1 week intervention period. In the second trial, 50 volunteers ingested daily a placebo beverage during the first 1 week intervention period and a beverage supplemented daily with 10 g of GOS during the second 1 week intervention period. After ingesting 5 or 10 g of GOS daily, defecation frequency increased from 0.92 to 1.07 ($p<0.05$) and from 0.85 to 0.97 ($p<0.05$) times per day,

respectively, and faeces became softer ($p < 0.05$). The laxative effect of GOS was more marked in those with low defecation frequency.

The results of studies investigating the laxative effects of GOS in adults with normal bowel habits are contradictory. Teuri et al. (17) investigated the effects of yoghurt supplemented with 15 g of GOS daily in 12 healthy volunteers. The median frequency of defecation increased ($p < 0.05$, Friedman's ANOVA) from eight times per week during the 1 week control period to nine and 10 times per week during the first and second administration weeks, respectively. The number of faecal bifidobacteria, analysed from six volunteers, showed no change, but the growth of bacteria on *Lactobacillus*-selective agar (MRS) increased ($p < 0.05$). Ito et al. (9) investigated the effects of an apple juice supplemented with GOS in a single-blind study. During four 1 week intervention periods, 12 healthy adults ingested 0, 2.5, 5 and 10 g of GOS daily according to a Latin square design. One-week washout periods separated the intervention periods. In this study, stool frequency showed no significant change after the ingestion of GOS, but the number of bifidobacteria increased and the stools softened. Van Dokkum et al. (18) examined the effects of an orange juice supplemented with indigestible oligosaccharides in a randomized, double-blind, Latin square study. Ingestion of GOS (15 g per day) for 3 weeks did not affect stool frequency in 12 healthy volunteers, but a significantly lower percentage of faecal dry weight was measured during the GOS period than during the placebo period. In contrast, Alles et al. (19) reported that ingestion of GOS (7 or 15 g per day) for 3 weeks did not significantly affect bowel habits or stool composition in adults with normal bowel function. It seems that in adults with normal bowel function, the effects of GOS are less clearcut.

Studies in infants

Intestinal microbiota plays an important role in the postnatal development of gastrointestinal functions. Several clinical trials have shown that the supplementation of infant formula with a mixture of GOS and FOS benefits bowel function in both preterm and term infants; these data were summarized in a recent review by Fanaro et al. (5). Thus, infant formula supplemented with a mixture of GOS and FOS stimulated the growth of intestinal bifidobacteria and lactobacilli in infants. In addition, the

supplementation of infant formula with GOS and FOS has modified stool consistency and increased defecation frequency to levels similar to those found in breastfed infants. In these studies, mixtures of GOS and FOS (GOS 90%, FOS 10%) resembling human milk oligosaccharides have been used (5), and it is impossible to separate the individual effects of the oligosaccharides (25). However, because the prebiotic mixtures contained mainly GOS, these studies provide supportive evidence of the benefits of GOS on bowel function.

Possible adverse effects of galacto-oligosaccharides

The bacterial fermentation of undigested carbohydrates increases the production of gases in the colon (26) and may cause adverse gastrointestinal symptoms such as flatulence, which are common side-effects of increasing fibre intake (24). Because GOS are fermented in the colon, gastrointestinal symptoms may occur after their ingestion (16, 17). Usually, tolerance to fibre depends on the amount of the product eaten (27). Similarly, the frequency of gastrointestinal symptoms increases when the dose of GOS increases (9, 16). In most of the studies, amounts of 12 g of GOS or less daily were well tolerated (14, 15), but 15 g of GOS per day increased flatulence (17). However, individuals vary considerably in their response to GOS (15), as with their response to any other easily fermented fibre (27).

Mechanisms behind the laxative effect

The laxative effect of GOS is believed to be caused by its action as a soluble fibre. Oligosaccharides pass undigested into the large intestine and stimulate bacterial fermentation in the colon. The bacterial fermentation of oligosaccharides increases bacterial mass, which in turn increases faecal bulk. Undigested oligosaccharides and fermentation products may also produce an osmotic effect in the gut, which increases the water content of faeces (28). The increased bowel content stimulates peristalsis in the colon (26). However, studies so far with 10 g (9) or 15 g (19) have been unable to demonstrate any significant effect of GOS on stool weight.

In addition, GOS may alter bowel function through a change in the colonic environment. *In vitro* studies have shown that the bacterial fermentation of oligosaccharides increases the production of short-chain fatty acids (SCFAs) (11, 29), which

lowers colonic pH (28). The lower colonic pH may stimulate the growth of lactobacilli and bifidobacteria and suppress the growth of undesirable bacteria (29). SCFAs may also affect intestinal motility, but the clinical relevance and mechanisms of this action remain uncertain (30). In humans, the results of the studies examining the effects of GOS on the concentration of SCFAs in the faeces are contradictory (18, 19). It should be noted that the increase in the production of SCFAs in the colon is difficult to determine in humans, because SCFAs are rapidly absorbed in the gut, and thus the amount of SCFAs in the faeces does not necessarily correspond to their intracolonic production (11).

Conclusions

Several clinical trials have shown that the use of GOS may reduce the severity of mild constipation. In constipated people, the ingestion of GOS has softened stools, increased defecation frequency and facilitated defecation. The laxative effect of GOS is more marked in people with low defecation frequency, and in adults with normal bowel function the effects of GOS may be limited. In infants, the supplementation of formula with a prebiotic mixture of GOS/FOS can modulate bowel function and stool characters in the same direction as does breast-feeding. Gastrointestinal symptoms, which are common side-effects of all fibre, may occur after the ingestion of GOS. However, amounts of 12 g or less daily are usually well tolerated. The bulking capacity of GOS remains to be clarified in future studies.

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