**Original article**

# The prebiotic effects of a new mixture of soluble fermentable fibres in the treatment of chronic constipation

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## INTRODUCTION

Chronic constipation is a multifactorial polysymptomatic disorder very common in the western population. Though constipation is a widespread condition, its real prevalence and incidence are difficult to quantify because of the definition itself, which varies among physicians and laypersons, and because only a small part of people who perceive they have constipation seek health care. Chronic constipation has become a significant health problem, especially in the female population. It is associated with impairment of quality of life and high levels of psychological distress.[1]

A recent systematic review estimates the prevalence of constipation in Europe to be 17.1% (median value 16.6%) [2] and epidemiologic studies based on householder surveys in North America suggest a prevalence of 15% to 20% especially in people over 65 years old with a ten year cumulative incidence estimated at 17.4%.[3-6] These prevalence rates were calculated using the Rome II criteria. However for self-reported constipation the prevalence rises up to 29.5% with approximately 1/3 of subjects dissatisfied with their bowel function.[7-8]

Idiopathic chronic constipation can be divided into slow transit constipation, outlet defecation syndrome and functional constipation but it is possible for different types to exist in the same patient with an overlapping of different subtypes. Many factors are implicated in the causation of chronic constipation: age, sedentary lifestyle, insufficient intake of fluid and fibre and a wide range of conditions such as medication, endocrine and metabolic disorders, neurological and gastrointestinal disease.[9]

Fibres are an important index of quality of a balanced diet.[10] Epidemiological studies have suggested that there is a critical faecal wet weight of 160-200 gr/day for adults below which transit time falls.[11] Using this critical faecal mass the adequate daily intake of dietary fibre ranges from 30 to 40 gr/day (14g per 1000 Kcal).[12] Fibres are a wide variety of substances that belong to the family of carbohydrate and are not absorbed by the human digestive tract.[13]

High-fibre diet and prescription of fibre like bulking agents are very common in primary and secondary care management of constipation. Products with different types of fibres have been available for constipated people: wheat bran and dietary supplements with active ingredients like arabic gum, partially hydrolyzed guar gum, psyllium pectins, methylcellulose.

In our study we decided to treat constipated patients with the association of gum arabic (GA) and fructo-oligosaccarides (FOS). GA is a soluble fermentable resin containig 85% of fibre obtained from the natural agricolture with a prebiotic effect favouring the growth of Bifidobacteria, Bacterioides and acidogenic bacteria.[14]

The GA is a dried exudate of the acacia tree (Acacia senegal), a tree commonly encountered in various tropical and subtropical regions of the world and prevalently in Sudan. It is a heteropolysaccharide of high molecular weight (approximately 350-850 kDa) containing galactose, rhamnose, glucuronic acid and arabinose residues and also minerals like calcium, potassium and magnesium.[15] GA is a fermentable soluble substance with mechanical and metabolic effects: delaying gastric emptying, increasing faecal bulk and frequency of bowel movements, regulating colonic transit time, slowing glucose absorption from the small intestine with reduction of postprandial blood, serum total cholesterol and low density lipoproteins.[16-19]

The FOS and inulin when present in diet are the only short-chain carbohydrates prebiotics that had shown a significant increase in stool output in constipated patients, due to a modification of micro-organisms in the gut.[20-22]

The aim of our pilot study is to evaluate the effectiveness of an association between GA and FOS (FD Fibre Liquid, Dalco srl, Mirano-Venice, Italy) in the treatment of chronic constipation. The blend would combine effects of the soluble fibre with prebiotic effect of the short chain carbohydrate.

## PATIENTS AND METHODS

Patients were recruited from the outpatient clinic of the Department of Surgery, University of Padua, Italy (Clinica Chirurgica 2) and were observed over a fifteen week period. Inclusion criteria were age 18-90 years with functional constipation as defined by the Rome III criteria.[23] Exclusion criteria were concomitant medication that could modify bowel transit, inflammatory bowel diseases, previous gastrointestinal surgery, severe liver, cardiac and kidney diseases, pregnancy, uncontrolled diabetes. All subjects gave written informed consent.

Patients were evaluated with the I.P.G.H. scoring system (Incontinence, Pelvic floor, General, Handicap) [24-25] and constipation was quantified by the "*constipaq score system*" (Tab. 1) a modified Constipation Scoring System (CSS).[26] Constipation was classified as mild for a constipaq score 6-10, moderate for 11-15 and severe for score >15. To exclude obstructive causes of constipation all patients had a colonoscopy or a barium enema.

A basal intestinal transit time study was performed in all patients. In patients with suspected obstructed defecation (Obstructed Defaecation Syndrome Score >9),[27] also a defecography was done.

Constipation was evaluated with a diary where the patients indicated the time of bowel movements, obstruction/straining/anal pain at defecation (yes/no), sense of incomplete evacuation (yes/no), abdominal discomfort/bloating/pain (yes/no), time spent in toilet (minutes), help for defecation (laxatives, suppositories, enema, digitations), number of unfruitful attempts, impairment of the daily activities (mild, moderate, severe, i.e. quality of life scale 0-3).

At visit 1 medical history was collected, a physical examination performed and the constipaq score calculated.

At visit 2, after a 21-days washout period, when the patients avoided laxatives or enemas, the score was calculated according to the diary. If the score was more than 5, patients were given daily active treatment for three weeks: 11.7 g of GA plus 4.7 g of FOS. During the treatment period

Table 1. – *Constipaq system code*.

| | | | | | |
|---|---|---|---|---|---|
| **C** | *stool frequency (number of defecation)* | | **O** | *obstruction, pain, straining* | |
| | **0** | >2 per week | **0** | never | |
| | **1** | 2 per week | **1** | < 1 per month | |
| | **2** | 1 per week | **2** | 1-4 per month | |
| | **3** | <1 per week | **3** | 1-2 per week | |
| | **4** | <1 per month | **4** | >2 per week | |
| **N** | *incomplete defecation* | | **S** | *abdominal discomfort, pain, bloating* | |
| | **0** | never | **0** | never | |
| | 1 | < 1 per month | **1** | < 1 per month | |
| | 2 | 1-4 per month | **2** | 1-4 per month | |
| | 3 | 1-2 per week | **3** | 1-2 per week | |
| | 4 | >2 per week | **4** | >2 per week | |
| **T** | *time spent in toilet (minutes)* | | **I-P** | *helps for defecation* | |
| | **0** | <5 | **0** | <1 per week | |
| | **1** | 5-10 | **1** | laxatives, suppositories ≥1 per week | **I** |
| | **2** | 10-20 | | | |
| | **3** | 20-30 | **2** | enema, digitation ≥1 per week | **P** |
| | **4** | >30 | | | |
| **A** | *unfruitful attempts(n°)* | | **Q** | *duration of constipation (year)* | |
| | **0** | never | **0** | <1 | |
| | **1** | 1-3 per day | **1** | 1-5 | |
| | **2** | 4-6 per day | **2** | 6-10 | |
| | **3** | 7-9 per day | **3** | 11-20 | |
| | **4** | >9 per day | **4** | >20 | |

***constipaq*** = CCS (0..30) + ***number of capital letters*** (0..9) + ***QoL*** (0..3) x ***n***

no other medications were allowed for constipation. The score was calculated at the end of the treatment (visit 3) and at the end of the following 9 weeks (visit 4).

At each visit patients returned the diary and underwent a physical examination. At visit 3 they were asked about tolerability of treatment (smell, taste, modality of intake). The presence of other symptoms including abdominal pain or cramps, bloating or nausea was recorded. Serious adverse events were communicated immediately by the patients.

## STATISTICAL ANALYSIS

The population size of the study could not be determined previously due to the lack of information on the subject; this is the reason why the study is defined as pilot. A descriptive analysis was performed by evaluating sex, age, weight and height distribution in the study population. The treatment efficacy was studied comparing the data at the three visits by means of homoschedastic "t" test; the results were considered significant for $p < 0.05$.

Table 2. – *Demographic data*.

| ***Parameter*** | ***Group A (15) AG-FOS*** |
|---|---|
| *Sex, n (%)* | |
| Female | 15 |
| Male | 0 |
| *Age (years)* | |
| Mean | 60.2 |
| Range(min-max) | (41-71) |
| *Weight (Kg)* | |
| Mean | 64.9 |
| Range(min-max) | (55-84) |
| *Height* | |
| Mean | 160.3 |
| Range(min-max) | (154-170) |

## RESULTS

From November 2006 to February 2008 fifteen women were enrolled. The demographic features of the population study are summarized in Tab. 2.

Seven patients (47%) had been constipated for more than 10 years. Fourteen patients (93%) had consulted less than three doctors for their problem.[28-30] The mean constipaq score at the enrolment was 21.4±4.7 with 14 (93%) severely and 1 (7%) mildly constipated patients (Tab. 3, Fig. 1-2). The mean Obstructed Defaecation Syndrome Score was 9.4±2.2.

After the treatment (visit 3) the mean score decreased significantly to 16±7.7 ($p<0.001$) (Tab. 3, Fig. 1-2): 12 patients showed a reduction of the score from severe to mild (7) or moderate (5) constipation. A reduction in the score was anyway observed in the three patients still suffering for a severe constipation. The Obstructed Defaecation Syndrome Score fall to a mean value of 6.8±3.

Before the treatment patients were mildly (9) and moderately (4) limited in their daily activities due to difficult defecation, sense of incomplete evacuation and abdominal discomfort/bloating/pain. After treatment there was a significant improvement in quality of life. In Tab. 3 the quality of life score is the result of QoL scale (0-3) multiplied for the number of doctors consulted for constipation. At visit three the improvement in constipation symptoms was related to

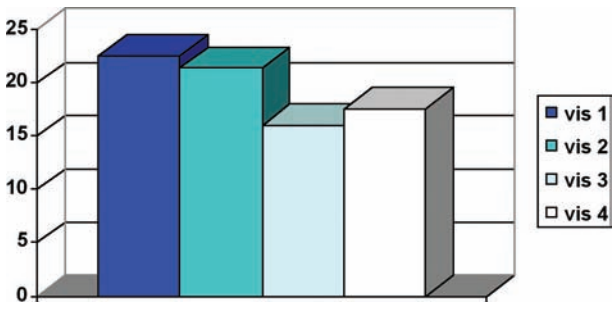

Fig. 1. – Constipaq score.

a better quality of life with the reduction of the score ($p < 0.05$) (Tab. 2).

The score reduction after 9 weeks (visit 4) was also significant compared to visit 2, with an improvement of QoL ($p<0.05$) (Tab 2).

## DISCUSSION

From 1990 to 2005 in our Proctology and Pelvic Floor Unit 4823 constipated patients with a score >5/30 sought a solution for their problem. The three different subtypes of chronic constipation (functional, slow transit, outlet obstruction) could be treated with nutritional lifestyle measures (physical activity, fibre-enriched diet, fibre supplements) and/or with outpatients treatment (pelvic floor muscle rehabilitation, rubber band legation). Surgical options for severe constipation resistant to conservative treatment consist of abdominal or perineal procedures: subtotal colectomy in case of inertia coli and correction of internal rectal prolapse or rectocoele. Recently sacral nerve stimulation became an option for intractable constipation. Quite often however different subtypes coexist and one treatment does not solve the problem.[31]

Dietary modification with improvement of daily intake of fibres is the first step in the treatment of this chronic bowel dysfunction. Patients' low compliance for fibre bulking agents is usually due to their taste and/or the discomfort related to abdominal pain and bloating. Moreover fibre must be introduced continuously to be effective. The association of GA (a resin and not a common fibre obtained by seeds) and FOS thanks to their prebiotic action is indicated to overcome these problems.

In order to achieve the prebiotic effects favouring the proliferation of lactic acid-producing bacteria and Bifidobacteria in faecal specimen, 5-10 g per day of GA is neaded.[14, 32]

The FOS and inulin are the only oligosaccharides able to increase the faecal mass and a daily dose of 5-20 g can stimulate the growth of health promoting species (Bifidobacterium and Lactobacillus) in the stool.[22-22, 33] The FOS are rapidly fermented in the proximal bowel with a gas production increase and bloating.[34] This complaint has seldom been reported by a patient.

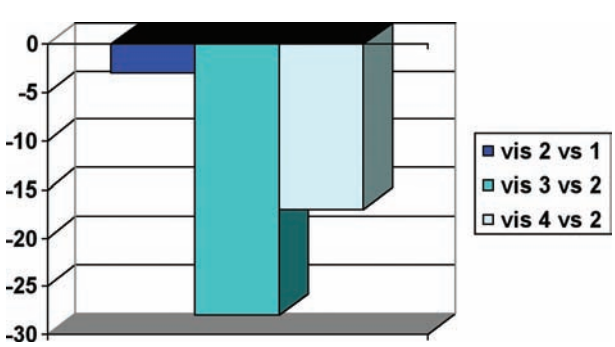

Fig. 2. – Reduction of constipaq score (%).

TABLE 3. – *Constipaq score in population study.*

| *Parameter* | *Group A (15) GA-FOS* |
|---|---|
| **C** | |
| Visit 1 | 0.53 |
| Visit 2 (wash-out) | 0.07 |
| Visit 3 | 0.07 |
| Visit 4 | 0.00 |
| **O** | |
| Visit 1 | 3.00 |
| Visit 2 (wash-out) | 2.67 |
| Visit 3 | 1.93 |
| Visit 4 | 2.93 |
| **N** | |
| Visit 1 | 3.40 |
| Visit 2 (wash-out) | 3.67 |
| Visit 3 | 2.8 |
| Visit 4 | 3.2 |
| **S** | |
| Visit 1 | 3.00 |
| Visit 2 (wash-out) | 3.53 |
| Visit 3 | 2.93 |
| Visit 4 | 3.04 |
| **T** | |
| Visit 1 | 0.8 |
| Visit 2 (wash-out) | 0.8 |
| Visit 3 | 0.6 |
| Visit 4 | 0.33 |
| **I P** | |
| Visit 1 | 1.53 |
| Visit 2 (wash-out) | 1.4 |
| Visit 3 | 0.93 |
| Visit 4 | 1.07 |
| **A** | |
| Visit 1 | 0.93 |
| Visit 2 (wash-out) | 0.87 |
| Visit 3 | 0.53 |
| Visit 4 | 0.47 |
| **Q** | 2.47 |
| constipaq score (± SD) | |
| Visit 1 | 22.6±5.5 |
| Visit 2 (wash-out) | 21.4±4.7 |
| Visit 3 | *16±7.7 |
| Visit 4 | ***17.6±6.8 |
| Quality of life score(±SD) | |
| Visit 1 | 2.9±2.1 |
| Visit 2 (wash-out) | 2.1±2.5 |
| Visit 3 | ***1.1±1.4 |
| Visit 4 | ***0.8±1.3 |

*p<0.001; **p<0.005; ***p<0.05 per visit 3 vs visit 2 and visit 4 vs visit 2.

The patients' quality of life was low due to the need to straining, feeling of anal obstruction and of incomplete defecation, abdominal discomfort, pain and bloating. Following treatment there was a significant improvement in patient satisfaction with a reduction of the QoL as well as of the CSS/constipaq scores. A 37% decrease in the obstructive defecation score was also observed, but the difference was not statistically significant probably due to the sample size.

In the literature the use of FOS as a dietary supplement has been reported in association with cereals and partially

hydrolysed guar gum.[35-36] The good taste and the long term effects of the association between GA and FOS make this mixture a promising new first option for the treatment of functional constipation.

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