Probiotics

Primary literature

Koebnick C, Wagner I, Leitzmann P, et al. Probiotic beverage containing Lactobacillus casei Shirota improves gastrointestinal symptoms in patients with chronic constipation. 2003;17(11): 655-59.

Study objectives: The aim of the study was to determine the effect of a probiotic beverage containing *Lactobacillus casei* on the gastrointestinal symptoms in patients suffering from chronic constipation.

Methods:

Design: Placebo-controlled, randomized

Allocation: Not stated

Blinding: Double-blinded

Setting: Did not state

Participants: The participants were recruited from a naturopathic practice and consist of 70 men and women aged 18 to 70 years old who suffered from chronic idiopathic constipation but were otherwise healthy.

Interventions: The treatment arm consumed a 65mL probiotic drink containing at least 6.5×10^9 *Lactobacillus casei* Shirota (LcS) and the placebo group consumed a drink of similar taste and appearance that did not contain the LcS. The study started with a run-in period of two weeks followed by the intervention of four weeks. The first assessment was performed one week after the intervention period using questionnaires.

Follow up period: Only the two weeks run in and the four weeks interventions. No long term follow ups performed.

Outcomes: The primary outcome looked at the severity of constipation, stool consistency and defecation frequency.

Patient follow up: All participants stayed in the study

Main results: The treatment group had a significantly higher improvement in self-reported severity of constipation and stool consistency that started in the second week of the intervention period ($P<0.0001$). The treatment group also experienced less moderate and moderately severe constipation and no side effects were reported. A statistically significantly higher defecation frequency from baseline in the treatment group was found during the intervention phase but this improvement became statistically insignificant after the intervention. It was also noted that the treatment group reported an improved general well being ($P<0.008$)

Conclusions: Comments/critical appraisal (including assessment of internal and external validity)

- Strengths: Randomized, double blinded and placebo-controlled trail; the treatment and placebo arms were similar; blinding of the drink was strong; no drop out rates (especially important for determining how safe the product is)
- Weaknesses: Run in period may have been unnecessary and might have impacted the results; self reported questionnaire may be inaccurate as there is potential for recall issues
- Internal validity: The sample size was relatively small and the patient's diet was not disclosed. Hence, the improvement in the severity of constipation, stool consistency and defecation may not solely be caused by the probiotic but it may be from other component of the drink or from diet/lifestyle confounding factors.
- External validity: These results are hard to validate for the general population (e.g. Canada) as the study did not provide specific details about the location of the trial. As each culture and area of the world have different diets and lifestyle, the results of this study may not applied to other cultures/areas of the world. It was mentioned briefly in the discussion that more studies were needed in Europe in order to validate the results. Hence, the study may have been performed in Europe. This study also did not exclude patients with irritable bowel syndrome.
- Overall, this study can only provide preliminary evidence for probiotics and larger and better-designed studies are needed to re-evaluate/confirm its efficacy in chronic constipation.

Yang YX, He M, Hu G, et al. Effect of a fermented milk containing Bifidobacterium lactis DN-173010 on Chinese constipated women. World J Gastroenterol. 2008;14:6237-43.

Study objectives: To determine the effects of fermented milk containing *Bifidobacterium lactis* DN-173010 and yogurt strains (BIO) on adult Chinese women with constipation in Beijing.

Methods:

Design: Randomized controlled trial

Allocation: unclear

Blinding: unblinded

Follow-up period: No further follow up period after the 2 weeks intervention

Setting: Beijing Hospital

Participants: 135 women, 35-65 years old, Diagnosed with constipation which was defined to be the following conditions: less than 3 stools per week, increased stool hardness, non-organic constipation and habitual constipation

Intervention:

- Treatment group consumed for two weeks 100g of test fermented milk
- Control group consumed for two weeks 100g of an acidified milk with non-living bacteria

- Stool frequency, defecation condition scores, stool consistency and food intake were recorded at baseline, and after the first and second week of intervention.

Outcomes: "Following consumption of test product, stool frequency was significantly increased after 1 wk (3.5 ± 1.5vs 2.4 ± 0.6,P < 0.01) and 2 wk (4.1 ± 1.7vs 2.4 ± 0.6,P < 0.01),vs baseline. Similarly, after 1 and 2 wk, of test product consumption, defecation condition (1.1 ± 0.9 vs 1.9±1.2, P<0.01and0.8±1.0 vs 1.9±1.2, P< 0.01, respectively) and stool consistency (1.0 ± 0.8 vs 1.5±1.1, P<0.01and0.6±0.8 vs 1.5±1.1, P < 0.01, respectively) were significantly improved. Compared with the control group, stool frequency was also significantly increased (3.5 ± 1.5 vs 2.5 ± 0.9,P < 0.01 and 4.1 ± 1.7vs 2.6 ± 1.0,P < 0.01, respectively), and defecation condition (1.1 ± 0.9 vs 1.6 ± 1.1, P < 0.01 and 0.8 ± 1.0 vs 1.6 ± 1.1, P < 0.01, respectively) and stool consistency (1.0 ± 0.8 vs 1.4 ± 1.0, P < 0.05 and 0.6 ± 0.8 vs 1.3 ± 1.0, P < 0.01, respectively) significantly decreased after 1 and 2 wk of product consumption."

Patient follow-up: Intention to treat protocol with 126 patients.

Main results: Statistically significant improvements were shown in all the primary outcomes. The food intake between the two arms was same. There were also no safety issues as all the safety laboratory parameters (blood, urine and stool analysis) were within the normal range.

Conclusions: The consumption of fermented milk with B. lactis DN-173010 showed an improvement in the stool frequency, defecation condition and stool consistency for adult Chinese women with constipation.

Comments/critical appraisal (including assessment of internal and external validity):
Weaknesses:
- Small sample size
- Not blinded (This un-blinding may lead to skewed results and lessen the "placebo" effect which may have influenced the results.)

Strengths:
- Controlled

External validity:
- Not applicable to all patients as the study was performed in only females and in the Chinese population in Beijing
- Not applicable to all patients as the definition of a chronic constipation is different.

Clinical Practice Guidelines

P Paré, R Bridges, MC Champion, et al. Recommendations on chronic constipation (including constipation associated with irritable bowel syndrome) treatment. Can J Gastroenterol 2007;21(Suppl B):3B-22B

Study objectives: Provide recommendations for chronic constipation as this condition has a high prevalence and there are currently no guidelines available.

Scope: Under each recommendation, different types of studies are presented. These studies include randomize controlled trials to meta-analysis. It is also specified whether these patients have chronic constipation or irritable bowel syndrome associated constipation. The Rome III criteria for functional constipation and constipation associated with irritable bowel syndrome (IBS-c) was used in identifying patients in some studies but other criteria were used as well. This guideline states the definition of chronic constipation to be the following: "The definition of chronic constipation (at least six months duration) or functional constipation is symptom based, including a combination of fewer than three stools per week, stool form that is mostly hard or lumpy, and difficult stool passage (need to strain or incomplete evacuation). Alarm symptoms should not be present. (Level B; vote: a 40%, b 60%)."

The following search terms were used for MEDLINE, PubMed or EMBASE: 'chronic constipation', 'irritable bowel syndrome', 'biofeedback', 'behavioural therapy', 'tegaserod', 'domperidone', 'erythromycin', 'lactulose', 'polyethyl- ene glycol', 'milk of magnesia', 'laxatives', 'suppositories', 'enemas', 'epidemiology', 'quality of life', 'antispasmodics', 'bisacodyl', 'miso- prostol', 'trimebutine', 'psyllium', 'ispaghula', 'bulking agents', 'docusate', 'methylcellulose', 'mineral oil', 'paraffin oil', 'diet', 'lifestyle', 'intestine function', 'gastrointestinal symptoms' and 'side effects'. An English language restriction was also used and the research time period was limited to studies adults and between 1966 and April 2006.

The consensus process for the recommendations for each therapy involved the use of a five point Likert scale. Moreover, the quality of data available was also evaluated. A recommendation was only passed if 80% of the participants voted either "accept completely" or " accept with some reservations". If less than 80% voted either one of those options aforementioned, another vote would take place after a discussion.

Methods: A consensus group of 10 gastroenterologists was formed to put together recommendations for treating chronic constipation. An outline was developed and it had addressed the following: 1) epidemiology; 2) quality of life; 3) threshold for treatment; 4) definition and diagnostic criteria; 5) lifestyle changes; 6) bulking agents and stool softeners; 7) osmotic agents; 8) prokinetic; 9) stimulant laxatives; 10) suppositories; 11) enemas; 12) other drugs; 13) biofeedback and behavior approaches; 14) surgery; and 15) probiotics. This group then developed a treatment algorithm for chronic constipation and irritable bowel syndrome associated constipation. This treatment algorithm used both evidence based approaches as well as expert opinion.

Main Results: There is not enough information to recommend the use of probiotics in chronic constipation. Only one RCT involving *Lactobacillus casei* showed some improvement in symptoms. This study did not exclude IBS patients.

Conclusions: Below is the recommendation the use of probiotics in chronic constipation: "Statement 37: There is insufficient evidence to support the use of probiotics in the treatment of CC. (Level C; vote: a 60%, b 40%)."

Comments/critical appraisal: This guideline is very comprehensive. Each recommendation was based on both evidence based medicine and expert opinion. The process of determining how a recommendation was approved was well done.

Only one trial was mentioned as it was a randomized controlled trial but including other trials would have been helpful. The critical appraisal was also very useful pointing out that IBS patients were not excluded. By not excluding these patients, it is unclear whether having IBS patients, who may be more likely to respond, lead to skewed results.

Other Literature Types

Canadian Pharmacist Association. Patient Self Care. 2010. Chapter 31: Constipation. Page 262-80.

Source of description:
Type: Textbook resource
Provided by: Canadian Pharmacist Association
Last updated in: 2012

Summary: There may be some initial data supporting the use of certain strains of probiotics for improving defecation frequency and stool consistency. These strains include the following:

- *Bifidobacterium lactis*
- *Lactobacillus casei Shirota*
- *Escherichia coli Nissle*

There is also some evidence for L. casei rhamnosus being helpful in children.
Overall, there is not enough evidence to support using probiotics for treating constipation.

Comments/Critical appraisal: The reference used for all that was stated about probiotics in the textbook was from a meta-analysis that examined the use of probiotics in patients with functional constipation. Hence, the proportion of patient with chronic constipation is unclear. The information cannot be transferred to patients suffering from chronic constipation but it is a good starting point for looking at the common strains of probiotics that have been studied.

Storr M. Chronic constipation: Current management and challenges. Can J Gastroenterol 2011;(Suppl B):5B-6B.

Source description: Narrative review, reviewed by Can J Gasteroenterol

Summary: A critical appraisal of a recent double-blinded placebo controlled RCT that consisted of patients with chronic constipation was performed in this review. This trial by Del Piano et al, involved 300 chronically constipated patients and separated these patients into three treatment arms of the following: 1) placebo, 2) lactobacillus plantarum LP01 and 3) Bifidobacterium breve BR 03 or Bifidobacterium lactis BS01. Both treatment groups showed significant improvements in symptoms compared with placebo but no differences were found between the treatment groups. The following were the critically appraisal points of the author:

- Despite the large sample size, the study included patients with very mild constipation
- Did not use the Rome diagnostic criteria
- Generalizability of study for chronic constipation is questionable

The bottom line generated in this review is that the use of probiotic is still experimental.

Comments/critical appraisal: This review provided a chart showing all the studies using probiotics specifically for chronic constipation, which makes it very easy for the reader to find more information and to compare the studies in terms of specific strains studied and duration of study. The author also provided a bottom line for the overall use of probiotics, which again is very useful for the reader. More information about each of the trial would have been more helpful.

Foxx-orenstein AE, McNally MA, Odusns ST. Review: Update on constipation: One treatment does not fit all. Cleveland Clinic Journal of Medicine. 2008;75(11): pp 813-24.

Source description: Document produced for continuing education purposes (i.g. CME credits). Approved and published in Cleveland Clinic Journal of Medicine

Summary: Probiotics may help relieve constipation. These effects are dependent on the strain of bacteria used. In one double blinded parallel study, the use of B animalis strain DN-173 010 in 70 healthy adults for 11 days reduced colon transit time by 20% from baseline. Bifodobacteria and lactobacilli have also been found in a review to have no health risk to consumers.

The use of probiotics in constipation remains inconclusive, as there are only a few well-controlled studies to date.

Comments/critical appraisal: This review is very useful for a quick update on pharmacological and non-pharmacologic treatment for constipation. However, the focus was not on chronic constipation. Hence, the summary above is not fully applicable in this situation. Moreover, only one study was presented. More trials would have been more helpful.