

Treating people with IBS:

A randomised double-blind placebo controlled trial of IntestAid® IB in people with Irritable Bowel Syndrome.

Professor Christine Dancey

and Elizabeth Attree

Presentation given by Prof C Dancey at the CAM Show, 2007

IBS is a chronic disorder with no clearly-defined cause or causes, and no general treatments which are lastingly effective. It may be that IBS consists of sub-groups of people, for which there are different causes. For instance, IBS may, in part, be heritable. Stress, food intolerances, gastroenteritis and abdominal surgery have all been implicated in IBS, as has a history of sexual abuse. Experts disagree about the contribution of these factors to IBS. IBS is defined by reference to frequency and severity of a set of symptoms; it is not a positive diagnosis. It is diagnosed in the absence of any known disease such as bowel cancer or IBD.

Participants suffer from abdominal pain which varies from mild to extremely severe, as well as diarrhoea, constipation, or an alternation of both. Urgency to have a bowel movement, a feeling of incomplete evacuation, flatulence and bloating are also present. People with diagnosed IBS suffer from 3 or more of these symptoms on a regular basis for many months or more commonly, many years. Around 15% of the population in Britain suffers from IBS, costing the healthcare and economic system millions of pounds, as well as untold misery for *millions* of people. Medical treatments can only be targeted at present for each symptom separately, since for any individual we are unlikely to know the cause. People with IBS take prescribed medicines and over-the-counter remedies, and often restrict their food intake in order to control their IBS. Some are living on extremely restricted – and therefore unhealthy – dietary regimes

We were asked to carry out a double blind randomised placebo controlled study to determine whether there were any benefits of IntestAid®IB on some of the common symptoms of IB. Symptoms which bother participants the most are pain, diarrhoea, and urgency to have a bowel movement.

IBS symptoms: Seven symptoms of IBS were analysed by time-series. These were abdominal pain, diarrhoea, urgency to have a bowel movement, incomplete evacuation after a bowel movement, flatulence, bloating, and constipation.

- ▶ Double-blind, randomised, placebo controlled cross-over
- ▶ Symptom rated from 1 to 7 every day
- ▶ 4 weeks baseline, 8 weeks
- ▶ IntestAid® IB /placebo, 4 weeks washout
- ▶ Main analysis: time-series

Participants rated symptoms every day on a scale of 1 (“no discomfort at all today”) to 7 (“very severe discomfort today”). All participants completed daily diaries throughout the trial. After an initial 4 weeks baseline, they were allotted to condition A or condition B. The capsules were taken three times a day with meals.

Seven separate interrupted time-series analyses were carried out for the seven symptoms for all participants combined. Time series evaluates the impact of the intervention(s), taking into account the patterns in the data at baseline.

Mean % improvement of IntestAid® IB over baseline and placebo

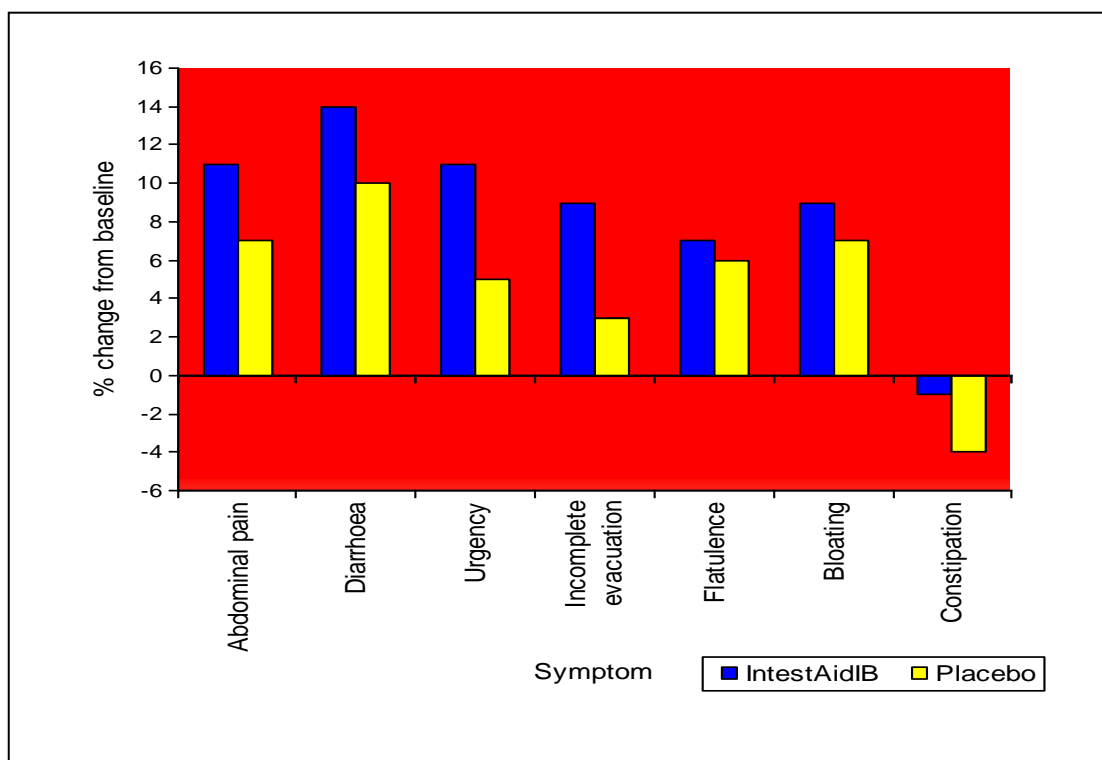
Symptom	% improvement over baseline	% improvement over placebo	Statistical significance	Reduction in severity over time
Pain	10.36	3.50	.01	YES
Diarrhoea	13.76	3.96	.08	NO
Urgency	11.09	5.96	.0001	NO
Incomplete evacuation	9.40	6.38	.001	YES
Flatulence	7.08	1.20	.60	YES
Bloating	8.37	1.47	.30	YES

The percentage of participants who showed a significant response to the condition varied from 13.9% (urgency to have a bowel movement) to 35.1% (bloating). The mean % of patients improved is 17.93 for placebo and 23.73% for IntestAid®IB, thus 5.8% of patients improved overall.

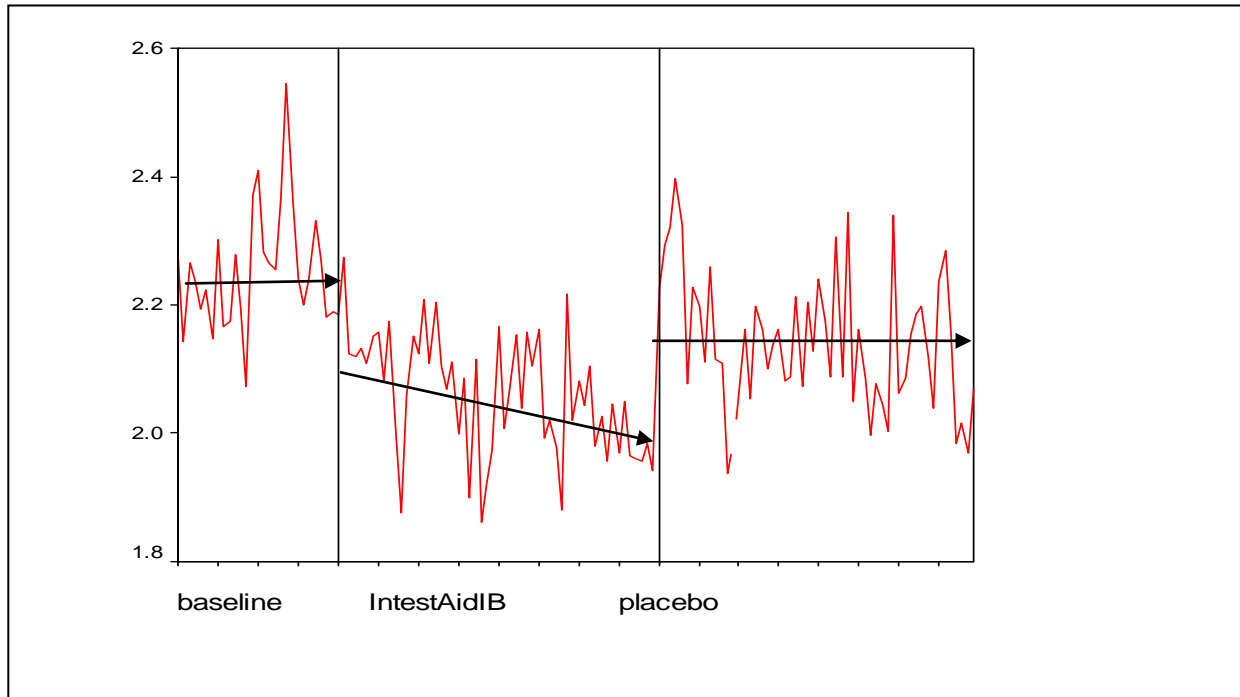
Flatulence and bloating also reduced over time in the placebo condition.

Emphasize that for all symptoms, IntestAid®IB improved symptom more than placebo, even when it wasn't statistically significant.

Sequence graph for the average participant on mean severity of total symptoms



Sequence graph for the average participant on mean severity of total symptoms



The percentage of participants who showed a significant response to the condition varied from 13.9% (urgency to have a bowel movement) to 35.1% (bloating). The mean % of patients improved is 17.93 for placebo and 23.73% for IntestAid®IB, thus 5.8% of patients improved overall.

▶ A mean of 23.73% improved on IntestAid®IB

Placebo response

▶ placebo response varied according to symptom, from 13.9% to 35.9%

▶ This gives a mean placebo response of 17.93,

So what Robin Spiller said is correct, the placebo response (approx 18%) is 3 times as higher as the size of the difference between placebo and IntestAid®IB response (6%) showing the importance of reassurance and nonspecific therapeutic effects of being in an IBS trial!. However 6% of the IBS population being improved translates into thousands of IBS sufferers. And there were no side effects reported for IntestAid®IB.

Conclusions

▶ Benefits of IntestAid®IB over placebo

▶ Variability between patients

▶ No exclusion policy in baseline means probably underestimating benefits

▶ General pattern of results all in same direction – positive effect

▶ Implications of severity of symptoms

What have we learned from this trial?

- That the **benefits of IntestAid®IB are greater** than taking a placebo – an extra 6% of people can be helped by taking IntestAid®IB, although this obscures the variability between patients – some patients were helped a lot, and some weren't.
- Also, that IntestAid®IB helps certain symptoms more than others – abdominal pain, urgency to have a bowel movement and incomplete feeling of evacuation. **Many studies exclude patients whose symptoms improve** over the run up period – but we didn't, thus we have probably underestimated the percentage of people benefitting from IntestAid®IB.
- Also, since some of the **symptoms showed improvement over time** – such as abdominal pain, a longer trial may have shown larger benefits, especially as the placebo effect does not begin to decrease until the 12 week period (Spiller, 1998). *Those participants who showed an improvement on IntestAid®IB are continuing with the product, and will be assessed to consider whether the improved response is real or a placebo effect.*