

Treatment of Patients with Irritable Bowel Syndrome with Eucarbon® Tablets

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Introduction

Irritable bowel syndrome (IBS) is a benign relapsing chronic disorder, characterised by recurrent abdominal pain and altered bowel function.

Patients complain of general symptoms of abdominal pain (most frequently located in the lower left quadrant), changes in bowel habits / stools, (e.g., stools may be soft-formed with pencil-size diameter), flatulence and / or abdominal distension with the onset of symptoms usually weeks or months prior to seeking medical attention.

The cause of IBS is still unknown and abnormalities in gut motility fail to explain the diverse features of IBS. Symptoms of IBS may be related with stress, depression, anxiety or other psychological manifestations, and food intolerance (most commonly lactose and gluten).

Clinical trials to evaluate optimal treatments for IBS face the dilemma of selection of appropriate endpoints, because no biological markers for this disease have been identified and patients usually complain of a wide range of symptoms, some being more prominent than others.

In the present study a simple, self-administered scoring system was used as key endpoint which proved to be sensitive and reliable to various changes of patients' complaints (Francis et al. 1997).

Eucarbon® is a mild laxative and intestinal adsorbent. Compounded tablets contain only vegetable ingredients (senna leaves and rhubarb extract) and carbo ligni (vegetable, non-activated charcoal). Carbo ligni is known to act as mild adsorbent. Dried senna leaves contain anthraquinone glycosides, calculated as sennoside B for standardisation of pharmaceutical preparations. Dried senna leaves and Rhubarb extract contain similar anthraquinone glycosides as main active components.

Methods

The design of this trial was a multinational, multicentre prospective, double blind, randomised phase III trial with a parallel control group. Two groups received tablets of identical size and appearance for a study period of 12 weeks.

The study was conducted at 35 centres in 4 countries (Austria, Belgium, Israel, Morocco). A total of 5 visits was planned (screening, baseline, 3 control visits after 4, 8 and 12 weeks after start of therapy).

At regular 4 weeks intervals during treatment, patients were assessed for severity of complaints using questionnaires (slightly modified Francis Score, with an open upper boundary). Response was assessed up to the end of week 12, according to the Francis Score.

Patients fulfilling the Roma Criteria for IBS for at least 3 months and fulfilling all in- and exclusion criteria were eligible. All forms of IBS could be included.

Other organic intestinal diseases in particular malignant diseases were to be excluded (diagnosis of IBS "per exclusionem").

Each patient received Eucarbon or carbo ligni tablets. During the first 4 weeks, the physician was allowed to adapt the dosage to individual needs, starting between 1x1 tablets to 8 tablets per day.

Eucarbon is a registered product (Eucarbon®, produced and distributed by F. TRENKA GMBH, Vienna, Austria). Tablets have the following composition:

Extr. Rhei 25.00 mg
Fol. Sennae 105.00 mg
Carbo Ligni plv. 180.00 mg

Carbo ligni tablets were identical in size, taste and appearance, but did not contain senna and rhubarb.

Primary endpoint was the overall well being of patients, measured by a Visual Analog Scale (VAS) 0 - 100 mm and was analysed by confirmatory statistics (Mann Whitney test, two sided, alpha = 0.05, beta = 0.10).

Results

284 patients were treated with Eucarbon or carbo ligni. A total of 262 and 144 patients were evaluated for Intention-to-treat (ITT) and Per-Protocol-Analysis (PP) resp., the remaining had missing data sets.

There was no difference in the demographic parameters between the two treatment groups (Table 1), nor in the other baseline clinical features.

Table 1 Patient characteristics at entry

	Eucarbon (ITT)	Carbo ligni (ITT)
All	131	131
Female	91	85
Male	40	46
Age (years)	42	42,5
Mean (±STD)	(±11,2)	(±11,6)
Height (cm)	165,7	166,8
Mean (±STD)	(±8,2)	(±8,7)
Weight (kg)	68,8	69,6
Mean (±STD)	(±12,8)	(±13,1)

Disease characteristics

Tenderness	n=89 (68%)	n=80 (61%)
Tympany	n=89 (68%)	n=83 (63%)

The number of patients who had been prescribed a daily dose of 1-3 tablets, 4-6 tablets or more than 6 tablets respectively, was similar although a trend could be observed (Table 2):

Table 2 Study medication given at the beginning (V2) and after 4 weeks, visit V3 (change of dosage was possible)

	Eucarbon (n=131)	Carbo ligni (n=131)
Prescribed 1-3 tablets / day		
at start of study	62	74
at visit V3	77	72
Prescribed 4-6 tablets / day		
at start of study	65	55
at visit V3	45	49
Prescribed > 6 tablets / day		
at start of study	4	2
at visit V3	4	6
Compliance (%)	96,2	96,9

In the Eucarbon-group after 4 weeks of treatment a much greater number of persons got 1-3 tablets (62 → 77 patients, versus carbo ligni: 74 → 72 patients).

Patients receiving 4-6 tablets: this change also was more pronounced in the Eucarbon-group (65 → 45 versus 55 → 49 patients).

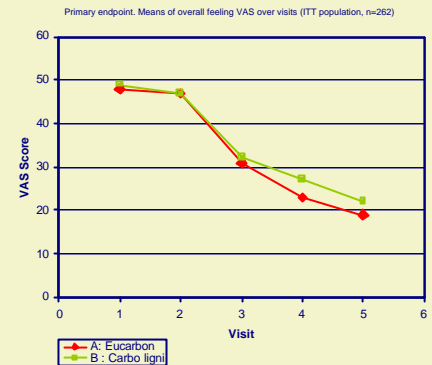
Patients receiving more than 6 tablets: Eucarbon patients remained constant (4 → 4), control patients increased 3 fold: 2 → 6.

This might be interpreted as meaning that in the Eucarbon group the pain and symptom relief is faster and greater, therefore the drift to use fewer tablets was stronger.

Improvement of the "overall feeling" (VAS scale) is very pronounced in both treatment groups (Figure 1), the difference between the treatments being consistently better in the group treated with Eucarbon (both ITT and PP-analysis) in all aspects analysed.

The relative gain in terms of efficacy of the final formulation Eucarbon compared to its basic component charcoal is about 8-9 %.

Figure 1 Primary endpoint. Means of overall feeling VAS over visits



Both treatments, Eucarbon and carbo ligni, were well tolerated. Adverse events occurred with a similar frequency in both groups (21% of patients treated with Eucarbon vs. 17% treated with carbo ligni). Most of them were mild or moderate and of gastrointestinal nature, therefore not to distinguish easily from symptoms related to IBS.

Discussion

Both treatments, Eucarbon and surprisingly carbo ligni, the main component of Eucarbon tablets as well, improved gastrointestinal symptoms of patients suffering from IBS. Overall improvement is by more than 50%, in the population analysed according to the principle of "intent-to-treat" as well as "per protocol". More patients of their carbo ligni group (25 versus 19) showed worsening of their overall Francis Score. A further interesting aspect is that in the carbo ligni group, three times as many patients (9 vs. 3) needed treatments for gastrointestinal problems during the 12-weeks study period. As there is no experience with carbo ligni in this indication, further research has to be done to evaluate if this component may be effective in some subgroups of IBS in a special manner, in cases of infection e.g.

Conclusions

The herbal drug Eucarbon® is considered to be effective and safe in the indication IBS. This is particularly important in view of the fact that IBS is a chronic disease needing long term treatment and in view of a recent withdrawal of alosetron hydrochloride from the market for reasons of serious adverse events (death due to ischemic colitis).

Reference

Francis CY, Morris J, Whorwell PJ.

The irritable bowel severity scoring system: a simple method of monitoring irritable bowel syndrome and its progress. Aliment Pharmacol Ther. 1997; 11: 395 - 402

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