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Efficacy and safety of bisacodyl in the acute treatment of constipation: a double-blind, randomized, placebo-controlled study

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SUMMARY

Background
Although laxatives are a first-line treatment for constipation, there are few randomized placebo-controlled trials assessing their efficacy.

Aim
To determine the effect and safety of oral bisacodyl on stool frequency and consistency in patients with idiopathic constipation.

Methods
55 patients (age 19–89 years) with idiopathic constipation were recruited from eight primary care practices and randomized to receive bisacodyl, 10 mg once daily, or placebo, on three successive days following a 3-day run-in period. Patients recorded stool frequency and consistency and adverse events.

Results
In each treatment group, 27 patients were evaluable for efficacy. The mean number of stools per day was significantly greater in the bisacodyl-treated group (1.8/day) compared with placebo (0.95/day) over the treatment phase ($P = 0.0061$). Mean stool consistency score improved from 'hard' (run-in) to between 'soft' and 'well-formed' during bisacodyl treatment, remaining between 'moderately hard' and 'hard' for placebo treatment ($P < 0.0001$). The investigator's global efficacy score was superior for the bisacodyl group compared with placebo. Both treatments were well tolerated. Serum electrolyte levels and incidence of adverse events were comparable between treatment groups.

Conclusions
Bisacodyl is effective and safe in improving stool frequency and consistency in acute treatment of idiopathic constipation.

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INTRODUCTION

Chronic, idiopathic constipation, described as decreased bowel frequency or the excessive need to strain during defecation,[1] affects up to 28% of the population in developed countries.[2–4] It has a significant impact on quality of life and represents a considerable burden on healthcare systems. It is a particular issue in the elderly.[2, 5–7] In the United Kingdom, it is estimated that 3 million general practitioner consultations per year relate to constipation.[8] Modifications to diet, including an increase in fibre-containing foods, can bring benefit to certain patients but, often, additional medical treatment is required. Of the alternatives available, laxatives are a preferred first-line treatment,[9] given a general acceptance of their rapid onset of action (especially the stimulant laxatives), overall efficacy and safety profiles. Surprisingly, however, there is a relative paucity of reports on formal clinical studies of their efficacy and safety and only very few double-blind, placebo-controlled trials are available.[10–15] Indeed, Ramkumar and Rao have concluded recently that there are very few laxative preparations for which there are sufficient clinical trials data to support or reject their use in the treatment of constipation.[13]

Bisacodyl [4,4′-diacetoxy-diphenyl-(pyridyl-2)-methane] has been used as a first-line laxative throughout the world for many years. Clinical experience suggests that it is highly effective, yet only few controlled studies are available that examine its efficacy. Bisacodyl is a prokinetic with a hydrogogue effect, a contact laxative, which acts locally in the large bowel by directly enhancing motility, reducing transit time[16–23] and increasing the water content of the stool.[24] Its delivery is therefore targeted at this part of the gastrointestinal tract. Administered as a sugar-coated formulation, bisacodyl is resistant to cleavage in the stomach and small intestine, and is therefore delivered to the colon essentially intact. Deacetylation of bisacodyl, under the influence of endogenous enzymes in the colon, leads to formation of the active diphenol; the time to onset of action (stimulation of colonic peristaltic activity) being approximately 6–12 h after oral administration.[25, 26]

As is the case for all laxatives that have been in use for a long time, most published studies on the efficacy of bisacodyl are of uncontrolled design, with a few exceptions of randomized-controlled studies.[27–29] Nevertheless, there is general acceptance of the efficacy of bisacodyl and it is used frequently as the rescue medication in studies of other agents being tested for their effect in patients with constipation.[30, 31]

The 'Rome II Committee' has developed guidelines with regard to diagnostic criteria for functional bowel disorders and the conduct of clinical trials to evaluate new treatments and these have often been adopted, particularly for registration studies with new drugs.[32–34] However, the diagnostic criteria and some aspects of the recommendations for study design within these guidelines do not necessarily reflect normal clinical practice. For example, laxatives are often used in the short-term for acute intermittent constipation; the benefit of laxatives used in the short-term needs to be established.

The aim of the present randomized-controlled study was to establish the efficacy and safety of once daily treatment for 3 days with bisacodyl tablets vs. placebo in adult patients with a history of constipation, and presenting with an acute episode. The study was intended to reflect the situation in a general practice setting, where patients present, not infrequently, requiring short-term or intermittent therapy.

MATERIALS AND METHODS

Patient population

The study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee of the Landesärztekammer Hessen in Frankfurt, Germany. All patients gave their written, informed consent and were free to withdraw from the trial at any time. They were not compensated for the time and effort involved in their participation in the study.

Male or female patients, aged 18 years and above, presenting with an acute episode of constipation and who had a documented history of constipation well known to the investigator, but otherwise were in good health, were eligible for the study. The duration of the history of constipation was not recorded. Constipation was defined[35] as <3 bowel movements per week, on average, during the last 3 months, and/or with excessive need for straining, hard stool, low stool weight or sensation of incomplete evacuation in more than a quarter of the evacuations.[31, 32] Previous studies have found a good correlation between patient reported

constipation and a diary record.[30] No diary was used prior to entry.

Patients with constipation associated with drug treatment, organic disease such as tumours, strictures, inflammatory disease, obstructive conditions, other gastrointestinal disorder, or a history of gastrointestinal surgery were excluded. Patients who, during the previous week, had ingested any drug that, in the opinion of the investigator, would have an effect on gastrointestinal motility were also not entered into the study. The patients were requested not to take milk or antacids at the same time of the ingestion of the enteric-coated tablets, as these would dissolve the enteric-coating prematurely. Female patients of child-bearing potential were included on confirmation of a negative serum pregnancy test and were obliged to use contraception during the study.

The concomitant use of any agents likely to cause changes in gastrointestinal motility or electrolyte balance was not permitted.

Trial design

This was a Phase IV, multicentre, double-blind, randomized, placebo-controlled, parallel group design study in patients attending out-patient general practice clinics. Eight general practices in Germany participated in the trial.

The study consisted of a 3-day run-in (days 0, 1 and 2), which was the baseline period, three treatment days (medication administration at bedtime of days 2, 3 and 4) and three treatment recording days (the days following medication administration the previous evening; days 3, 4 and 5).

Patients were randomized to receive either 10 mg bisacodyl, as two 5 mg sugar-coated tablets (Dulcolax, Boehringer Ingelheim, Ingelheim, Germany), or matching placebo tablets, to be taken orally, once daily. Patients were assigned a patient number in sequential order as they presented and were enrolled into the study. The randomization ratio was 1:1. Unused medication was collected at the end of the treatment period.

Patients were examined by the investigator prior to commencement of the study, prior to dosing following the 3-day run-in period and on completion of the study.

Blood samples were taken on study days 2 and 5 for haematological and serum chemistry tests. Samples were analysed for haemoglobin, haematocrit, white blood cell count (with differential count), platelets, blood urea nitrogen (BUN), lactose dehydrogenase (LDH), creatinine, alkaline phosphatase, serum glutamic oxaloacetic transaminase (=aspartate aminotransferase; SGOT), serum glutamic pyruvic transaminase (=alanine aminotransferase; SGPT), total bilirubin, total protein, γ-glutamyl transferase (GGT), albumin and serum electrolytes (Ca^{++}, K^{+}, Na^{+}, Cl^{-}), as well as serum hCG in female patients of child-bearing potential.

Patients were asked to keep a diary during the run-in period and throughout the course of the treatment phase. Information recorded included the number of bowel movements per day, consistency of stools and the occurrence of any adverse events.

Primary efficacy variables

There were two primary efficacy end points.

1 Mean of the total number of stools per day during the three treatment days.

2 Mean stool consistency during the three treatment days.

The first primary end point was calculated for each subject as the arithmetic mean of the total number of stools per day averaged over the three treatment days. The calculation of the co-primary end point was based on the daily stool consistency score obtained by the sum of the individual consistency scores of the stools divided by the number of stools on that day. The mean stool consistency score during the treatment days per subject was the arithmetic mean of the three daily stool consistency scores from this subject. Consistency of stools was scored on a 5-point rating scale (1 = liquid, 2 = soft, 3 = well formed, 4 = moderately hard, 5 = hard).

Secondary efficacy variable

A global assessment of efficacy was made by the investigator on the basis of their evaluation of the severity of constipation compared with baseline, using a 4-point rating scale.

1 Worsened = worsening of either the number of bowel movements or the consistency of stools while the other either worsened or remained unchanged.

2 Unchanged = number of bowel movements and consistency of stools remained unchanged.

3 Somewhat improved = improvement of either the number of bowel movements or consistency of stools while the other remained unchanged.

4 Significantly improved = improvement in both the number of bowel movements and consistency of stools.

Safety and tolerability

Patients were asked to record any adverse events in the diary on a daily basis. Adverse events were mapped to preferred terms and body systems and coded using the WHO-Adverse Reaction Terminology (ART) dictionary. In addition, the occurrence of any adverse event identified through questioning by the investigator was recorded. All adverse events were assessed and recorded in detail by the investigator and reported, in accordance with regulatory definitions, in terms of severity, duration and outcome, aetiology and relationship to the study drug.

The investigator recorded any interruption of treatment and made a global assessment of tolerability at the end of the study, using a 4-point rating scale (very good, good, fair or poor).

Haematology and serum chemistry tests, including serum electrolytes, were evaluated on study days 2 (baseline phase) and 5 (conclusion of treatment phase). Analyses were undertaken at an accredited laboratory local to each investigator site. Where values for a given sample were outside the normal range, the analysis was repeated to confirm the findings. Abnormal values were recorded by the investigator on the case report form and an assessment was made of their likely aetiology.

Statistical analysis

The required sample size was estimated to be 28 patients per treatment group, giving the study a power of at least 80% to detect a difference of 40% between the bisacodyl and the placebo group in the percentage of patients with improvement in both the total number of stools per day and stool consistency.

The null hypothesis being tested was that there was no difference between the two treatment groups in at least one of the two primary efficacy end points, i.e. either in the mean of the total number of stools or in the mean stool consistency vs. the alternative hypothesis that there was a difference between the two treatment groups for both primary efficacy end points, i.e. in the mean of the total number of stools and in the mean stool consistency. In order to conclude superiority of bisacodyl to placebo the *P*-values of the comparisons for both primary efficacy end points had to be lower than the predefined significance level of 0.05 (two-sided).

All patients who received at least one tablet of study medication were included in the safety analysis (safety set). All patients who received at least one tablet of study medication and provided at least one efficacy measurement on treatment were included in the full analysis set (FAS). All patients who maintained compliance with the inclusion/exclusion criteria, did not take any prohibited concomitant medications, remained in the study through the complete treatment period, and completed at least 75% of the diary comprised the per-protocol set (PPS).

The safety end points were evaluated descriptively for each patient treated. The efficacy end points were evaluated comparatively for both the FAS (primary analysis) and the PPS (ancillary).

For each day that a patient reported no bowel movement, a stool consistency score of 6 was assigned, and used in the calculations.

The mean of the total number of stools per day and the mean stool consistency were evaluated by analysis of variance with treatment as fixed factor. In order to assess the robustness of the results for possible departure from normal distribution the analyses for the primary end points were repeated using the Wilcoxon test.

The investigator's global assessment of efficacy and tolerability was analysed with the Wilcoxon test. The incidence of adverse events was summarized by treatment group and Fisher's exact test was used to compare the overall incidence of adverse events and those adverse events reported by at least 5% of patients in the two treatment groups. The number of patients experiencing significant changes in serum electrolytes or other laboratory measures was summarized by treatment group and a descriptive comparison was made between the groups.

RESULTS

Patients

Eight centres participated in the study. Fifty-five patients were entered, of whom 28 were randomized to receive bisacodyl, and 27 to receive placebo. One patient in the bisacodyl group was lost to follow-up prior to receiving study medication and so was not included in analyses of safety and efficacy. All

patients who received study medication completed the study and were included in the safety and primary efficacy evaluation (FAS population). Two patients (one in each treatment group) were excluded from the per-protocol analysis, both having taken prohibited concomitant medication.

Patient demographics were comparable among the two treatment groups except for age. The mean ages were 61.8 and 53.7 years, respectively, for the bisacodyl and placebo groups. This apparent difference (which was not statistically significant; $P = 0.0726$) was likely to reflect the wide range of ages and was considered to be a chance occurrence, unlikely to affect the efficacy or safety outcome measures (see Table 1).

There was a predominance of female patients in the study (39 females; 17 males), reflecting the overall higher proportion of women suffering from constipation (Table 1). All patients were Caucasian.

Sixteen of the 27 patients in the bisacodyl-treated group and 12 of the 27 patients in the placebo-treated group were taking concomitant medication during the course of the study. The most commonly treated conditions were hypertension (seven bisacodyl; eight placebo group), coronary heart disease (four bisacodyl group) and goitre (two bisacodyl; two placebo group).

Baseline data

The baseline data for vital signs and for the primary efficacy variables (mean number of stools per day and mean stool consistency) were very similar for the two treatment groups during the run-in phase (Table 1).

Table 1. Demographics and baseline characteristics (full analysis set)

	Bisacodyl	Placebo
Number of patients	27	27
Age (years)		
Mean (s.d.)	61.8 (15.2)	53.7 (17.0)
Range	33–89	19–82
Sex, *N* (%)		
Male	8 (29)	7 (26)
Female	19 (70)	20 (74)
Mean number of stools (run-in phase)		
Median	0.67	0.67
Mean stool consistency (run-in phase)		
Median	5.0	5.0

Efficacy assessment

The analysis of the two primary efficacy end points (mean number of stools per day and mean stool consistency during the treatment phase) for the FAS population indicated a statistically significant difference between the group treated with bisacodyl and the group treated with placebo, in favour of bisacodyl.

The mean number of stools per day over the 3-day treatment phase (days 3–5) for the bisacodyl treatment group (1.8 ± 1.5/day, mean ± s.d.) was statistically significantly greater ($P = 0.0061$) than that for the placebo group (0.95 ± 0.60/day). This increase in the number of stools (0.86/day; 95% CI: 0.26–1.5) in patients treated with bisacodyl brought patients into the normal population range for stool frequency. The frequency of patients in the bisacodyl group reporting at least two stools per day increased to approximately 50% on the first treatment day (day 3) compared with <15% at baseline and remained constant over the 3-day treatment period (Figure 1). In the placebo-treated group, the frequency of patients with at least two stools per day increased from 7% at baseline initially to 30% on the first treatment day, but steadily decreased during the remaining treatment days to <20%.

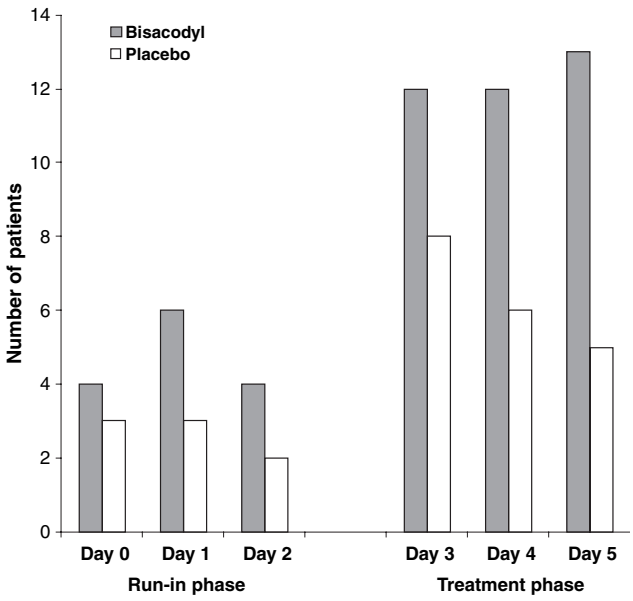

Figure 1. Number of patients with at least two bowel movements per day during the run-in and treatment phases by treatment (full analysis set).

The mean stool consistency at baseline for both groups was 5.0 ('hard'). Over treatment days 3–5 this improved substantially in the bisacodyl-treated group (score 2.8 ± 1.1, mean ± s.d.) compared with a minimal change in the placebo-treated group (score 4.2; $P < 0.0001$). In terms of the designation of stool consistency, this change of −1.4 (95% CI: −2.0 to −0.76) represented a difference between a value signifying between 'soft' and 'well-formed' in the bisacodyl group and between 'moderately hard' and 'hard' in the placebo group, suggesting a significant improvement in clinical status for the bisacodyl-treated group.

The investigator's global assessment of efficacy provided further indication of improvements in the bisacodyl group. In the bisacodyl-treated patients, 19 of 27 were assessed as being significantly or somewhat improved, compared with 14 of 27 in the placebo group although this did not reach statistical significance ($P = 0.423$ by Wilcoxon test). However, the study was not powered for this secondary end point.

Evaluation of the primary efficacy end points using the Wilcoxon test instead of the analysis of variance, as well as the analysis of the per-protocol population, yielded similar results as the primary analysis with the FAS population, supporting the robustness of the results.

Table 2. Summary of the number of patients with adverse events during the randomized treatment phase (safety set)

	Bisacodyl	Placebo
Number of patients	27	27
Patients with any adverse event	15	18
Mild	15	16
Moderate	0	2
Severe	0	0
Patients with any possibly drug-related adverse event	4	5
Mild	4	4
Moderate	0	1
Severe	0	0
Adverse events observed in at least 3 patients		
Constipation	2	5
Eosinophilia	3	4
Monocytosis	2	4
Neutropaenia	3	1
BUN increased	3	1

There was no statistically significant difference in the occurrence of adverse events between the two treatment groups. BUN, blood urea nitrogen.

Safety analysis

Of the 54 patients (27 in each treatment group) who received at least one dose of study medication, all completed the 3-day dosing regimen and were included in the safety analysis. In the bisacodyl treatment group, 15 (56%) reported a total of 37 adverse events whereas, in the placebo group, 18 (67%) patients had a total of 29 adverse events (Table 2). No serious adverse events were reported. The adverse events reported for the bisacodyl group were all rated as mild in intensity. Twenty-four (65%) of these were attributed to a concurrent condition, three (8%) were considered to be not related and 10 (27%) possibly related to the study drug. Two of the events in the placebo group were classed as moderate and the remainder as mild in intensity. Twenty-three (79%) were attributed to concurrent conditions, one (4%) was considered to be not related and five (17%) possibly related to the study drug. Only one non-related adverse event (one patient with lumbar pain in the placebo-treated group) required treatment.

The most frequently reported adverse events (Table 2) were associated with white cell and reticuloendothelial systems and related to blood counts slightly outside the normal range. Other frequently reported events included gastrointestinal, metabolic and nutritional disorders. Although most adverse events were reported as occurring during the treatment phase, there was no pattern suggesting predominance of a particular event in either treatment group. Within the bisacodyl group, the most common adverse events were an increase in urea, eosinophilia and neutropaenia (three of 27 in each case); however, only one report of mild eosinophilia was considered possibly drug related. In the placebo group five of 27 patients reported constipation, and eosinophilia and monocytosis were each reported for four of 27 patients; however, none of these was reported as possibly drug related.

There were 28 treatment emergent changes with regard to out of normal range laboratory values. Twelve of these occurred in the bisacodyl group and 16 in the placebo group. Within the bisacodyl-treated patients, three of 12 were for lymphocyte count and two of 12 for neutrophil count. All of the treatment emergent out of range values for this group were of unknown origin. In the placebo-treated patients, four of 16 were for monocytes, two of 16 for eosinophils

and two of 16 for haemoglobin. In this group, two cases (one each for monocytes and chloride) were attributed to sampling errors and three (one each for haemoglobin, haematocrit and red blood cell count) were attributed to concurrent disease or medication.

None of the adverse events, in either the bisacodyl or placebo groups, was considered to be of clinical significance. In addition, there were no clinically meaningful differences between treatment groups for any measures of haematology, serum chemistry or electrolytes (calcium, potassium, sodium or chloride).

DISCUSSION

The double-blind, randomized, placebo-controlled study reported here has evaluated the clinical efficacy and safety of bisacodyl used for the acute (3 days) treatment of constipation in a group of patients of either sex and over a wide range of ages. The study was conducted in a primary care setting.

The summary of the demographic data revealed no trends suggestive of any confounding factors when comparing the two treatment groups. None of the incidental factors, such as pulse rate and blood pressure, was considered likely to influence the key efficacy parameters.

Taking the findings for efficacy together, on the objective measures of stool number and consistency and the blinded global assessment of efficacy by the investigator, there was a clear improvement in symptoms of constipation in the group treated with bisacodyl over the 3-day period compared with those in the placebo group. The magnitude of changes in stool frequency and consistency, together with the investigators' subjective assessments, suggests that the treatment effect was clinically relevant.

The global rating of tolerability for bisacodyl was rated as 'very good' or 'good' in 26 of 27 patients. In this comprehensive assessment of safety, bisacodyl produced no clinically significant adverse effects. The hydrogogue effect of bisacodyl is considered as having the potential to cause an electrolyte imbalance. The 3 days treatment period with bisacodyl had no effect on serum electrolytes. This shows that short-term use of the recommended dose of bisacodyl does not result in such an electrolyte imbalance.

Whilst there is a substantial literature comparing the safety and efficacy of bisacodyl with other laxatives in bowel preparation for colonoscopy or colonography, there is a paucity of data on randomized-controlled trials of laxatives in general in the treatment of idiopathic constipation.[10–12] A review by Petticrew *et al.*[10] focused on studies in the elderly. The authors identified 10 studies that involved placebo-controlled or normal diet comparisons and 12 studies where two or more laxative regimens were compared. They concluded that there was insufficient evidence on which to base judgements of efficacy or cost-effectiveness. In a more general review of clinical trials of laxatives, focussing on the relatively few randomized, placebo-controlled trials found in the literature, Jones *et al.*[12] concluded that there was an overall lack of objective evidence of efficacy of laxatives in chronic constipation. Furthermore, the reported magnitude of beneficial effect of some laxative treatments, relative to placebo, was small. The data presented here, whilst in a relatively small group of patients, show clear differences between bisacodyl- and placebo-treated individuals.

Ewe *et al.*[23] compared the effects of lactose (45 g, p.o.), lactulose (30 g, p.o.) and bisacodyl (10 mg, p.o.) on gastrointestinal transit in healthy volunteers, before and after dosing with loperamide to simulate constipation. They found that, whereas lactose and bisacodyl (but not lactulose) significantly shortened small intestinal transit time, only bisacodyl shortened colonic transit time. Following administration of loperamide (4–6 mg), only bisacodyl significantly shortened transit times and was effective in doing so in the small and large intestines. In the colon, transit times were reduced by bisacodyl to 23% and 31% of controls (loperamide-free and loperamide-treated conditions, respectively). In the same study, lactulose treatment had a significant effect on stool weight (25% increase) and consistency, as did bisacodyl (more than 100% increase in stool weight). When comparing historical data from similar studies, the rank order of effectiveness as laxatives was lactulose being least effective, sennosides with intermediate efficacy, and bisacodyl most effective.

The effects of bisacodyl are mediated through a direct action on the gastrointestinal mucosa,[16–22] combined with an influence on the water content of the stool.[24] The pharmacokinetics of acid-resistant coated tablets of bisacodyl, as used in the present study, has been compared with a solution of bisacodyl, in healthy volunteer subjects. The peak plasma levels of the active metabolite bis-(*p*-hydroxyphenyl)-pyridyl-2-methane were obtained at 4–10 h postdosing with the tablet formulation, compared with 1.7 h for the solution, and reached only 3–20% of the levels observed

with the solution.[36] There was no apparent relationship between the plasma level of the metabolite and the laxative effect, suggesting that systemic absorption was not required for the laxative action and the effect was mediated locally.

The impact of constipation on the quality of life and the enormous costs to the health service (see Ref.[4, 10]) demand that simple, safe and effective treatments are available. In certain patients, changes in dietary habits and/or patterns of exercise are effective in reducing the incidence of constipation.[37] However, where dietary habits and life style are not considered to be the major cause of constipation,[38] these measures often fail to bring adequate relief, and medical intervention is required. For the majority of patients, this should be self-administered, relatively mild and predictable in its action, and free from adverse effects. Laxatives are generally considered as an appropriate treatment in patients with normal colon transit times, but impaired evacuation, and in those with slow transit.[9, 39] The choice of the most appropriate laxative will be determined by a number of factors, but principal amongst these should be efficacy, safety and tolerability. These characteristics should be established from controlled clinical trials.

The definition of constipation for the purposes of this study (<3 bowel movements per week during the previous 3 months, and/or the need for excessive straining, low stool weight and sense of incomplete evacuation in more than 25% of evacuations), although in line with the principal elements of the Rome II criteria, did not adhere strictly to them. Nevertheless, it did reflect the approach adopted by primary care doctors when presented with cases of acute constipation and, as such, was a relevant approach.

A treatment period of at least 8 weeks in duration is suggested by the Rome II Committee for studies in functional bowel disorders[34] and this is appropriate for certain drug development programmes. The treatment period adopted for the present study was shorter as the aim was to evaluate bisacodyl in the treatment of acute episodes of constipation in a primary care setting. The run-in period was also shorter than is adopted in some studies of chronic constipation. This was also considered appropriate in relation to acute episodes of constipation. Given the equivalence of baseline characteristics for the two groups and the observation of a statistically (and clinically) significant difference between them at the end of the treatment period, the short run-in period does not appear to detract from the validity of conclusions. Other studies will focus on the long-term safety and efficacy of the compound.

No attempt was made to stratify outcome in terms of possible underlying causes of constipation (e.g. 'outlet obstruction', inertia, functional). Such subclassification was not felt to be relevant in the primary care setting, was felt to be potentially poorly reproducible, and has not been shown to be predictive of a drug response in patients with constipation.[30]

The management of patients with idiopathic constipation requires a full and careful investigation[9, 40, 41] before embarking on a course of treatment. Given that, to date, there have been relatively few placebo-controlled trials of the safety and efficacy of laxatives[12] to support selection of the most appropriate alternative, further studies are warranted. Taken overall, the results of the present double-blind, placebo-controlled study demonstrate that bisacodyl is a safe, well-tolerated and effective treatment in patients with idiopathic constipation. This provides valuable supporting evidence for bisacodyl as being suitable for use in patients for whom dietary and exercise regimens have been unsuccessful, or as part of a management programme.

The use of laxatives on a long-term basis has evoked controversy. Concern has been raised previously about potential enteric toxicity from contact laxatives, although recent studies have not confirmed adverse effects.[38] Further studies are required to demonstrate long-term efficacy, although clinical experience suggests that such laxatives retain efficacy in some patients in the long-term.

In conclusion, this study has demonstrated that bisacodyl is an effective and safe laxative for the treatment of acute episodes of idiopathic constipation.

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