CURRENT MEDICAL RESEARCH AND OPINION®
VOL. 23, NO. 4, 2007, 691–699

0300-7995
doi:10.1185/030079907X178865

ORIGINAL ARTICLE

Comparison of bisacodyl and sodium picosulphate in the treatment of chronic constipation

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Key words: **Bisacodyl – Chronic constipation – Laxative – Long-term treatment – Picosulphate**

ABSTRACT

Background: Chronic constipation is a widespread condition. Although laxatives are generally accepted as being effective treatments, few studies have made formal comparisons of their efficacy and safety in chronic use.

Objective: To compare the safety and efficacy of bisacodyl and sodium picosulphate in the treatment of chronic constipation over a 4-week period.

Methods: Patients with chronic constipation (N = 144), recruited from out-patient clinics, were analysed for safety and efficacy in this open-label, randomised, parallel-group study. Patients were treated daily for 4 weeks (bisacodyl, 5–10 mg daily: 70 patients; sodium picosulphate, 5–10 mg daily: 74 patients). Primary efficacy criteria consisted of the number of bowel movements and stool consistency. Secondary efficacy criteria were straining at stool and physicians' global efficacy assessment. Safety assessments included adverse event monitoring, tolerability and changes in laboratory parameters.

Results: Both treatments were equally effective in treating chronic constipation, providing sustained improvement in symptoms. Compared to baseline, there were significant ($p < 0.001$) improvements in stool frequency and consistency and in the occurrence of straining at 14 and 28 days for both treatment groups. Based on the physicians' global assessment, a significant improvement was observed in 74.6% (bisacodyl) and 79.2% (sodium picosulphate) of patients. Neither treatment had significant effects on serum electrolytes. There was a trend for better tolerability in patients receiving bisacodyl treatment based on the number of drug-related adverse events (bisacodyl: 7; sodium picosulphate: 14, two patients withdrawn).

Conclusions: Bisacodyl and sodium picosulphate are equally well tolerated and effective in the treatment of chronic constipation over a 4-week period.

Introduction

Chronic constipation is a common condition, particularly amongst the young and the elderly and has an adverse effect on quality of life. It places considerable demands on clinical practice at the primary, secondary and tertiary levels and accounts for significant healthcare costs[1–8], and it affects about

one-quarter of the population at any time[9]. A recent estimate of the tertiary-care costs, inclusing diagnostic evaluation on patients presenting with constipation in the USA was put at $6900 million per year[10].

The symptoms of chronic constipation may be caused by structural or systemic diseases of the anus, colon and rectum, by medications that have a direct or indirect effect on the bowel and by diet and lifestyle factors. However, the symptoms of constipation frequently have no apparent physical cause.

The nature of functional disorders of the gastrointestinal tract is such that there is considerable variation in their diagnosis and management. The 'Rome II' criteria have been proposed as the basis for diagnosis of functional bowel disorders and for determining inclusion/exclusion criteria for clinical trials on therapeutic interventions[11,12]. In the case of constipation, it is proposed that positive diagnosis should be based on the occurrence of at least two of six symptoms (straining, hard stools, sensation of incomplete evacuation, sensation of anorectal obstruction, or need for manual manoeuvres to facilitate defecation in more than 25% of defecations or <3 defecations per week) for 12 weeks within a 12-month period. The Rome criteria represent useful guidelines towards achieving greater unanimity in diagnosis, especially in the design of clinical trials. Nevertheless, differences in expectation as to what constitutes normal bowel movements lead to differences in diagnostic criteria for constipation in normal clinical practice[5,13–15].

It is important to obtain clear evidence of the safety and efficacy of potential treatments. Non-pharmacological treatments for constipation may be effective in ameliorating constipation. These include a fibre-rich diet to enhance faecal bulk and stool frequency, increased fluid intake, physical exercise, abdominal massage, biofeedback and hypnosis. Many such interventions, though, have not been formally evaluated and patient compliance is often relatively poor[15–18]. Treatment with a laxative preparation is the most common pharmacological intervention and there are four main types: bulking agents, stimulant laxatives, faecal softeners and osmotic laxatives. Clinical experience of laxatives in the treatment of constipation is that, in general, they provide rapid and positive results. Surprisingly, however, despite their widespread use, there are only a few well-designed placebo-controlled studies of single agents or of comparator studies to support selection of the most effective and well-tolerated laxative preparations[18–21]. Recently, two studies showed the efficacy of both bisacodyl and sodium picosulphate in the acute treatment of constipation[22,23].

Bisacodyl is a locally-acting, triarylmethane stimulant laxative. Its sugar-coated tablet formulation means that it can reach the colon without appreciable dissolution and absorption in the upper gastrointestinal tract. The action of enzymes in the enteric mucosa and of the bacterial flora in the colon leads to the formation of the active form – free diphenol – effectively targeting the drug to the colon[24,25]. Here, it stimulates the intestinal mucosa, causing peristalsis[26]. The active moiety also causes reduction in the resorption of sodium ions and water through inhibition of the sodium and potassium-dependent ATP-ase pathway and it exerts a positive hydragogue effect on the flux of water and electrolytes in the intestine[27]. Onset of action is 6–12 h post-ingestion and clinical studies have demonstrated its safety, effectiveness and tolerability for relief of occasional constipation and irregularity[28–30]. It is also an effective bowel-cleansing agent in patients being prepared for surgery or colonoscopic examination, post-operative care (e.g., restoration of bowel function), antepartum and postpartum care and preparation for delivery[31].

Sodium picosulphate is a locally-acting, stimulant laxative, also of the triarylmethane class, with a similar mode of action to bisacodyl[25]. Taken orally, in liquid form, hydrolysis of sodium picosulphate is brought about solely by the colonic microflora and onset of action is normally 4–6 h post-ingestion[24,25,32,33].

Both compounds are employed for the treatment of chronic constipation, for bowel preparation prior to radiological or colonoscopic examination and in post-operative management[34,35]. This study compared the safety and efficacy of bisacodyl and sodium picosulphate during a 4-week treatment period in patients with chronic constipation.

Patients and methods

The purpose of this phase IV, open-label, randomised, parallel-group study was to compare the safety and efficacy of bisacodyl sugar-coated tablets versus sodium picosulphate drops as once-daily therapy for the treatment of chronic constipation over a 4-week period in an outpatient setting.

The study protocol was reviewed and approved by the Freiburger Ethik-Kommission International and the Ethik-Kommission of the Hessen Regional Medical Association. All patients provided witnessed, written informed consent prior to participating in any study-specific procedures.

A total of 146 adult patients with chronic constipation were enrolled in the study from 15 centres in Germany comprising general practice, hospital outpatient departments and specialist gastroenterology units. In order to be included in the study, patients of either sex had to be ≥18 years of age with a confirmed diagnosis of chronic constipation (i.e., fewer than three stools per week for

at least 6 months and/or a preponderance of painful stools requiring straining for the past 6 months).

Patients were excluded from the study if they had a history of organic disease of the colon, ileus, any acute surgical abdominal conditions or organic diseases of the rectum and anus. Presence of active gastrointestinal disease, obstruction or dehydration, as well as ingestion of any drug affecting gastrointestinal motility or hypersensitivity to triarylmethane compounds were also excluding factors. In order to avoid any risk associated with changes in electrolyte balance, concomitant use of diuretics, adrenocorticosteroids or cardiac glycosides was not permitted. Use of tetracycline antibiotics was not permitted. Recent (within the past 7 days) use of bisacodyl or sodium picosulphate was also prohibited. In addition, female patients of child-bearing age had to have a negative pregnancy test and to use reliable contraception throughout the study.

The study schedule comprised a total of four visits: an initial screening visit (visit 1) followed by a 7-day baseline period, randomisation to study treatment at visit 2, and two further follow-up visits at days 15 and 29. Patients were required to complete diary cards throughout the course of the study, including the run-in period, detailing consistency of stools, frequency of bowel movements, amount and severity of straining, as well as details of concomitant medications and adverse events. These diary cards were reviewed by the investigator at the clinic visits to ensure accuracy and completeness.

Blood samples were taken at visits 2, 3 and 4 for standard clinical chemistry and serum electrolyte (Na^+, K^+, Cl^-) tests.

Patients were randomised on a 1 : 1 basis to receive either bisacodyl (Dulcolax, Boehringer Ingelheim, Germany) 5–10 mg (1–2 tablets orally) or sodium picosulphate solution (Laxoberal, Boehringer-Ingelheim, Germany) 5–10 mg (10–20 drops orally). The study treatments were taken each night, just before bedtime, over a period of 4 weeks (28 days). Bisacodyl was not allowed to be taken with milk or antacids. In view of the different presentations of the two study medications (bisacodyl as 1–2 tablets once daily, and sodium picosulphate solution, taken as 10–20 drops once daily), no attempt was made to blind the study. The number of bisacodyl tablets or volume of sodium picosulphate solution returned at the end of the treatment period was cross-checked against diary records to confirm compliance.

Primary efficacy measures

The primary efficacy criteria comprised the number of bowel movements per day and the consistency of the stools. The number of bowel movements was recorded by the patient on a daily basis. The average daily number of stools was determined for the baseline and treatment periods.

A 5-point scale was adopted for stool consistency, corresponding to liquid = 1, soft = 2, well-formed = 3, moderately hard = 4, hard = 5. The daily stool consistency score was obtained as the number of stools of each consistency class multiplied by the appropriate score and divided by the total number of stools for that day.

Secondary measures of efficacy

The secondary measures of efficacy included degree of straining at stool and the physicians' global assessment of efficacy.

Straining at stool was scored on a daily basis as: absent = 0, mild = 1, moderate = 2, severe = 3, very severe = 4.

During visits 3 and 4, as a global assessment of efficacy, the investigator assigned a severity of constipation rating on the basis of the frequency and consistency of stools as reported by the patient and relating this to the status at the end of the baseline period. A 4-point rating scheme was employed (worsened, unchanged, somewhat improved, significantly improved).

Safety assessment

Safety was assessed according to adverse events spontaneously reported during the study, the patients' assessment of tolerance, and changes in laboratory parameters. Adverse events and laboratory variables, with particular attention to serum electrolytes, were monitored throughout the study.

Patients underwent a physical examination, including monitoring of vital signs, at screening and on days 1, 15 and 29 of the treatment period. Blood samples for laboratory tests were obtained on days 1, 15 and 29 and were submitted for a panel of tests including liver enzymes, blood urea nitrogen, creatinine and serum electrolytes (K^+, Na^+, Cl^-).

Statistical analysis

The null hypothesis was that there was no difference between bisacodyl and sodium picosulphate over a 4-week period in the treatment of patients with chronic constipation.

The sample size was calculated to detect a difference between treatments of 0.21 in the mean number of bowel movements over a 14-day period (assumed standard deviation of 0.31). It was estimated that a total of 126 evaluable patients (63 per treatment arm) would provide at least a 95% chance to rule out

this difference of 0.21 between the treatments with a two-sided test at the 0.05 significance level. It was estimated that a total of 180 patients (90 per treatment arm) should be enrolled to account for a drop-out rate of approximately 30 patients per arm (30%).

The primary efficacy parameters were summarised using descriptive statistics by treatment group per 14-day period and analysed by ANOVA. Changes from baseline were also analysed with ANOVA. Ninety-five percent confidence intervals (CI) for the mean difference between treatments in the change from baseline in stool frequency and consistency were generated after 14 and 28 days of treatment.

The secondary efficacy parameters were summarised by treatment group per 14-day period using descriptive statistics, and changes from baseline in severity of straining were summarised by treatment group after 14 and 28 days of treatment using descriptive statistics. Ninety-five percent CI for the mean differences between treatments were calculated.

The primary efficacy analysis was based on all patients who received at least one dose of study medication and who provided any data on treatment (intention-to-treat (ITT) data set). An evaluation with the per-protocol data set including all randomised patients who reasonably adhered to all protocol conditions was carried out for all efficacy endpoints to support the results with the primary ITT data set.

The incidence of adverse events and numbers of patients reporting clinically significant shifts in serum electrolytes and other laboratory parameters were summarised by treatment group. Comparisons between groups were made using Fisher's exact test with all randomised patients included (safety data set).

Results

A total of 144 patients (104 of whom were female), age range 23–94 years, received at least one dose of study medication and were assigned to the safety population (70 in the bisacodyl group and 74 in the sodium picosulphate group). The demographic distribution between the two treatment groups was similar with ratios of male : female patients of 1 : 2.3 and 1 : 2.9 in the bisacodyl and sodium picosulphate groups respectively (safety data set). There was no significant difference between mean ages (safety data set; p = 0.83 by ANOVA) or other demographic measures (Table 1).

Two patients were excluded from the ITT data set as they did not provide any efficacy data on treatment, leaving 142 patients in this analysis (69 in the bisacodyl group and 73 in the sodium picosulphate group) (Figure 1). An additional eight patients were excluded from the per-protocol (PP) population for reasons of protocol violation (non-compliance, missing baseline data, or prohibited concomitant medication).

Table 1. *Summary of demographic characteristics (randomised patients)*

Parameter	Bisacodyl (n = 70)	Sodium picosulphate (n = 74)
Age (years)		
Mean (SD)	63.7 (17.4)	61.8 (21.1)
Range	25–90	23–94
Sex n (%))		
Males	21 (30.0)	19 (25.7)
Females	49 (70.0)	55 (74.3)

SD = standard deviation

Of the 144 patients in the safety population, 136 (94.4%) completed the study (bisacodyl: 65 patients; sodium picosulphate: 71 patients). The eight patients who withdrew from the study did so due to adverse events (sodium picosulphate: two patients), lack of eligibility (bisacodyl: two patients), patient request (bisacodyl: one patient) and non-compliance (bisacodyl: two patients, sodium picosulphate: one patient).

In the ITT population, baseline characteristics were similar for both treatment groups for all parameters (vital signs and stool characteristics), with a mean number of bowel movements per day of 0.46 (SD: 0.32) in the bisacodyl group and 0.45 (SD: 0.38) in the sodium picosulphate group. The mean baseline values for consistency of stools were 4.1 (SD: 0.76) and 4.2 (SD: 0.72) for the bisacodyl and sodium picosulphate groups, respectively, and the mean values for straining at stool were 3.0 (SD: 0.82 and 0.92) for the two treatment groups (Table 2).

Both treatments were associated with substantial changes in both the primary and secondary measures of efficacy, with statistically significant improvements in the scores for stool frequency, stool consistency and incidence of straining at the 14 and 28 day time points (Table 2).

After 14 and 28 days of treatment, results in the ITT population showed that for both primary efficacy parameters (mean number of stools per day and mean consistency score) and for the respective changes in these measures since baseline, there were no statistically significant differences between the treatment groups (Table 2). Similar results were seen in the PP population, with the exception that the change in the number of stools since baseline appeared slightly greater in the sodium picosulphate group, although this failed to reach statistical significance (p = 0.062, CI: –0.014–0.134).

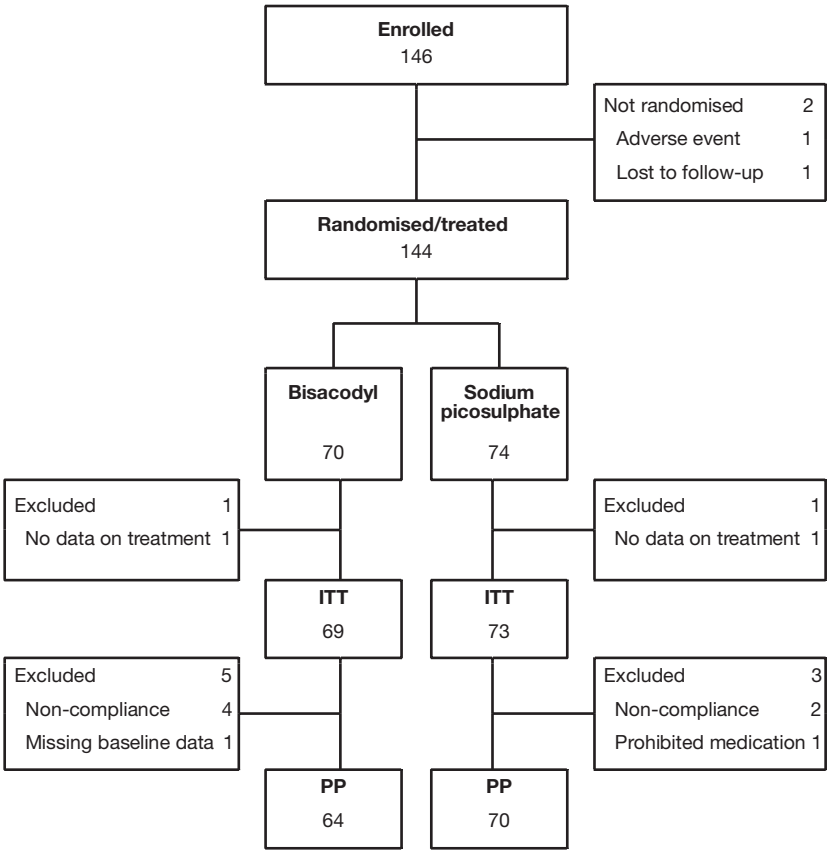

Figure 1. *Profile of the subject disposition during the course of the study and inclusion in the analysis data sets*

Evaluation of the secondary efficacy criteria corroborated the results of the primary analyses with no significant differences being seen between the treatment groups with respect to comparisons of mean straining scores, or in the magnitude of the respective changes from baseline in straining scores or changes in global efficacy parameters at both the 14 day and 28 day assessments (Table 2). There was a statistically significant improvement in straining scores relative to baseline for both treatment groups.

In the global assessment of change, 71.0% of patients in the bisacodyl and 63.0% in the sodium picosulphate groups were judged to have shown 'significant improvement' by day 14 and 74.6% and 79.2% respectively at day 28. One patient in the bisacodyl group and two in the sodium picosulphate group were considered to be unchanged at day 28 with one further patient in the latter group lost to follow-up. The remaining patients were judged to be somewhat improved.

There were no significant differences between the two treatment groups with respect to the numbers of patients reporting adverse events, severity of adverse events, actions taken in response to adverse events or relationship of adverse events to study medication. Fifteen of 70 patients (21.4%) in the bisacodyl group reported 27 adverse events compared to 17 of 74 patients (23.0%) reporting a total of 24 adverse events in the sodium picosulphate group. The majority of events were considered mild (87.5%). The most commonly reported adverse events were flatulence (bisacodyl group 7.1%, sodium picosulphate 9.5%), headache (bisacodyl group 8.6%, sodium picosulphate 6.8%) and abdominal pain (bisacodyl group 7.1%, sodium picosulphate 6.8%). No serious adverse events or deaths were reported. A total of nine patients reported adverse events that were considered related to study medication (bisacodyl: three patients; sodium picosulphate: six patients). Two patients in the sodium picosulphate group were discontinued from study medication due to adverse events (one occurrence of vertigo and one of meteorism) which were considered to be study drug-related. Administration of study medication was interrupted in another patient, while a fourth patient had a reduction in dose. No such changes in dosage regimen were required in the bisacodyl group.

With respect to laboratory parameters, most values did not change over the course of the study, although some individual patients in each group did show changes which were of unknown cause. Changes in laboratory measures between baseline and visit 3 (day 15) and visit 4 (day 29) were similar for the two treatment groups. There were statistically significant differences in values between groups for total bilirubin ($p = 0.026$) and sodium ($p = 0.0085$), but the mean changes were small and considered by the investigators to be not clinically significant; total bilirubin change between baseline and

Table 2. *Efficacy parameters at baseline and at days 14 and 28 (ITT data set)*

Efficacy parameter	Baseline		Day 14 assessment		Day 28 assessment	
	Bisacodyl (n = 69)	Sodium picosulphate (n = 73)	Bisacodyl (n = 69)	Sodium picosulphate (n = 73)	Bisacodyl (n = 67)	Sodium picosulphate (n = 72)
Number of bowel movements per day						
Mean (SD)	0.46 (0.32)	0.45 (0.38)	1.07 (0.39)	1.08 (0.42)	1.06 (0.35)	1.11 (0.45)
Change since baseline						
Mean (SD)			0.61 (0.41)	0.63 (0.34)	0.59 (0.39)	0.67 (0.43)
95% CI			0.52–0.70	0.54–0.72	0.49–0.69	0.57–0.77
p-value			< 0.0001	< 0.0001	< 0.0001	< 0.0001
Consistency score						
Mean (SD)	4.1 (0.76)	4.2 (0.72)	2.62 (0.55)	2.65 (0.51)	2.43 (0.54)	2.51 (0.50)
Change since baseline						
Mean (SD)			1.51 (0.82)	1.57 (0.71)	1.68 (0.75)	1.74 (0.69)
95% CI			1.31–1.71	1.40–1.74	1.49–1.87	1.58–1.90
p-value			< 0.0001	< 0.0001	< 0.0001	< 0.0001
Straining score						
Mean (SD)	3.0 (0.82)	3.0 (0.92)	1.33 (0.64)	1.36 (0.62)	1.20 (0.62)	1.17 (0.64)
Change since baseline						
Mean (SD)			1.69 (0.92)	1.59 (0.88)	1.81 (0.96)	1.80 (0.86)
95% CI			1.47–1.91	1.38–1.80	1.59–2.04	1.59–2.01
p-value			< 0.0001	< 0.0001	< 0.0001	< 0.0001
Global assessment of change (n (%))						
Significant improvement			49 (71.0)	46 (63.0)	50 (74.6)	57 (79.2)
Somewhat improved			18 (26.1)	25 (34.2)	16 (23.9)	13 (18.1)
Unchanged			2 (2.9)	2 (2.7)	1 (1.5)	2 (2.8)
Worsened			0	0	0	0

SD = standard deviation. Stool frequency, consistency, and occurrence of straining scores as assessed at 14 and 28 days after commencing treatment with bisacodyl and sodium picosulphate and respective differences from baseline values. p-values are for comparison between baseline and 14 day or 28 day scores. There was no significant difference between scores for the bisacodyl and sodium picosulphate groups at any time point. Analysis of data for the per protocol population yielded similar results

Global assessment of change in overall clinical status relative to baseline as determined by the investigator at 14 and 28 days

visit 4: bisacodyl –0.1 (SD 0.24) mg/dL, sodium picosulphate 0.0 (SD 0.25) mg/dL; serum sodium change between baseline and visit 4: bisacodyl 0.1 (3.44) mmol/l; sodium picosulphate: –1.5 (3.98) mmol/l (Table 3). No significant differences in vital signs emerged between treatment groups at any visits.

Based on amounts of study medication returned by patients at the end of the study, the mean consumption as a proportion of the maximum possible total dose for each treatment group over the 28 day treatment period was 63.3% (bisacodyl) and 64.6% (sodium picosulphate).

Discussion

Analysis of both primary and secondary efficacy parameters indicated that bisacodyl and sodium picosulphate are equally effective in the treatment of chronic constipation over a treatment period of 28 days. The change in the mean number of stools since baseline was slightly greater in the sodium picosulphate group compared to the bisacodyl group.

Importantly, both treatments were associated with more than doubling of stool frequency from baseline values, and a change in average stool consistency from 'moderately hard'/'hard', to 'soft'/'well-formed' at day 28. These changes represent clear improvements in clinical status.

This view is further supported by the observed improvements in secondary measures of efficacy. Thus, the score for straining improved from baseline values of 'severe', for both treatment groups to 'mild' to 'moderate' on the rating scale. The physicians' global assessment, based on the patients' diary records, concluded that significantly improved results were seen both in patients on bisacodyl and on sodium picosulphate.

Table 3. *Changes in key laboratory measures between baseline and end of 28 day treatment period*

Laboratory measure	Treatment	Baseline Mean (SD)	Final Mean (SD)	Change Mean (SD)	*n*
Total bilirubin (g/dL)	Bisacodyl	0.6 (0.27)	0.5 (0.26)	–0.1 (0.24)	62
	Sodium picosulphate	0.5 (0.25)	0.6 (0.27)	0.0*	67
Potassium (mmol/l)	Bisacodyl	4.6 (0.78)	4.5 (0.58)	–0.1 (0.68)	61
	Sodium picosulphate	4.6 (0.72)	4.7 (0.83)	0.1 (1.03)	71
Sodium (mol/l)	Bisacodyl	141.5 (4.17)	141.6 (3.48)	0.1 (3.44)	59
	Sodium picosulphate	141.3 (3.57)	139.8 (3.60)	–1.5 (3.98)**	71
Chloride (mol/l)	Bisacodyl	100.5 (5.27)	101.2 (4.97)	0.7 (6.40)	55
	Sodium picosulphate	102.0 (4.79)	100.9 (5.41)	–1.1 (7.11)	60

Baseline, measurement at visit 2 before administration of first dose of study medication; final, measurement at visit 4 after administration of final dose of study medication

*Indicates statistically significant differences ($p < 0.05$) or **($p < 0.01$) between groups by ANOVA

The tolerability profile of both treatment groups was similar, and overall, neither of the two laxatives had a detrimental effect on serum electrolyte levels. Bisacodyl and sodium picosulphate both exhibited good tolerability profiles over the 4-week treatment period. The difference in tolerability between bisacodyl and sodium picosulphate was marginal.

Patients were permitted to vary the dose of study medication within the prescribed range (5–10 mg both for bisacodyl and sodium picosulphate). Based on returned supplies at the end of the study, patients in both treatment groups took about two-thirds of the maximum prescribed dose over the 28-day treatment period, suggesting that there was a significant amount of individual titration of dose. This is an advantage of the dosage forms for both preparations with sodium picosulphate being particularly amenable to dose adjustment by 0.5 mg (dropwise) increments.

It may be argued that the absence of a placebo arm in the study leaves open the possibility that the significant and substantial improvement in the clinical status of more than 75% of patients in both treatment groups during the 4-week treatment period may incorporate a large placebo effect. In general, the placebo effect in studies of constipation tends to be lower than that seen in clinical trials in other functional gut disorders and rarely exceeds 40%[36]. Furthermore, the consistent and marked change in all of the measures at 14 and 28 days is unlikely to be attributable to a placebo response.

For both bisacodyl and sodium picosulphate, a clinically significant response, in comparison with placebo, has recently been shown in the acute treatment of constipation[22,23]. This is in full agreement with daily medical experience. However, for evidence-based medicine, efficacy and safety/tolerability over a longer period needs to be shown, in a setting answering to the current (GCP and Rome) requirements. The study reported here is aiming in this direction. More studies, especially placebo-controlled ones, should be performed.

The efficacy of lactulose was comparable to or better than that of a group of stimulant laxatives, in which bisacodyl was included; no details for the individual stimulants were given[37]. A further study showed the comparable effect of both bisacodyl and lactulose on stool weight and consistency. However, there was a pronounced shorter intestinal transit time for bisacodyl in comparison to lactulose[30]. These results are important, as lactulose is positively evaluated in evidence-based medicine reviews[21].

The primary efficacy parameter is a simple counting of daily bowel movements, an objective measure, which has been used in many clinical trials evaluating constipation. The secondary parameters are mainly based on the patients' own subjective observation and feeling. However, these parameters are generally accepted and have been widely used in studies evaluating constipation[38–40]. The parameters are judged by the patients throughout the whole study, including the run-in period, confirming an individual consistency over the whole study. The general acceptance of the efficacy and tolerability of bisacodyl can be concluded from the use of bisacodyl as rescue medication in studies on other medications for constipation[38–40].

The global assessment of efficacy was based on the investigators' observation of overall change in clinical status rather than that of the patients. Whilst this might be considered a shortcoming in the design of the study[12], the investigators' assessments were derived largely from the patients' own diary records and verbal reports during clinic visits on days 1, 15 and 29. Thus, the predominant input to the global assessment was from the patients themselves.

Patients experiencing chronic idiopathic constipation are likely to need regular therapeutic intervention over periods of many months or years[5]. The study reported here was limited to daily treatment for 28 days. This

period of exposure to the drugs should be sufficient to detect any important changes in electrolyte levels and other adverse effects. Overall, both treatments were well-tolerated. This result is in agreement with a comparative study of sodium picosulphate with standardised senna, where the possibility for individual dosing was shown to be a special advantage in elderly patients[41]. The current study does not address potential long-term changes in mucosal status. However, a retrospective long-term study (median time of 10 years) in patients with constipation treated with sodium picosulphate showed an absence of serious side-effects and there is little evidence to support the view that long-term treatment results in damage to the bowel[5,42].

Conclusion

In conclusion, the results from this study show that both bisacodyl and sodium picosulphate are well tolerated and effective agents for the treatment of chronic constipation over a 4-week course of treatment. Whilst the study detected a slight trend for sodium picosulphate to demonstrate superior efficacy, bisacodyl treatment was associated with a tendency towards better patient tolerability, based on the relative frequency of drug-related adverse events and required changes to the treatment regimen. This demonstrates that bisacodyl and sodium picosulphate laxative treatments are equally advantageous in the treatment of chronic constipation over a 4-week period.

Acknowledgements

Declaration of interest: This study was funded by Boehringer-Ingelheim GmbH.

Susanne Kienzle-Horn, Chris C. Jordan and Michael A. Kamm are consultants to Boehringer-Ingelheim GmbH.

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Paper CMRO-3836_2, *Accepted for publication*: 06 February 2007
Published Online: 21 February 2007
doi:10.1185/030079907X178865