Multicenter, 4-Week, Double-Blind, Randomized, Placebo-Controlled Trial of Sodium Picosulfate in Patients With Chronic Constipation

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OBJECTIVES: **Although it has been used as a laxative for many years, high-quality trials assessing the efficacy of the laxative sodium picosulfate (SPS) are lacking. The purpose of this study was to assess the efficacy and safety of 4-week treatment with SPS in patients with functional constipation as defined by the Rome III diagnostic criteria.**

METHODS: **This study was a randomized, double-blind, placebo-controlled, parallel-group study in 45 general practices in Germany. A total of 468 patients with chronic constipation presenting to their general practitioner and fulfilling the Rome III diagnostic criteria were screened. After a 2-week baseline period, 367 patients were randomized to either SPS drops or matching placebo in a 2:1 ratio for 4 weeks. Dose titration was permitted throughout treatment. Patients without a bowel movement for more than 72 h were allowed to use a "rescue" bisacodyl suppository. The primary end point was the mean number of complete spontaneous bowel movements (CSBMs) per week. A spontaneous bowel movement (SBM) was defined as a stool not induced by rescue medication, whereas a CSBM was defined as an SBM associated with a sensation of complete evacuation.**

RESULTS: **The mean number (±s.e.) of CSBMs per week increased from 0.9±0.1 to 3.4±0.2 in the SPS group and from 1.1±0.1 to 1.7±0.1 in the placebo group ($P<0.0001$). The percentage of patients reaching an increase of ≥1 in the mean number of CSBMs per week compared to baseline was 65.5% vs. 32.3%, respectively ($P<0.0001$). The percentage of patients reaching a mean number of at least three CSBMs per week was 51.1% in the SPS group and 18.0% in the placebo group ($P<0.0001$). After 24 h, approximately 69% of patients in the SPS group and 53% in the placebo group had their first SBM. The SPS dose was titrated down during the study by nearly 50% of patients. Assessment of quality of life (QoL) by the constipation-related Patient Assessment of Constipation (PAC)-QoL questionnaire showed significant improvement in SPS-treated patients compared to the placebo group.**

CONCLUSIONS: **Treatment of chronic constipation with SPS improves bowel function, symptoms, and QoL and is well tolerated. The dose can be adjusted individually while maintaining benefit.**

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INTRODUCTION

Constipation occurs in at least 10–20% of adults, depending on demographic factors, sampling techniques, and definitions. It affects all ages and is more common in women than in men (1). In the majority of cases, no cause can be identified. Risk factors such as lack of exercise, food, and reduced fluid intake are often mentioned as causes but evidence for most of these factors is scarce, if not absent (2). Moreover, diet and lifestyle changes often fail to relieve symptoms. In chronic constipation, treatment may be long term or, alternatively, involve

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recurring courses of short-term treatment (e.g., on demand or as a defined regime).

Bisacodyl was first developed and distributed in the 1950s and sodium picosulfate (SPS) in the late 1960s. They are both prodrugs that are both converted in the gut into the same active metabolite, bis-(*p*-hydroxyphenyl)-pyridyl-2-methane (BHPM), which causes the desired laxative effect. BHPM has a dual action, namely, an antiabsorptive-secretory effect and also a direct prokinetic effect (3,4). Bisacodyl is activated by the action of endogenous deacetylase enzymes found in the mucosa of the small intestine and colon, whereas SPS is converted by desulfatases of the colonic microflora (5,6). To have the desired effect of BHPM in the colon, we sealed bisacodyl in coated tablets that dissolve in the colon after oral intake. In contrast, SPS travels unchanged through the gut to the colon and can hence be given in any form.

Only small amounts of bisacodyl and SPS are systemically absorbed. There is no relationship between the laxative effect and plasma levels of the active diphenol because the active metabolite behaves locally and absorption is no prerequisite of activity (7). Urinary excretion reflects low systemic burden after oral administration, and no excretion in breast milk can be detected by current analytical methods (8).

Not surprisingly, much of the clinical documentation for the efficacy and safety of both compounds is relatively dated and was generated in accordance with the requirements of that time. Although the clinical efficacy of bisacodyl and SPS is generally not questioned, knowledge derived from good-quality GCP trials has until recently been rather scant. Consequently, in a paper published in 2005, bisacodyl was assigned a low level of evidence (9). Likewise, the 2005 American College of Gastroenterology Chronic Constipation Task Force stated that there were insufficient data to make a recommendation about the efficacy of these laxatives for the management of chronic constipation (10). Therefore, bisacodyl and SPS would continue to be classified as 'nonevidence-based' until results of more recent and state-of-the-art clinical trials with these products are published. Thus, we performed a randomized, double-blind, placebo-controlled, parallel-group clinical trial in accordance with ICH GCP guidelines in patients with functional constipation, as defined by the Rome III diagnostic criteria.

METHODS

This study was a randomized, double-blind, placebo-controlled, parallel-group study to assess the efficacy and safety of 4-week treatment with SPS drops (Dulcolax/Laxoberal), 10 mg administered orally once daily, in patients with functional constipation. Eligible patients entered a 2-week baseline period throughout which they were instructed to use an electronic diary (eDiary) to record bowel symptoms. Patients whose functional constipation was confirmed by the eDiary data at the end of the baseline period, and who were compliant with use of the eDiary and with the rescue medication rule, were entered into the 4-week, randomized, double-blind treatment phase.

During the 4-week trial, patients received either SPS drops (18 drops = 10 mg) or matching placebo in a 2:1 ratio. Treatment allocation and concealment were conducted by a computerized random-number generator and numbered containers of identical appearance, respectively. The SPS-matching placebo drops were identical in appearance and taste (tasteless) to the active SPS drops. Study medication was administered orally, once daily in the evening, and patients were instructed to use the eDiary throughout the 4-week treatment phase. Dose reduction, from 18 drops SPS liquid or matching placebo liquid, for the once daily intake, to 9 drops SPS liquid or matching placebo liquid, was permitted during the 4-week treatment phase of the trial on the basis of the patient's tolerability (e.g., if a patient experienced excessive diarrhea or severe abdominal discomfort). If a patient wished to reduce the dose, he/she was to inform the investigator before implementing the dose reduction. In this way, both the patient and the investigator had an opportunity to discuss the appropriateness of the dose reduction. Similarly, a patient could return to the original dose without restrictions. Multiple dose reductions and up-titrations were also permitted.

Rescue medication, in the form of 10 mg bisacodyl suppositories, was provided to the patient on entry into the baseline period, for use as required, during the entire study period. Patients who did not experience a bowel movement for more than 72 h were allowed to use a bisacodyl suppository. The use of this rescue medication was not permitted on day −1 nor on the day of randomization (day 1). Following study visits were scheduled for day 16 and day 30.

Male and female patients, ages 18 and above suffering from functional constipation according to the Rome III diagnostic criteria, (1) were eligible for the trial if able and willing to complete a daily eDiary, able and willing to use the rescue medication, and had signed written informed consent. At visit 2 (end of the baseline period), patients had to comply with the following additional inclusion criteria to be eligible for entry into the treatment phase. Functional constipation was confirmed by eDiary data according to the following definition: less than three complete spontaneous bowel movements (CSBMs) per week on average, together with at least one of the following symptoms occurring at least 25% of the time: straining, incomplete evacuation, and/or lumpy or hard stools (i.e., type 1 or type 2 stools according to the seven-point Bristol Stool Form Scale (11)). They had to be compliant with the use of the eDiary throughout the baseline period (defined as completing 80% of the eDiary evening reports) and with the use of the rescue medication.

The following exclusion criteria were applied at screening: eating disorders such as anorexia nervosa and bulimia as a cause of excessive use of laxatives; constipation caused by organic disease, metabolic, or neurological disorders; severe psychiatric disorders or any other significant disease or intercurrent illness that, in the investigators' opinion, would have interfered with participation in the trial; restricted mobility (e.g., wheelchair bound or bedridden) that, in the investigators' opinion, would have interfered with participation in the trial; known hypersensitivity to SPS or bisacodyl; ileus; intestinal obstruction; acute surgical abdominal conditions; anal fissure; ulcerative proctitis; clinically significant abnormal electrolyte values; concomitant opioid medication; constipation caused by medication in the investigators' opinion; premenopausal women who were breast-feeding or pregnant or who were of

childbearing potential and were not using an acceptable method of birth control throughout the study; participation in another trial with an investigational product within 1 month before enrollment into this study; drug or alcohol abuse; and concomitant use of antibiotics.

At the end of the baseline period, further exclusion criteria were applied: clinically significant abnormal electrolyte values, identified after the central laboratory analysis at screening visit; loose or watery stools (i.e., type 6 or type 7 according to the Bristol Stool Form Scale) for 3 or more days during the baseline period.

The primary end point was the mean number of CSBMs per week during the 4-week treatment phase of the trial. A spontaneous bowel movement (SBM) was defined as a stool not induced by rescue medication and a CSBM was defined as an SBM with a sensation of complete evacuation. Secondary efficacy end points were the number of CSBMs per week at each weekly time point during the treatment; number of SBMs per week; number of patients who had an increase of ≥1 CSBM per week compared with the last 7 days of the baseline period; number of patients who had ≥1 CSBM a day; number of patients who had ≥3 CSBMs per week; number of patients who used rescue medication; change from baseline at each of the weeks 1, 2, 3, and 4 in the mean score per week for the symptoms associated with constipation; the time (24-h clock) of the first SBM after intake of the first dose of study medication.

Scores for four additional constipation-related symptoms were collected in the eDiary: (i) the degree of straining, using the following five-point ordinal Verbal Rating Scale (VRS) and in response to the question: 'Please describe the degree of straining, if any, associated with this bowel movement' (0 = absent, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe); (ii) the stool quality, using the seven-point Bristol Stool Form Scale (1 = hard lumps, 7 = watery); (iii) the sensation of anorectal obstruction or blockage using the following five-point ordinal VRS and in response to the question: 'Did you feel a blockage in your anus (back passage) that made it difficult to pass this bowel movement?' (0 = absent, 1 = mild, 2 = moderate, 3 = severe, 4 = very severe); and (iv) Whether or not a manual maneuver was required to facilitate defecation (e.g., digital evacuation, support of the pelvic floor); a nominal scale (i.e., yes/no) was displayed to the patient on the eDiary screen in response to the following question: 'Did you need to press around your anus (back passage) or vagina to try to remove the stool to complete this bowel movement?'.

The time of the first SBM after intake of the first dose of study medication was assessed.

Scores for patients' overall satisfaction with their bowel habit over the past week were obtained using the following five-point ordinal VRS and in response to the question: 'How satisfied are you with your bowel habits over the past week?' (0 = a very great deal, 1 = a good deal, 2 = moderately, 3 = hardly, 4 = not at all). The scores for a patient's bother with constipation, abdominal bloating, and abdominal discomfort, respectively, were scored using the following five-point ordinal VRS and in response to three separate questions: 'How bothersome was your constipation over the past week?'; 'How bothersome was abdominal bloating over the past week?'; 'How bothersome was abdominal discomfort over the past week?' (0 = not at all bothersome, 1 = hardly bothersome, 2 = moderately bothersome, 3 = a good deal bothersome, 4 = a very great deal bothersome).

Global assessment of efficacy was scored using the following four-point ordinal VRS and in response to the question: 'How satisfied are you with the effect of your treatment over the past 4 weeks?' (1 = good, 2 = satisfactory, 3 = not satisfactory, 4 = bad). The investigator's global assessment of efficacy was scored using the following four-point ordinal VRS (1 = good, 2 = satisfactory, 3 = not satisfactory, 4 = bad). The score for this VRS was recorded in the electronic case report form by the investigator at the end of the 4-week treatment phase. The investigator rated the severity of constipation on the basis of the stool frequency and stool quality reported by the patient at the end of the 4-week trial compared to the end of the baseline period.

Quality of life (QoL) was assessed using both the SF-36v2 health survey and the Patient Assessment of Constipation (PAC)-QoL questionnaire. The SF-36v2 is a multipurpose, short-form health survey with 36 questions. It comprises an eight-scale profile of physical functioning, performance in physical role, performance in emotional role, vitality, social functioning, bodily pain, general health perceptions, and mental health. The PAC-QoL is a 28-item self-administered QoL instrument designed to evaluate a patient's assessment of constipation over time. It generates five scores, a total scale score, and four specific scale scores (worries and concerns (11 items); physical discomfort (4 items); psychosocial discomfort (8 items); satisfaction (5 items)).

The study protocol was registered under the EudraCT No. 2007-002087-10. It was approved by the local ethical committee.

Statistics

The sample size calculation was based on the primary end point. An efficacy as reported for other laxatives was assumed based on published trials with a similar study design. Assuming that the common standard deviation is 2.5, a sample size of 200 patients in the study group receiving SPS and 100 patients in the placebo group would have a 90% power to detect a difference of 1 in the mean number of CSBMs per week with a 0.05 two-sided significance level. Anticipating a dropout rate of 20%, approximately 240 patients in the active and 120 patients in the placebo group were to be entered (randomized) into this trial.

All randomized patients who took at least one dose of trial medication were part of the patient set for the evaluation of safety, those who took at least one dose of trial medication and who provided any data for the primary efficacy end point constituted the full analysis set, and those who adhered to all protocol conditions (with exception of minor deviations that were no clear basis for exclusion) constituted the per protocol set.

RESULTS

Patient disposition

The disposition of patients is shown in **Figure 1**. Demographic data are given in **Table 1**.

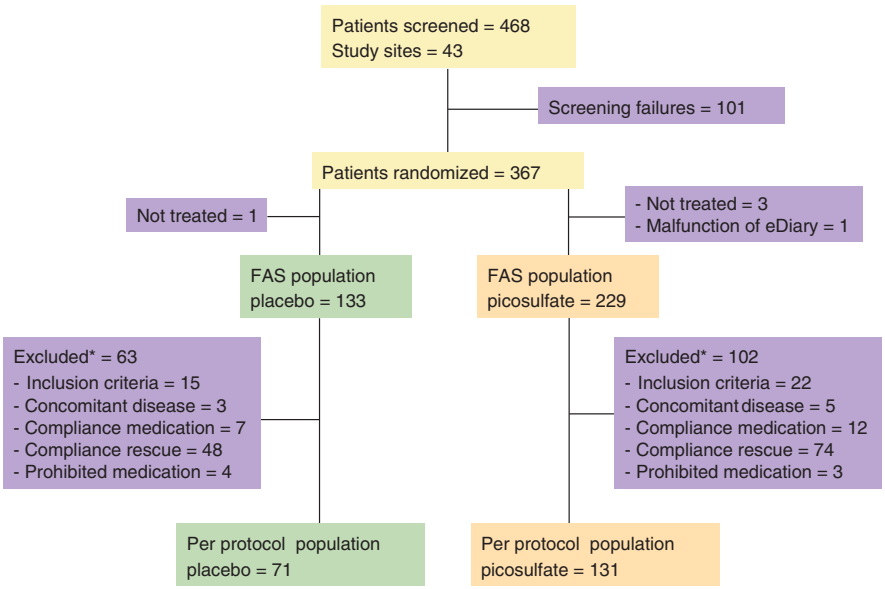

Figure 1. Disposition of participants. *Some patients fulfilled more than one exclusion criterion.

Table 1. Demographic data (full analysis set)

		Placebo	Picosulfate	Total
Number of patients treated	*n* (%)	134 (100)	233 (100)	367 (100)
Female		115 (85.8)	170 (73.0)	285 (77.7)
Age (years)	Mean (s.d.)	51.9 (16.5)	50.2 (17.2)	50.8 (16.9)
Body mass index (kg/m^2)	Mean (s.d.)	26.1 (5.1)	26.4 (4.6)	26.3 (4.8)
Duration of constipation (years)	Mean (s.d.)	13.2 (13.4)	13.3 (14.3)	13.2 (14.0)

Compliance

Compliance rate (defined as the proportion of recorded days with a correct study medication intake being 80% or more) was 94.7% in the placebo group and 94.8% in the SPS group. During the 4 weeks treatment period, 5.2% of the patients treated with SPS and 3.8% of the patients treated with placebo discontinued the study prematurely. The slightly higher dropout rate in the active drug group was due to the increased occurrence of diarrhea.

Primary end-point CSBM

During the 4 weeks of treatment, the mean number (±s.e.) of CSBMs per week (primary efficacy variable) was statistically significantly higher in the SPS than in the placebo group (**Table 2**). Analysis restricted to the per protocol population confirmed the superiority of SPS over placebo. The time course of SBMs and CSBMs is shown in **Figure 2**.

Secondary end points of bowel function

The percentages of patients reaching an increase of ≥1 in the mean number of CSBMs per week over the 4 weeks treatment period compared to baseline and the percentage of patients reaching a mean number of at least three CSBMs per week were significantly higher in the SPS group than in the placebo group over the 4 weeks treatment period (**Table 2**).

The time to the first SBM after the first dose of study medication was captured by the eDiary. After 1 day, 69% of patients in the SPS group had their first bowel movement compared to 53% in the placebo group (**Figure 3**).

Straining with defecation, stool consistency, incomplete evacuations, feeling of anal obstruction, and need for manual maneuvers all decreased much more on SPS than on placebo (all $P<0.01$). The overall satisfaction with bowel habit, constipation, abdominal bloating, and abdominal discomfort improved much more with SPS than placebo (all $P<0.0001$).

Dose adjustment and use of rescue medication

Nearly all patients assigned to placebo took the full dose of medication throughout the trial. In contrast, approximately 40% of patients treated with SPS quickly tapered the dose according to their needs. This proportion increased to nearly 50% by the

Table 2. Effects of treatment with SPS and placebo on the number of CSBMs

	Placebo	SPS	*P* value	NNT
CSBM per week (FAS)				
Baseline (mean±s.e.)	1.1±0.12	0.9±0.09	$P<0.0001$	NA
Treatment (mean±s.e.)	1.7±0.14	3.4±0.20		
CSBM per week (PPS)				
Baseline (mean±s.e.)	0.7±0.12	0.6±0.10	$P<0.0001$	NA
Treatment (mean±s.e.)	1.7±0.19	3.4±0.24		
ΔCSBM per week ≥1[a] (number of patients) (FAS)	32.3%	65.5%	$P<0.0001$	3
≥3 CSBM per week (number of patients) (FAS)	18.0%	51.1%	$P<0.0001$	3
≥1 CSBM per day (number of patients) (FAS)	0%	9.6%	$P<0.0001$	10

CSBM, complete spontaneous bowel movement; FAS, full analysis set; NA, not applicable; NNT, number needed to treat; PPS, per protocol set; SPS, sodium picosulfate.
[a]Increase of at least one CSBM during treatment as compared to baseline.

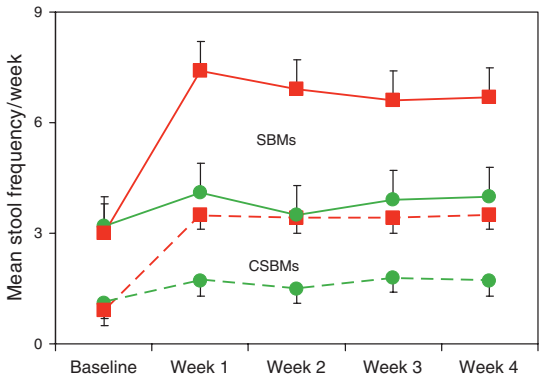

Figure 2. Time course of spontaneous bowel movements (SBMs, solid lines) and complete spontaneous bowel movements (CSBMs, broken lines) in the SPS group (red symbols) and the placebo group (green symbols) (FAS analysis). FAS, full analysis set; SPS, sodium picosulfate.

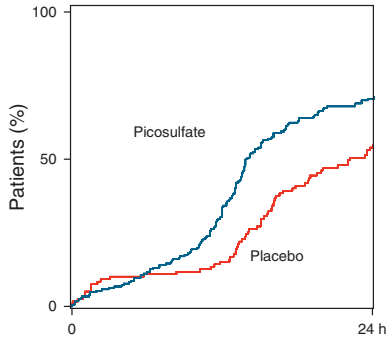

Figure 3. Time to first bowel movements after the first dose of study medication.

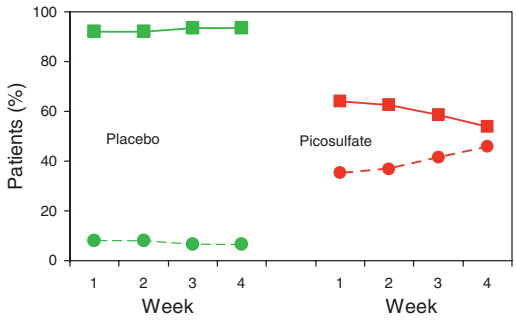

Figure 4. Dose of medication taken on day 7 of each week of the trial. Full dose, squares and solid lines; down to half dose, dots and broken lines. Percentage of patients falling into either of the categories is shown.

end of treatment (**Figure 4**). During treatment, 20.5% of the SPS group and 44.4% in the placebo group used rescue medication at least once. Similarly, the weekly proportion of patients using rescue medication was much lower in the SPS group ($P<0.002$) (**Figure 5**).

Quality of life measures

The analysis of SF-36v2 scores showed that the improvement in the dimensions general health and mental component summary was significantly greater in the SPS than in the placebo group ($P=0.008$ and $P=0.048$, respectively). There were no significant improvements for the other dimensions. The overall PAC-QoL score as well as all the single scores were significantly improved in favor of SPS (**Figure 6**).

Global efficacy and satisfaction

The final global efficacy as assessed by the investigator after 4 weeks of treatment was rated as 'good' or 'satisfactory' in 86.9% of the patients of the SPS group and in 48.2% of the patients on placebo ($P<0.0001$). In the final global efficacy assessment by the patient, 87.7% of SPS-treated patients and 45.8% of the placebo-treated patients rated efficacy as 'good' or 'satisfactory' ($P<0.0001$).

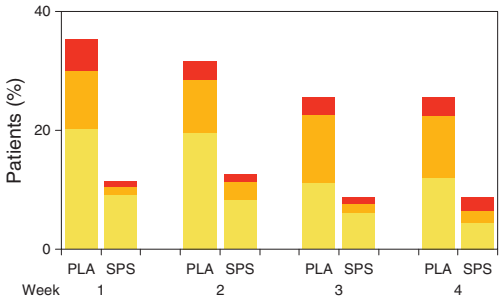

Figure 5. Proportion of patients taking rescue medication during the trial. PLA, placebo group; SPS, sodium picosulfate group; yellow, orange, red, 1, 2, 3 suppositories per week, respectively. The number of patients as well as the number of suppositories is significantly lower in the SPS group.

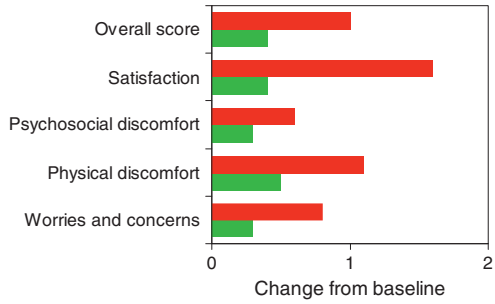

Figure 6. Change from baseline in the Patient Assessment of Constipation Quality of Life (PAC-QoL) scale scores (means, adjusted for center effects and baseline value; all $P<0.001$ in favor of SPS). SPS, sodium picosulfate.

Safety and tolerability

Tolerance of treatment was generally good. All reported adverse events (AEs) in the course of this study, except diarrhea and to a lesser degree abdominal pain, were observed with a similar frequency in both treatment groups. The most frequent AE was diarrhea, which occurred in 4.5% of the placebo group and 31.8% of the SPS group. Diarrhea was graded as 'mild' by 3 patients (2.2%) and 'moderate' by 3 patients (2.2%) on placebo; and 'mild' by 35 patients (15.0%), 'moderate' by 37 patients (15.9%), and 'severe' by 2 patients (0.9%) on SPS. Abdominal pain was reported by 3 patients (2.2%) on placebo and by 13 patients (5.6%) on SPS. There were no significant changes in the laboratory variables assessed during the course of the study. No drug-related serious AEs occurred in either group.

DISCUSSION

SPS is thought to be effective by many physicians, and efficacy has been shown in our study from a number of perspectives. In addition, although bisacodyl, the compound metabolized to the same active metabolite as SPS, has been used as rescue medication in numerous trials in chronic constipation, (12–14) the data gathered in this prospective trial provides further insight into various aspects of SPS treatment.

To exert its laxative effect, SPS must be activated by the colonic flora to its active moiety BHPM (5,6). The onset of action occurs between 6–12 h after ingestion and this is reflected by the divergence of curves for the first bowel movement between SPS and placebo after 6 h (**Figure 3**). No loss of effect over the 4 weeks of the study was observed (**Figure 2**). The benefits of SPS included not only increased bowel frequency and improved stool consistency but also decreased need to strain during defecation, incomplete evacuation, feeling of anal obstruction, and the need for manual maneuvers. This is in keeping with the results of a previous trial showing the therapeutic equivalence of bisacodyl and SPS (15).

Patients had a mean stool frequency of once daily after treatment with picosulfate. This suggests greater efficacy than other compounds such as the 5-HT_4 partial agonist tegaserod (12) and the chloride channel activator lubiprostone (14) and is similar to that achieved with the new 5-HT_4 full agonist prucalopride (13).

Because mean stool frequency on active treatment was approximately once per day (**Figure 1**), a proportion of patients had more than one evacuation per day that may not be desirable. If a patient felt that the effect of daily dosing was too strong, they were allowed to titrate down the daily dose. This was done by nearly 50% of the patients over the 4 weeks of treatment (**Figure 4**). Both the high stool frequency on SPS and the dose reduction by many patients suggest that the full dose taken every day is not necessary for many constipated patients. Rather, an individually chosen dose, e.g., between 5 and 10 mg, a longer interval between doses, or both, could be preferable depending on the individual patient's needs. Treatment with SPS may therefore be well suited for individualized treatment, either on a fixed schedule or on demand.

The improvement in constipation symptoms was not reflected in all of the dimensions of the global SF-36v2 assessment. However, the observed improvement in the PAC-QoL score in SPS-treated patients compared to patients in the placebo group shows that the treatment of constipation resulted in an increase in the patients' everyday functioning and well-being. Generic questionnaires as the SF-36v2 focus on broad aspects of QoL, and are intended for use in general populations or across a wide range of disease conditions. Distinct disease and treatment-related effects are generally better detected by disease-specific instruments. The latter are developed to detect health states that are likely to be experienced by patients in a study. Thus, the disease-specific PAC-QoL seems to be more suitable for detecting treatment-induced changes in patients with constipation than the generic questionnaire SF-36. Using this instrument, we proved SPS to be clearly superior to placebo.

In the treatment of functional disorders such as chronic constipation, safety is of paramount importance. As for all laxatives, contraindications to its use are suspected bowel obstruction, bowel perforation, and dehydration. In the present trial, the only differences in frequency of AEs between the two treatment groups were the slightly increased occurrence of diarrhea and, on a lower level, abdominal pain in the SPS group. These probably relate to the starting dose of SPS. The number of investigator defined drug-related AEs decreased significantly after the first week of SPS treatment and was likely due to the reduction in SPS dosage by patients. In the following weeks 2, 3, and 4, the frequency of AEs was similar

between SPS and placebo. Hence, SPS treatment over 4 weeks on a daily basis can be considered safe. This confirms the clinical experience with both SPS and bisacodyl over several decades. In the vast majority of countries where bisacodyl or SPS are available, they are marketed OTC. Until now SPS is not registered in the United States. A Time and Extent Application submitted to the FDA to include SPS in the OTC-monograph for laxatives is pending.

In conclusion, treatment of chronic constipation with SPS improves many of the symptoms of chronic constipation, improves bowel function, and is well tolerated over a 4-week period. The dose can be adjusted easily as the drug is given in liquid form. It would be of considerable interest to compare SPS to other newer and more expensive drugs such as lubiprostone and prucalopride.

CONFLICT OF INTEREST

Guarantor of the article: Stefan Mueller-Lissner, MD.

Specific author contributions: S. Mueller-Lissner: study design, principal investigator, data analysis, and paper writing; M.A. Kamm: study design, data analysis, and paper review; A. Wald: data analysis and paper review; U. Hinkel: design of protocol, data analysis, and paper review; U. Koehler: design of protocol, study manager, data analysis, and paper review; E. Richter: statistical planning and analysis and paper review; J. Bubeck: review of protocol and paper. All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Financial support: Boehringer Ingelheim sponsored the trial.

Potential competing interests: S. Mueller-Lissner, M.A. Kamm, and A. Wald: consultants to Boehringer Ingelheim. U. Hinkel, U. Koehler, E. Richter, and J. Bubeck: employees of Boehringer Ingelheim.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Laxatives of the diphenylmethane group are "old" drugs mostly used over the counter.
- ✓ Although there is little doubt about their efficacy, high-quality clinical trials are sparse.

WHAT IS NEW HERE

- ✓ The efficacy and safety of sodium picosulfate in the treatment of chronic constipation has been shown in a 4-week trial.
- ✓ Patients quickly adjust the dose according to their individual needs.
- ✓ Patient's satisfaction with active treatment is very high, and measures of quality of life are significantly improved.

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