

## Comparing the Efficacy of Two Drugs Senalin and Bisacodyl in Treatment of Constipation in Intensive Care Units' Patients

### Abstract:

**Background:** Constipation is an intestinal syndrome that can be created alone or in the context of another disease in patients admitted to intensive care units (ICUs). Given the role of sennosides in increasing the transfer rate of materials from the large intestine, we aimed to compare the effect of senalin with bisacodyl on the treatment of constipation in patients admitted to ICUs. **Materials and Methods:** In this randomized, double-blind study, 70 patients admitted to the ICU were divided into two groups. The senalin recipient group received senalin with a dose of 500 mg daily for 3 days. The bisacodyl recipient group received bisacodyl with a dose of 10 mg daily for 3 days. **Results:** The mean of defecation frequency during the 2<sup>nd</sup> day of treatment of constipation was significantly higher in the group receiving bisacodyl than in the senalin group ( $P < 0.01$ ). There was no significant difference between the two groups in terms of fecal consistency in any of the study days ( $P < 0.05$ ). The prevalence of complications in the 3<sup>rd</sup> day of treatment was significantly higher in bisacodyl group than in the senalin group ( $P = 0.04$ ). **Conclusion:** Given the lack of difference in the efficacy of two drugs, fecal consistency, daily defecation frequency and fewer complications of senalin compared to bisacodyl, it seems that this drug can be used as an appropriate treatment for constipation in patients admitted to ICUs.

**Keywords:** *Bisacodyl, constipation, laxative, senalin*

### Introduction

Constipation is an intestinal syndrome, which can be developed alone or as a background disease.<sup>[1]</sup> Constipation is a common condition involving 2%–28% of people. Its prevalence increases by age and affects women more than men. It is estimated that constipation imposes about \$ 6.9 milliard cost annually to countries.<sup>[2]</sup> Intestinal movement problems are also common in patients admitted in the intensive care unit (ICU).<sup>[3]</sup> In studies conducted on constipation, the prevalence of constipation varies between 15% and 83%.<sup>[4-6]</sup> Several factors such as splenic hypoperfusion caused by shock, electrolyte disorders, and particularly hypocalcemia and hypomagnesemia, some of the drugs mainly used in ICUs, such as opiates, can cause constipation in patients admitted to these units.<sup>[7]</sup>

Previous studies have shown a significant relationship between constipation, organ dysfunction, and prolonged admission time in ICUs and failure to separate

from mechanical ventilation.<sup>[4-6]</sup> To treat constipation, there are various drug groups such as osmotic, volumetric, and stimulating laxatives, and they have different mechanism of action and complications. Stimulating laxatives such as bisacodyl and senalin apply their effect by changing the transfer of electrolytes through intestinal mucosa.<sup>[8]</sup> Their effects appear in the form of oral prescription between 6 and 12 h and if used rectally, it appears about 20 min later.<sup>[9,10]</sup> Stimulating laxatives may be associated with side effects such as salt overload, hypokalemia, and protein-losing entropy. Bisacodyl is used for many years as the first-line laxative around the world, and clinical experience suggests that this drug can be very effective in treating constipation.<sup>[11]</sup>

Bisacodyl is a stimulating laxative, which acts locally in the large intestine and increases the intestinal movement and decreases the intestinal transit time and rises the watery feces portion.<sup>[12]</sup> In addition to the drugs produced so far, Goldaru

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Company in Iran has produced a laxative with the brand of senalin by combining three substances of the senna leaves, fennel seeds, and rose petals at ratios of 34.2, 45, and 15.1%, respectively. It is expected that the side effects of this drug, including abdominal cramps, to be reduced by adding two herbal substances to the senna. The ingredients of the senna leaf are anthraquinones, including dianthrone glycosides, mainly sinusoids A and B, along with sinusoids C and D.<sup>[13]</sup> Anthraquinone glycosides are absorbed in the gastrointestinal tract and glycons released during metabolism and secretion into the large intestine lead to increased peristaltic intestinal movements.

Given the high prevalence of constipation in patients admitted to the ICU and high complications and costs imposed on the health-care system of countries, its treatment is considered to be an important issue and it can reduce the complications such as prolonged admission and mortality, as a result, the health system costs are reduced. In studies conducted on bisacodyl, its efficacy has been usually compared with placebo. As senalin drug is a domestic product and no study has been conducted so far, we decided to compare this drug with bisacodyl in the treatment of constipation in patients admitted to the ICUs of Al-Zahra Hospital in Isfahan.

## Materials and Methods

The present study was a randomized, double-blind clinical trial conducted on 70 patients admitted to Al-Zahra Hospital in Isfahan to compare the effects of senalin with bisacodyl in treatment of constipation. The sample size was calculated with the power of 80% and significance level of 5%. The inclusion criteria included age over 18 years, staying for >5 days in the ICU, lack of immunodeficiency, and nonpregnancy. Exclusion criteria were the use of laxatives before admitting to the care unit, a history of allergy to herbal compounds, anal fissure, ulcerative proctitis, and electrolyte disorders.

Before starting, all stages of the study and the possible complications were explained to the participants or their companions, and written informed consent was obtained. The present study was approved by the Medical Ethics Committee of Isfahan University of Medical Sciences. Patients were randomly assigned to two groups of received senalin and received bisacodyl. Randomization was performed using Random Allocation Software. Patients and researchers were not aware of intervention received, so the study was performed in double-blind form. The first group included 35 patients who received 10 mg of oral bisacodyl daily for 3 days. The second group also included 35 patients who received oral senalin 500 mg (Gol Daru Company, Iran) daily for 3 days [Figure 1].

Patients were examined during 3 days of treatment and 2 days after and the variables were evaluated. Patients in both groups were followed up daily for 5 days during

the study, and the variables studied in the research were checked and recorded. The measured variables included demographic characteristics (age by year and gender), cause of admission, duration of admission in the ICU, frequency of feces excretion during the day, feces consistency score, vital signs, and side effects. The feces consistency score was evaluated based on Bristol Stool Scale in a 5-point scale, in which point 1 means watery feces, point 2 means soft feces, point 3 means well-formed feces, point 4 means relatively tough feces, and point 5 means tough feces [Figure 2]. The collected data were analyzed using SPSS software (Version 20.0. Chicago: SPSS Inc. IBM Corp).

Quantitative variables were presented as mean  $\pm$  standard deviation and qualitative variables were presented as numbers (percentage). Using the Kolmogorov–Smirnov Z-test, the normal distribution of data was examined, and accordingly, parametric or nonparametric tests were used for quantitative data analysis. To compare the quantitative variables between two groups, independent sample *t*-test and Mann–Whitney U-test were used. Chi-square test was also used for qualitative variables. The significance level in all cases was considered to be  $<0.05$ .

## Results

The mean age was  $42.91 \pm 21.02$  years in the bisacodyl group and it was  $41.05 \pm 20.65$  years in senalin group, which no significant difference was seen between the two groups in terms of age ( $P = 0.56$ ). In bisacodyl and senalin groups, 88.6% and 71.4% of patients were male, respectively, which no significant difference was seen between the two groups in terms of gender ( $P = 0.13$ ). The mean admission time was  $12.74 \pm 5.80$  days in bisacodyl group and it was  $13.20 \pm 5.40$  in senalin group, which showed no significant difference in this regard ( $P = 0.42$ ). The mean score was  $19.17 \pm 1.58$  in bisacodyl group and  $19.34 \pm 1.30$  in senalin group with no significant difference ( $P = 0.43$ ). The mean frequency of excretion during the 2<sup>nd</sup> day of constipation was  $1.85 \pm 0.49$  in bisacodyl group and  $1.40 \pm 0.49$  in senalin group, which it was significantly higher in bisacodyl group than senalin group ( $P < 0.01$ ). While the mean frequency of excretion during the 1<sup>st</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> days in senalin group was higher than bisacodyl group, this difference was not statistically significant ( $P < 0.05$ ) [Table 1].

Regarding the complications observed during the 3<sup>rd</sup> day of treatment, 1 patient (9.1%) had vomiting and 9 patients had abdominal cramps (26.7%) in the bisacodyl group, and 1 patient (20%) had nausea and 2 patients (50%) had dizziness and 2 patients (40%) had abdominal cramps in senalin group. The prevalence of complications in the 3<sup>rd</sup> day of treatment was significantly higher in bisacodyl group than senalin group ( $P = 0.04$ ). However, no significant difference was found between the two groups

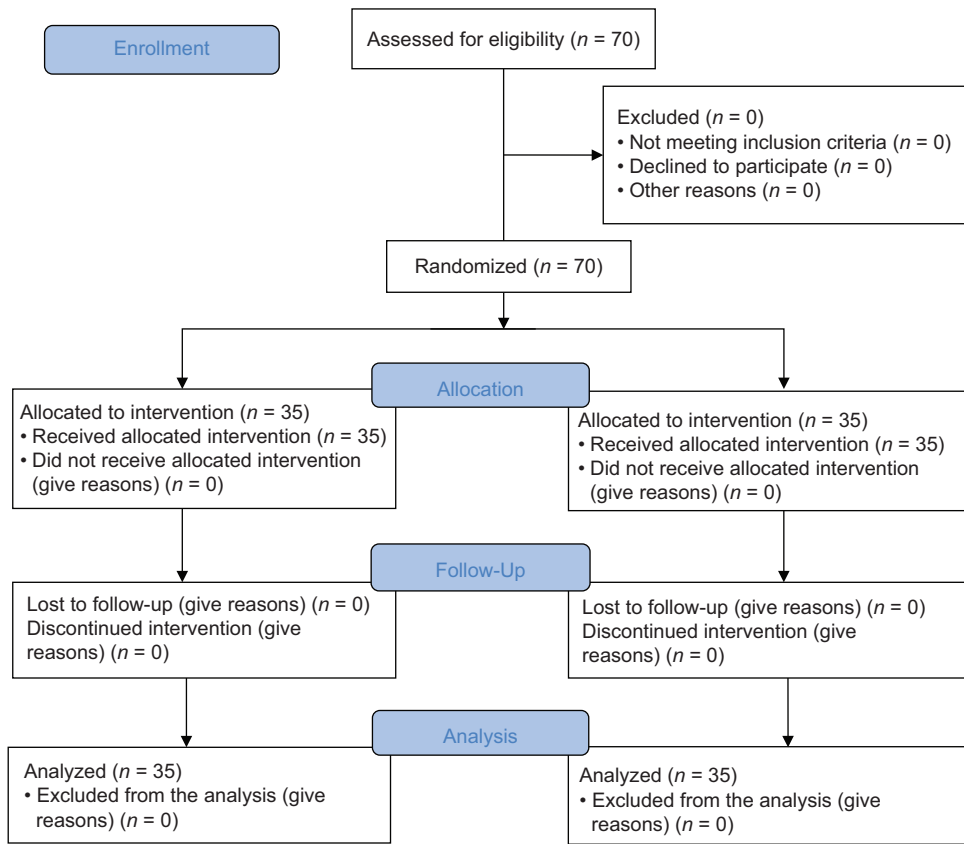


Figure 1: Study CONSORT flow diagram

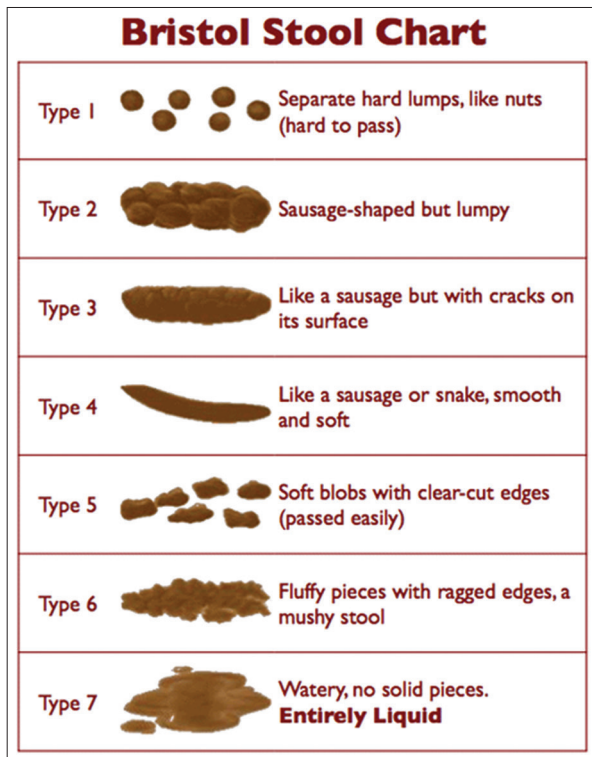


Figure 2: Bristol stool scale

regarding the prevalence of complications in the 1<sup>st</sup>, 2<sup>nd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> days of constipation treatment ( $P < 0.05$ ).

## Discussion

This study was conducted to compare the effects of senalin and bisacodyl on constipation in patients admitted to ICUs. The results of the study indicated no significant difference in the effect of two drugs of senalin and bisacodyl on feces consistency. On the other hand, the mean frequency of excretion during the 2<sup>nd</sup> day of treatment was significantly higher with bisacodyl than senalin. However, the mean frequency of excretion in the other days of the study was higher in senalin group, while these differences were not statistically significant. Regarding the evaluated complications in this study, except for the 3<sup>rd</sup> day, they were significantly lower in senalin group compared to bisacodyl group, but no significant differences were found between the two groups regarding the complications of constipation in other days. Most of the studies conducted in this area so far compared the use of bisacodyl with placebo or other existing drugs for the treatment of constipation, and no study tried to compare these drugs with each other.<sup>[14-16]</sup>

In a study conducted by Pachlo *et al.*, bisacodyl and sinusoids A and B, which are the active ingredient of senalin, were prescribed to mice. The results of this study showed that both bisacodyl and sinusoids A and B treatments similarly stimulated loose feces during 24 h and accelerated the transmission time to the large intestine, although the duration of transmission was longer for

**Table 1: Constipation symptoms and other clinical variables in bisacodyl and senalin receptors**

Variables	Group	1 <sup>st</sup> day	2 <sup>nd</sup> day	3 <sup>rd</sup> day	4 <sup>th</sup> day	5 <sup>th</sup> day
Daily fecal excretion	Bisacodyl	1.71±0.57	1.85±0.49	1.74±0.61	1.57±0.60	1.77±0.68
	Senalin	1.71±0.50	1.40±0.49	1.88±0.67	1.65±0.59	2.66±0.2
<i>P</i>		0.11	<0.01	0.38	0.51	0.11
Stool consistency scale	Bisacodyl	2.51±0.65	2.45±0.50	2.94±0.87	2.63±0.65	2.65±0.51
	Senalin	2.54±0.50	2.45±0.50	2.94±0.87	2.65±0.63	2.45±0.82
<i>P</i>		0.75	0.61	0.89	0.09	0.21
Heart beat	Bisacodyl	88.20±6.67	88.42±6.10	88.57±4.51	87.20±4.39	87.45±3.79
	Senalin	86.94±4.66	87.94±4.57	87.82±4.40	87.55±4.34	88.6±3.66
<i>P</i>		0.36	0.70	0.48	0.89	0.55
Number of breaths	Bisacodyl	18.37±2.12	18.54±2.7	18.62±2.35	18.77±2.22	18.57±2.47
	Senalin	18.11±1.85	18.00±2.24	19.20±2.64	18.77±2.14	18.57±2.68
<i>P</i>		0.94	0.92	0.87	0.68	0.34
Body temperature	Bisacodyl	37.24±0.46	37.34±0.49	37.33±0.55	37.43±0.53	37.39±0.52
	Senalin	37.30±0.42	37.37±0.49	37.34±0.53	37.64±0.52	37.33±0.48
<i>P</i>		0.94	0.92	0.87	0.68	0.34
Mean arterial blood pressure	Bisacodyl	90.54±4.96	89.62±4.66	91.00±4.73	90.08±4.86	90.47±4.23
	Senalin	88.60±4.67	88.05±4.30	88.85±4.47	89.85±3.56	90.57±3.57
<i>P</i>		0.01	0.06	0.02	0.51	0.85

bisacodyl. This study also showed that both bisacodyl and sinusoids A and B drugs have an effect on the colon movement and secretion, but the rate of colonic secretion in the group of treating with bisacodyl was higher than sinusoids A and B.<sup>[14]</sup> In a study conducted by Sitadini *et al.*, three regimens of polyethylene glycol along with bisacodyl, sinusoid along with magnesium sulfate, and sinusoid along with polyethylene glycol were examined.<sup>[15]</sup> The results of this study showed that the drug regimen containing the sinusoid resulted in a better intestinal cleansing, better mucosal coating, and colonic secretion compared to bisacodyl drug regimen. However, in our study, no significant difference was found between feces consistency and between bisacodyl and senalin groups. This difference can be due to different sample sizes, different drug regimens, as well as differences in dosage and active ingredients of senalin with sinusoid used in other studies. On the other hand, in other studies, sinusoids, which are active ingredients, were prescribed directly, which could cause different blood levels of the active ingredient compared with prescription of the senalin drug. In addition, in a study conducted by Setadini *et al.*, it was shown that sinusoid group experienced lower level of abdominal cramp compared to bisacodyl group, which is different from the results of our study.<sup>[15]</sup>

The differences in observed complications can be due to other substances used in senalin such as rose and fennel, which can prevent some of the complications of sinusoid, such as abdominal cramps. In another study conducted to evaluate the effect of adding bisacodyl and sinusoid to polyethylene glycol on intestinal evacuation and preparation for colonoscopy, it was showed that all three regimens of polyethylene glycol, polyethylene glycol along with bisacodyl, and polyethylene glycol in

addition to sinusoid had the same effect on intestinal function and preparation for colonoscopy as well as the same complications.<sup>[16]</sup> In another study conducted to compare several laxative drugs on constipation and gastrointestinal movements, it was showed that sinusoids' prescription at a dosage of 250–500 mg/kg has an effect on gastrointestinal movements.<sup>[17]</sup> However, in this study, sinusoids compared with other drugs, such as dantrolene, increase the rate of transmission in the large intestine. As constipation is usually caused by a disturbance in colon movement caused to remain feces in the large intestine for longer time and consequently more water absorbance, the use of drugs containing sinusoids such as senalin can reduce the constipation by reducing the duration of intestinal feces present in the large intestine. In other studies, drugs such as neostigmine had clinical effects on the incidence of constipation in ICU patients, which is suggested to compare these drugs in other studies.<sup>[18]</sup>

One of the limitations of the study was small sample size and lack of senalin and bisacodyl comparison with different doses and the control group.

## Conclusion

Regarding no difference in efficacy of the two drugs of senalin and bisacodyl in feces consistency and frequency of excretion during the study days, as well as less complications of senalin compared to bisacodyl, it seems that this drug can be used as an appropriate drug for treatment of constipation in patients admitted to ICUs. However, wider and more extensive studies are needed to confirm that this drug is an appropriate alternative for treatment of constipation in these patients.



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## Conflicts of interest

There are no conflicts of interest.

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