

Letter to the editor

Effect of magnesium oxide with probiotics on bowel movements in elderly orthopedic patients with chronic constipation: a retrospective chart review

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Elderly orthopedic patients have a higher prevalence of constipation due to a decreased defecation reflex with age and pain caused by illness. The primary cause of constipation in these patients cannot be identified but may include dehydration, lack of exercise, and therapeutic drugs [1]. Magnesium oxide (MgO) is recommended and used as the first choice for constipation, but there are some cases of low efficacy with MgO treatment [2]. We reported in this journal that the addition of probiotics to laxatives is effective for chronic constipation [3]. Therefore, a retrospective chart review was conducted to determine the effect of the addition of probiotics to MgO on bowel movements in elderly chronic constipation patients hospitalized for orthopedic diseases.

Elderly patients who were 75 years of age or older, had chronic constipation, were hospitalized for orthopedic diseases, and had received MgO for at least six weeks continuously between April 2021 and October 2022 were included in the study. Among them, those with probiotics added to MgO for at least 4 weeks were categorized as the probiotic group (P group). Patients without concomitant administration of probiotics were considered the control group (C group). The probiotics and daily doses administered were *Streptococcus faecalis*, 2×10^8 CFU/day; *Bacillus mesentericus*, 1×10^7 CFU/day; and *Clostridium butyricum*, 5×10^7 CFU/day. These probiotics have been shown to mildly improve defecation in preliminary studies of chronic constipation [3]. However, because this effect is thought to be due to recovery from dysbiosis, the improvement in defecation is not as rapid as with laxatives, often taking a month or more. For the P group, defecation scores were calculated before and after 4 weeks of probiotic use. For the C group, the change in defecation score for 4 weeks was calculated. Defecation scores were calculated using our previous method of weekly defecation,

with values determined using the Bristol Scale [3]. Defecation scores were obtained by recording the typical daily stool properties based on the Bristol scale, subtracting 4 (the Bristol scale value for normal stool) from that value, and summing those values for seven consecutive days. Note that on days when there was no defecation, 0 was assigned as the Bristol Scale value. The exclusion criteria were as follows: orthopedic surgery within the past 3 weeks, ulcerative colitis, irritable bowel syndrome, gastrointestinal cancer, and antimicrobial use. Concomitant use of other laxatives was permitted in both groups. Data were analyzed using the Easy R statistical software [4], with the Wilcoxon signed rank test used for comparison of means between the two groups and the χ^2 test used for comparison of proportions. Results are presented as the mean \pm standard error (SE) or number of patients (%). A p-value less than 0.05 was considered statistically significant. Informed consent was obtained via an opt-out form posted on a hospital bulletin board, and data were used only for analysis with consideration given to not identifying individuals.

During the study period, a total of 44 patients were analyzed: 12 patients who met the criteria for the P group and 32 patients who met the criteria for the C group. There were no differences in age, gender, orthopedic diseases, medications, concomitant laxatives, MgO dosage, or defecation scores at baseline (Table 1). The defecation score for the P group improved significantly from -10.3 ± 1.1 at baseline to -5.4 ± 1.2 after 4 weeks ($p=0.013$), whereas the defecation score for the C group was not statistically different over time ($p=0.417$; Fig. 1). At the end point, the defecation score for the P group was -5.4 ± 1.2 , and that for the C group was -10.4 ± 1.3 ; statistically, the P group did predominantly better ($p=0.022$), and the effect size of Hedge's g was 0.75, a value that seemed clinically meaningful.

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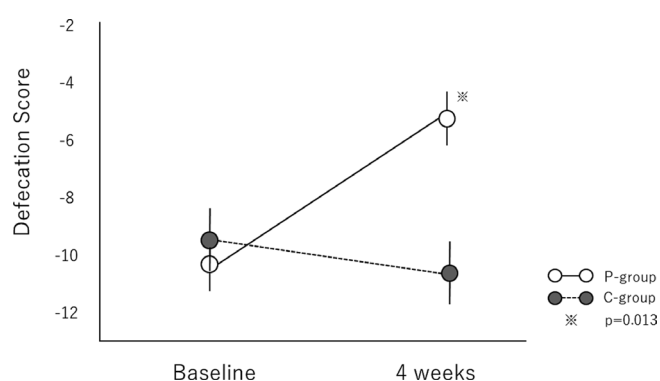
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Table 1. Comparison of background factors between the probiotic and control groups

	P-group	C-group	p-value
n	12	32	n/a
Age years, mean \pm SE	85.4 \pm 3.2	82.4 \pm 2.2	0.642
Sex, n (%)			
Male	4 (33.3)	9 (28.1)	0.736
Female	8 (66.7)	23 (71.9)	0.736
Orthopedic Disease			
compression fracture	6 (50.0)	19 (59.4)	0.576
femoral neck fracture	3 (25.0)	7 (21.9)	0.866
severe osteoporosis	3 (25.0)	6 (18.7)	0.647
Medication			
NSAIDs	6 (50.0)	12 (37.5)	0.453
acetaminophen	6 (50.0)	18 (56.3)	0.711
duloxetine	3 (25.0)	6 (18.8)	0.647
opioid	2 (16.7)	4 (12.5)	0.719
Concomitant Laxatives			
stimulant laxatives	4 (33.3)	12 (37.5)	0.798
Kampo stimulant laxatives	4 (33.3)	8 (25.0)	0.584
others	2 (16.7)	5 (15.6)	0.933
Magnesium oxide g/day, mean \pm SE	1.32 \pm 0.3	1.28 \pm 0.3	0.543
Defecation scores			
Baseline, mean \pm SE	-10.3 \pm 1.1	-9.6 \pm 1.2	0.314
Endpoint, mean \pm SE	-5.4 \pm 1.2	-10.4 \pm 1.3	0.022

P-group: probiotic group; C-group: control group; SE: standard error; NSAIDs: non-steroidal anti-inflammatory drugs.

**Fig. 1.** Changes in defecation scores with and without probiotics.

In the Japanese guidelines for chronic constipation, MgO is positioned as a first-line drug with a recommendation level of 1 and an evidence level of A [5]. However, continuous administration of MgO to elderly patients with chronic constipation does not always result in improvement of constipation, and in this study, 12 of 12 (100%) patients in the P group and 29 of 32 (90.6%) patients in the C group were constipated despite MgO administration. Unlike stimulant laxatives, MgO was thought not to lose its efficacy with continuous use, but in some cases, long-term administration of MgO has worsened defecation [6]. Recent animal experiments have shown that dietary fiber is fermented by intestinal bacteria to produce short-chain fatty acids (SCFAs), which improve the intestinal environment and chronic constipation, but this constipation-improving effect disappeared when MgO was

used [7]. The mechanism by which MgO eliminates this constipation-improving effect is an increase in intestinal pH together with a concomitant change in the composition of the intestinal microbiota and a decrease in the production of SCFAs [7]. On the other hand, the guidelines for chronic constipation place probiotics at a recommendation level of 2 and a level of evidence of B [5]. Their efficacy for chronic constipation has not yet been determined. However, in this study, defecation scores were improved when probiotics were used in combination with MgO. The probiotics used in this study have been shown to produce SCFAs and improve the intestinal environment [8], thereby providing protection against intestinal dysbiosis caused by MgO. In cases where constipation does not improve with MgO and defecation is worsened, the administration of probiotics that produce SCFAs may be a new way to treat constipation. Future prospective studies are needed to confirm this hypothesis.

CONFLICT OF INTEREST

The author has no conflicts of interest relevant to the content of the article.

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