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# Possible Effect of Concomitant Prokinetics and Herbal Medicines against Nausea in Patients Taking Lubiprostone

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## Abstract

**Aim and Background:** Lubiprostone is a novel laxative that sometimes causes nausea, but preventive strategies remain unconfirmed.

**Methods:** We retrospectively chose 126 patients prescribed lubiprostone from 2013 to 2016. Medical records were reviewed to clarify whether nausea developed after administration of the drug. Background characteristics, including concomitant medicines, were also reviewed.

**Results:** The most common adverse symptom was diarrhea (23.8%). Nausea occurred in 16 patients (12.7%). Patients taking either prokinetics or herbal medicines or both were unlikely to develop nausea ($p$ = 0.007).

**Conclusion:** Concomitant prokinetics and/or herbal medicines may help alleviate lubiprostone-induced nausea.

**Keywords:** Constipation; Vomiting; Nausea; Gastric; Bowel

## Introduction

Chronic constipation (CC) is a common condition that sometimes impairs a patient's quality of life. The number of patients with CC has recently increased in association with the advanced-aged society in developed countries [1]. Lubiprostone is a selective type 2 chloride-channel activator that increases the liquid component in the small intestine, enhances bowel motility, and improves constipation. This agent has become essential for clinicians in the management of patients experiencing CC and constipation-associated irritable bowel syndrome. On the other hand, lubiprostone has been reported to sometimes cause upper gastrointestinal symptoms such as nausea and vomiting, which is one of chief reasons for discontinuation of the drug. A possible mechanism is that an increase in luminal volume may cause distension of the small intestine, inducing a delay in gastric emptying and thus a sensation of nausea via vagal stimulation. However, it is difficult to predict the development of such troublesome symptoms before administration, and strategies for prevention remain uncertain. We conducted the present study to identify the key clinical factors associated with the development of lubiprostone-induced nausea.

Incessant stoppage (CC) may be a common wellbeing issue that altogether influences the quality of life of patients and places a burden on the economy. This disability of quality of life is comparable to or more extreme than that experienced in a few other constant maladies (e.g., joint pain asthma, or coronary supply route malady). Both coordinate and circuitous costs are related with CC. Roundabout costs incorporate lost school or work (non-appearance) or being less beneficial (presenteeism), though coordinate costs of treating obstruction incorporate office visits, demonstrative tests, and solutions. Administration of CC may include an expanded admissions of dietary fiber, bowel purges, and stimulant or osmotic purgatives. In spite of the accessibility of these treatments, roughly 50% of all patients with CC are not fulfilled with their treatment, which is generally ascribed to the need of adequacy. Lubiprostone, a unused medicine outlined for the treatment of CC in both men and ladies, was endorsed by the FDA [2].

We tentatively enlisted 35 patients who gotten lubiprostone from Eminent 2013 to December 2013 at our institution. The investigate and morals committee of Kunimoto Clinic endorsed this think about, and all patients given composed educated assent some time recently interest. Consideration criteria were as takes after: Japanese male and female patients matured >20 a long time with CC. All the patients had obstruction as characterized by the Rome III criteria, with diminished bowel recurrence (less than three times per week), a sensation of inadequate purging, difficult stools, or a history of troublesome clearing on at slightest a quarter of events. To center solely on the affect of CC and maintain a strategic distance from the commitment from related gastrointestinal comorbidities, all patients with touchy bowel disorder, visit the runs, Crohn illness, or ulcerative colitis were excluded. Each of the 35 patients was treated orally with a 24-μg lubiprostone capsule twice every day. The pharmaceutical was taken with nourishment and at slightest one glass [3].

## Materials and Methods

This is a retrospective study using the medical records of patients in Teikyo University Hospital (Tokyo, Japan). First, all 269 patients who had been prescribed lubiprostone (Amitiza, Mylan EPD, Tokyo) for CC in the Department of Internal Medicine (January 2013 to April 2016) were identified from patient lists. A diagnosis of constipation was made according to the Rome III criteria: bowel movements less than three times per week, hard stools, a sensation of incomplete emptying, or difficulty in evacuation on at least 25% of occasions. Then, 80 patients with an insufficient description of clinical effectiveness and 63 patients without follow-up after administration were excluded, with 126 patients finally enrolled as subjects. Medical records of the subjects were examined by two authors (T. Y. and H. A.), to judge their responsiveness to lubiprostone and development of

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adverse effects such as nausea, vomiting, diarrhea, or others within 1 month (as the endpoints of the study). If the drug was discontinued, the cause was identified, where possible. In addition, clinical data such as demographics and concomitant medications were examined to evaluate their influence on responsiveness and the development of adverse reactions [4].

In the statistical analysis, a $p$ value < 0.05 was regarded as significant. To clarify significant clinical factors related to responsiveness, univariate and multivariate analyses were performed using logistic regression analysis. All statistical evaluations were made using SPSS Statistics, version 19 (IBM Japan, Tokyo, Japan). This protocol was approved by the Institutional Review Board of Teikyo University prior to the study (TU-16-018) [5].

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The seriousness of clogging was evaluated based on the CSS (run: 0-30 at increases of 1; no side effects = 0). The taking after parameters were checked on a day by day premise for 1 week: the number of bowel developments; trouble in departure; feeling of deficient clearing; stomach torment; time within the latrine; the utilize of purgatives, douches, and computerized help; fizzled endeavors at bowel development; and length of constipation (Table 1). The entire score was gotten by including the scores of these 8 person parameters. To survey work efficiency, the WPAI for unremitting constipation (WPAI-CC) was utilized. As already depicted for the WPAI-CC, the entire work time missed or compromised since of clogging was calculated as a per-week rate of presenteeism, non-appearance, and in general disability (presenteeism also truancy) for patients utilized amid the think about. Also, the impact of clogging on non-work exercises (such as housework, working out, and examining) [7].

**Table 1:** Background characteristics and clinical response to lubiprostone.

| | |
|---|---|
| Number of patients | 126 |
| Age (year ± SD) | 65.4 ± 15.7 |
| Sex (male/female) | 61/65 |
| Mental disorder | 13 (10.3%) |
| Concomitant agents | |
| Laxatives | 69 (54.8%) |
| Prokinetics/herbal medicines | 56 (44.4%) |
| Probiotics | 10 (7.9%) |
| PPI/H2RA | 33 (26.2%) |
| Effectiveness | 95 (75.4%) |
| Diarrhea | 30 (23.8%) |
| Nausea/vomiting | 16 (12.7%) |
| Discontinuation | 53 (42%) |

## Results

Background characteristics of the study subjects are shown in Table 1. The subjects included 61 men and 65 women, and the average age was 65.4 years. It was noted that female patients were significantly younger than male patients. The rate of concomitant laxatives was almost 50%. The response rate reached up to 75.4%, while adverse effects were seen in about 40% of all subjects. Common adverse reactions were diarrhea (30 patients, 23.8%) and nausea, vomiting, or both (16 patients, 12.7%). Others included edema (2 patients), headache (1 patient), and palpitations (1 patient). The rate of discontinuation reached 42% of all the subjects. The major reason for discontinuation was an adverse effect such as nausea or diarrhea. Table 1 shows the impact of clinical factors on responsiveness and adverse effects, using univariate analysis. Effectiveness was significantly related to older age. Regarding adverse effects, no factors were associated with the development of diarrhea. On the other hand, development of nausea was less frequent in elderly patients and in those treated with prokinetics, such as mosapride, itopride, and/or Japanese herbal medicines, including rikkunshito, daikenchuto, mashiningan, or daiou (Rhei rhizoma), than in those without. These two groups of medicines were analyzed together because most of them were concomitantly prescribed. Women tended to be more susceptible to nausea than men during lubiprostone treatment. Multivariate analysis showed that age and concomitant prokinetics or herbal medicines were significant factors related to upper gastrointestinal symptoms [8].

## Discussion

Gastrointestinal symptoms are cumbersome reactions during treatment with lubiprostone. According to previous data, incidence reached 40%, and the most frequent symptom was nausea. In the present study, we found the incidence was similar, though diarrhea was the most common symptom. Unfortunately, because dose reduction has only a partial prophylactic effect against lubiprostone-induced nausea, discontinuation of the agent is necessary, and preventive treatment has not yet been established. In a recent study from Japan, it was reported that itopride, a prokinetic drug with antidopamine effect, might be useful in alleviating nausea. In the present study, we showed the possible effectiveness of concomitant herbal medicines. Daikenchuto is an herbal medicine that is effective for bloating in patients with CC, probably via action on the gut microbiota. Rikkunshito is a ghrelin enhancer and is effective against upper gastrointestinal symptoms. Daiou, or Rhei rhizoma, has been proven to have an inhibitory effect on reflux esophagitis in rats. Although it remains unclear which specific type of medicines was most effective for preventing nausea because of the small number of subjects in the present study, prokinetics and herbal medicines might help prevent nausea induced by lubiprostone. Further prospective studies are required to clarify clinical efficacy. Limitations must be considered in the interpretation of the present data. One is the retrospective study design. Second, this study was carried out at a single institution, and third, the sample size was small. Further multicenter prospective studies are required to determine which agents are appropriate for preventing lubiprostone-induced nausea [9].

## Conclusion`

Inveterate stoppage could be a exceedingly predominant clutter that's habitually safe to treatment with way of life alterations and over-the-counter cures. Treatment choices with medicine medicines are restricted, particularly given the later withdrawal of tegaserod from the commercial center. Lubiprostone, a modern course of medicine

endorsed for the treatment of inveterate clogging in both men and ladies (age 18 and over), was endorsed by the FDA on January 31, 2006 and is showcased beneath the exchange title Amitiza. It is accessible in a gelatin capsule and the prescribed dosing is 24 μg p.o. twice day by day. No confinements have been set on the length of its use [10]. Lubiprostone specifically fortifies sort 2 chloride channels in epithelial cells subsequently causing an efflux of chloride into the intestinal lumen. The resultant liquid discharge into the gastrointestinal lumen gives a bolus impact that relaxes stool, increments intestinal travel, and progresses side effects of clogging.

## Acknowledgement

None

## Conflict of Interest

The author declares that they have no conflict of interest.

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