

## Treatment of Chronic Constipation and Dysbiosis in Elderly Patients

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### STUDY DESCRIPTION

The Japanese population is aging at an accelerated rate, with people aged 65 and over encompassing nearly 25% of the total population [1]. One of the gastrointestinal symptoms characteristic of the elderly is abnormal bowel movements such as constipation, and there is no organic disease in the lower gastrointestinal tract. According to the statistics released by the Ministry of Health, Labor, and Welfare, the number of patients complaining about constipation increases rapidly after the age of 70 [2]. Abnormal bowel movements are always accompanied by abdominal discomfort and lead to a decreased Quality of Life (QOL) [3] as well as deterioration of nutritional status, especially in elderly people, due to decreased appetite and motivation.

Solving the constipation issue is critical to help extend the life expectancy of healthy individuals. However, constipation seldomly improves despite introducing various laxatives. In the past, constipation was thought to be caused by deteriorating intestinal peristalsis with aging, use of multiple drugs (steroids, NSAIDs, and neuropsychiatric drugs), and comorbidities [4]. However, dysbiosis has been recently reported to have a crucial role in constipation [5]. The population of harmful bacteria such as *Clostridium difficile* and *Clostridium perfringens* increases in the elderly due to gradual changes in environmental factors such as eating habits [6]. Dysbiosis is reportedly known to affect the peristaltic movement of the intestine and cause abnormal bowel movement, thereby causing chronic constipation in elderly people [3]. In addition, the intestinal flora is closely related to intestinal immunity [7,8]. Since probiotics such as lactic acid bacteria are known to reduce the population of harmful bacteria [9], they might help treat constipation more effectively and normalize intestinal environment.

We here present a short commentary on the usefulness of probiotics for treatment of chronic constipation from the viewpoint of improving intestinal bacteria using our preliminary data.

### SUMMARY

To illustrate the above hypothesis, we conducted the following preliminary intervention study. Elderly patients with chronic

constipation were categorized into two groups according to the International diagnostic criteria by Rome IV [10]. One group received only laxatives (Lubiproston) while the other was administered laxatives combined with probiotics (Lubiproston and Lactomin). The two groups were compared in terms of improvement in constipation symptoms and changes in the intestinal environment. In addition, we collected stool samples to determine the distribution of intestinal bacteria, the metagenomic analysis of which was performed using next-generation sequencing with the help of 16S rDNA detected in stool as an index (Techno Suruga Laboratory Co., Ltd). This interventional study was approved by the ethics and conflicts of the interest review committee of our hospital.

After interim analysis of results for a limited numbers of patients, chronic constipation tended to be resolved earlier by the use of probiotics combined with a laxative. Further, the population of harmful bacteria, which are considered the cause of opportunistic infections and presumed to deteriorate the intestinal environment, tended to decrease with improvement in constipation.

Several reports have showed that probiotics could help treat constipation. [11,12]. Our preliminary results also suggested that the combined use of probiotics with a laxative would be more effective in treating chronic constipation. Furthermore, easing of constipation was also speculated to lead to a better intestinal environment due to reduced load of harmful bacteria.

Since it has been reported that intestinal flora is closely related to intestinal immunity, probiotics might also improve gut immunity and health.

A systematic view of both the previous research as well as our data indicate that probiotics can improve the intestinal environment and constipation. The usefulness of probiotics should be further verified to understand their contribution to intestinal immunity.

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