Efficacy of Solifenacin on Irritable Bowel Syndrome With Diarrhea: Open-label Prospective Pilot Trial

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Background/Aims
Solifenacin, a muscarinic type 3 receptor antagonist, is used to treat overactive bladder in adults. The goal of this study is to examine the efficacy of solifenacin on the symptomatic relief of diarrhea predominant irritable bowel syndrome (IBS-D).

Methods
A total of 20 patients with IBS-D were enrolled. After a 2-week observation period, all participants received solifenacin for 6 weeks. Subsequently, the administration of solifenacin was discontinued and ramosetron, a serotonin 3 receptor antagonist, was administered for 4 weeks. Overall improvement, the IBS-symptom severity scale (IBS-SSS), and frequency of defecation were assessed.

Results
Six weeks after initiation of solifenacin treatment and 4 weeks after initiation of ramosetron treatment, overall improvement was observed in 19 out of 20 (95%) and 17 out of 20 (85%) participants, respectively. At 2 weeks after initiation of solifenacin, overall improvement was observed in 16 out of 20 participants (80%). Total IBS-SSS scores at 2 and 6 weeks after the administration of solifenacin, and at 4 weeks after administration of ramosetron, were significantly lower than those at week 0. Compared to before administration, the participants’ quality of life and frequency of defecation were significantly lower in all participants at 2 and 6 weeks after the administration of solifenacin and at 4 weeks after administration of ramosetron.

Conclusions
The efficacy of solifenacin in the treatment of IBS with diarrhea was not inferior to that of ramosetron. Further placebo-controlled parallel studies are needed.

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Key Words
Diarrhea; Overactive; Ramosetron; Solifenacin succinate; Urinary bladder
**Introduction**

Irritable bowel syndrome (IBS) is a condition characterized by the presence of chronic abdominal pain or abdominal discomfort accompanied by abnormal bowel movements, such as diarrhea or constipation. In IBS, symptoms are improved by defecation, and there appears to be no organic substance or biochemical abnormality that can explain the symptoms. In population-based Japanese surveys, the prevalence of IBS has been estimated as 10%-15% and the annual incidence as 1%-2%. Because gastroenterologists frequently focus mainly on inflammatory or malignant disorders, functional disorders such as IBS, that are associated with subjective symptoms, are less likely to be the target of aggressive treatment. The complaints of patients with IBS consist of general gastrointestinal symptoms, and differential diagnosis of complications such as infectious enteritis is necessary. Therefore, it is important to obtain a detailed history of the disease. The treatment for IBS tends to consist of merely the prescription of common gastrointestinal medications. For healthcare providers, IBS can be difficult to detect, and patients are often dissatisfied with the outcome even when they consult a physician, resulting in a low consultation rate at medical institutions. Currently, the majority of patients remain undiagnosed, including those who are themselves unaware of their disease. Although the disease is not life-threatening, the symptoms of IBS clearly cause deterioration in patients’ quality of life, and it affects a large number of patients. The societal losses due to IBS are immeasurable. Depending on the type of stool, IBS can be classified into 4 categories: constipation predominant IBS (IBS-C), diarrhea predominant IBS (IBS-D), mixed IBS (IBS-M), and unsubtyped IBS. Among those categories, IBS-D is a particularly serious problem for patients who commute to work or to school by public transportation. Anticholinergic drugs, the serotonin 3 receptor antagonist, ramosetron, high molecular weight polymers (polycarbophil calcium), gastrointestinal motility regulators, probiotics preparations (such as *Bifidobacterium infantis* 35624) and laxatives are used in the treatment of IBS. However, no medication for the treatment of IBS has been able to provide the same levels of efficacy as proton pump inhibitors that are used for the treatment of peptic ulcers or gastroesophageal reflux disease.

**Materials and Methods**

**Study Population**

The present study is a single-cohort prospective trial. The protocol for this study was approved by the ethics committee of Tokyo-Eki Center-Building Clinic (TEC-CC0005, Nov. 7, 2010, UMIN000005577). This study included IBS-D patients, age 20 years or older, who were treated as outpatients in Tokyo-Eki Center-Building Clinic. The required sample size for testing the equality of proportions was 16 patients based on a minimum expected difference of 10% and standard deviation of 10% in the overall improvement between solifenacin and ramosetron, with an alpha error of 5% and 80% power. Thus, after considering the number of patients who dropped out, a total of 20 patients were recruited for the present study. The IBS was diagnosed according to the Rome III criteria. Namely, participants were defined as having IBS if they had suffered recurrent abdominal pain or discomfort for more than 2 days in a week and also had 2 or more of the following: improvement with defecation, onset associated with change in (increased