Comparison of Adverse Gastrointestinal Effects of Acarbose and Miglitol in Healthy Men: A Crossover Study

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Abstract

Objective  The incidence of the gastrointestinal adverse effects is important to determine as these effects are the reason for lower compliance of α-glucosidase inhibitors (αGIs). There has been no direct investigation of the adverse effects with acarbose or miglitol, therefore we compared them in healthy subjects.

Methods  Twenty-two healthy men were administered 75 mg of miglitol or 100 mg of acarbose per every meal for three days. After four drug-free washout days, they were administered 100 mg of acarbose or 75 mg of miglitol per every meal, respectively. They reported the state of their stool, borborygmi, abdominal bloating, flatus, and abdominal pain on the 1st and 3rd day.

Results  Stool tended to be soft when miglitol was administered and to be firm when acarbose was administered. The flatus score of acarbose was greater than that of miglitol. The abdominal bloating score of acarbose was greater than that of miglitol on the 1st day.

Conclusion  Our results suggest that if diabetic patients have constipation, firm stool, or flatus they may be administered miglitol and if they have diarrhea or soft stool they may be administered acarbose.

Key words: miglitol, acarbose, α-glucosidase inhibitor, gastrointestinal adverse effect

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Introduction

The regulation of postprandial hyperglycemia is correlated with the risk of microvascular and macrovascular complications (1). However, medication noncompliance is prevalent among diabetic patients and is associated with adverse clinical outcomes (2). Hertz et al. reported that the initial treatment using insulin or an α-glucosidase inhibitor (αGI) was a risk factor for early nonpersistence and discontinuation of treatment (3). We previously reported that administration of αGI after meals improved compliance (4-7). One of the reasons for the poor compliance with αGI treatment is the incidence of adverse gastrointestinal effects. The efficacies and adverse gastrointestinal effects of acarbose and voglibose have been previously reported (8, 9). Although these agents have a similar glucose-lowering effect (9), the differences in their adverse gastrointestinal effects were unclear. Miglitol is the first pseudomonosaccharide αGI and the drug has been reported to be more effective at reducing the blood glucose levels at 30 and 60 minutes after a meal than voglibose (10). This can be explained by the fact that unlike acarbose or voglibose, miglitol is partially absorbed from the small intestine (11). Since the adverse gastrointestinal effects of acarbose and miglitol have not been previously reported, in the present study we compared these effects in healthy subjects except for the abdominal symptoms.

Methods

The present study was approved by the Institutional Ethical Review Committee; informed consent was obtained from all subjects prior to the start of the study. The study had a randomized open-label crossover design. Twenty-two healthy men aged 39.3±1.7 years with a mean height of 172.7±1.1 cm, a mean weight of 70.3±1.7 kg, and a mean BMI of 23.4±0.4 kg/m² who had never been diagnosed as having diabetes or impaired glucose tolerance were enrolled. They were divided into two groups by an alternate allocation method of randomization. Eleven men were instructed to...
Figure 1. Scores for stools, borborygmi, abdominal bloating, flatus, and abdominal pain during the administration of either miglitol or acarbose on days 1 and 3. Boxes and horizontal bars show 25th and 75th percentiles and the median, respectively. Outliers show maximum and minimum. The means of miglitol- and acarbose-treated groups are expressed as open diamonds (n=22) and filled diamonds (n=22), respectively. n.s. indicates not significant. *p<0.05, **p<0.01

The subjects were asked to complete a questionnaire regarding adverse gastrointestinal effects on days 1 and 3 of each administration period. The subjects rated the conditions of their stools as no change (0 points), soft (-1 point), moderate diarrhea (-2 points), severe diarrhea (-3 points), firm (1 point), moderate constipation (2 points), or severe constipation (3 points). Borborygmi, abdominal bloating, flatus, and abdominal pain were each rated as no change (0 points), mild (1 point), moderate (2 points), or severe (3 points). If drug administration was discontinued because of severe abdominal symptoms, the adverse gastrointestinal effects were rated on the day of discontinuation. The subjects were instructed to rate the abdominal conditions honestly and not to confer the results on another drug administration.

Data were expressed as the mean ± SE. Differences in the scores between the miglitol and acarbose administration periods were evaluated using a Wilcoxon signed test. Differences with a p value of less than 0.05 were considered statistically significant.

Results

One subject discontinued miglitol dosing on day 2 because of severe diarrhea; this subject rated the adverse gastrointestinal effects of miglitol on day 2 and the results were regarded as the subject’s response for day 3.

As shown in Fig. 1, the stool scores of the acarbose and miglitol groups were significantly different on both days 1 and 3. The stool tended to be soft in the miglitol group and firm in the acarbose group. The flatus score of the acarbose group was significantly greater than that of the miglitol group on days 1 and 3. The abdominal bloating score of the acarbose group was significantly greater than that of the miglitol group on day 1 but not on day 3. No significant differences in borborygmi or abdominal pain were noted between the administration groups.

In miglitol or acarbose-treated groups, there were no significant differences between days 1 and 3 in the score regarding stool, borborygmi, abdominal bloating, flatus, and abdominal pain.

Discussion

The most important finding of the present study was that the subjects’ stools tended to be soft in the miglitol group and firm in the acarbose group. The flatus score in the acarbose group was also greater than that in the miglitol group on days 1 and 3.

Acarbose not only inhibits disaccharidase activity, but also the activities of pancreatic and salivary α-amylase. Unabsorbed polysaccharides in the intestine are broken down by enterobacteria and increase intestinal gas production. Therefore, the flatulence and abdominal bloating scores are likely to be higher after acarbose administration than after

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<th>Gastrointestinal Symptom Score</th>
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Miglitol mean | Acarbose mean | Median
miglitol administration. In contrast, miglitol does not inhibit α-amylase (12). Therefore, the administration of miglitol increases unabsorbed disaccharides, rather than polysaccharides, in the intestine. Disaccharides are known to induce osmotic diarrhea or softening stools (13). The increased unabsorbed disaccharide may lead to osmotic changes and thus softening the stools during miglitol administration.

Given the fact that poor drug compliance is prevalent among diabetic patients and is associated with adverse clinical outcomes and that initial treatment using an αGI was a risk factor for early nonpersistence and discontinuation of treatment (2, 3), caution is necessary when starting the administration of αGIs. The results of this study may indicate that if diabetic patients are constipated, have firm stools, or flatus, they should be treated with miglitol for postprandial hyperglycemia. In contrast, if diabetic patient have diarrhea, or soft stools, they should be treated with acarbose. As here we have evaluated the differences of acarbose and miglitol in adverse gastrointestinal effects in healthy men, we would like to evaluate these effects in diabetic patients in the future.

As there were no reports which have evaluated the timing of the adverse gastrointestinal effects of acarbose and miglitol, it should be noted that they were observed on day 1, as shown in Fig. 1.

In conclusion, because stools tend to be soft when miglitol is administered and firm when acarbose is administered, the condition of the patient’s stools and gastrointestinal symptoms may be considered when starting αGI therapy.

Acknowledgement
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References