11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases

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1. Objectives

To clarify the effect of rikkunshito (六君子湯) on ghrelin secretion and symptoms and to clarify its mechanism of action in patients with functional dyspepsia (FD).

2. Design

Randomized controlled trial (RCT).

3. Setting

Not mentioned (the author belongs to the Department of Gastroenterology, Graduate School of Medicine, Chiba University), Japan.

4. Participants

Twenty-seven patients with FD fulfilling the Rome III criteria.

5. Intervention

Arm 1: TSUMURA Rikkunshito (六君子湯) Extract Granules 7.5 g/day for 4 weeks (n=13).
Arm 2: domperidone 30 mg/day for 4 weeks (n=14).

6. Main outcome measures

Blood acylated ghrelin (AG) levels, serum leptin levels, gastrointestinal symptoms (assessed by Gastrointestinal Symptom Rating Scale [GSRS] score), and depressive symptoms (assessed by Self-rating Depression Scale [SDS] score) before administration and 2 and 4 weeks after administration began.

7. Main results

All symptoms improved significantly in arm 1 in Week 2 of administration, while gastric acid reflux, abdominal pain, and dyspepsia improved in Week 4. Although in arm 2 these three symptoms improved significantly in Week 2, only dyspepsia had improved in Week 4. And while blood AG levels in arm 1 had improved significantly after 2 weeks compared to before administration ($P<0.05$), no significant change was observed in arm 2. The AG increase and gastrointestinal symptom improvement in arm 1 demonstrated a significant, positive correlation. There were no significant changes in serum leptin levels in either arm. Depression scores did not change significantly in arm 1, but showed a significant improvement in arm 2 in Week 4 ($P=0.04$).

8. Conclusions

Rikkunshito increases blood acylated ghrelin levels and improves gastrointestinal symptoms in FD patients.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

The authors mention that there were no adverse effects between the start and the completion of the trial.

11. Abstractor's comments

This is a valuable clinical study that demonstrated for the first time in an RCT that rikkunshito alleviates gastrointestinal symptoms by increasing blood AG levels in FD patients. In their 2010 paper, the authors did not specify the numbers of participants in each group, and AG levels showed a rising trend only in the week-four analysis. But in their 2012 paper they did specify the numbers of participants in the groups, they excluded two participants with diabetes because insulin resistance and blood sugar levels affect AG concentrations, and analysis in week two, not week four, resulted in a significant difference. Furthermore, they found that the extent of symptomatic improvement correlates to the increase in AG concentration. On the other hand, a study of the relationship of the increase in blood AG concentration and the effects of rikkunshito to the factors relevant to rikkunshito-pattern (六君子湯の証), including presence or absence of fatigue or sensitivity to cold and whether participants exhibit *kyo-sho* or *jitsu-sho* (虚証/実証, deficiency or excess pattern), might yield even more definitive and clinically significant results.

12. Abstractor and date

Motoo Y, 1 June 2010, 1 January 2012 , 1 June 2013.