

**11. Gastrointestinal, Hepato-Biliary-Pancreatic Diseases****References**

Tominaga K, Fujiwara Y, Shimoyama Y, et al. Rikkunshito improves PPI-refractory NERD: a prospective randomized multi-center trial in Japan. *Gastroenterology* 2010; 138: S655–6.

Tominaga K, Fujiwara Y, Arakawa T, et al. GERD — rikkunshito\*. *Shindan to Chiryō (Diagnosis and Treatment)* 2011; 99: 771–6 (in Japanese). [MOL](#), [MOL-Lib](#)

**Tominaga K, Fujiwara Y, Fujimoto K, et al. Rikkunshito improves symptoms in PPI-refractory GERD patients: a prospective, randomized, multi-center trial in Japan. *Journal of Gastroenterology* 2012; 47: 284-92. Pubmed ID: 22081052**

**1. Objectives**

To evaluate the effectiveness of rikkunshito (六君子湯) for patients with proton pump inhibitor (PPI)-resistant gastroesophageal reflux disease (GERD).

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

Department of Gastroenterology, Osaka City University Hospital, and four other research institutes (research groups), Japan.

**4. Participants**

One hundred and four PPI-resistant GERD patients who showed no improvement despite taking rabeprazole (RPZ 10 mg/day) for more than four weeks.

**5. Intervention**

Arm 1: combination group: Participants continued taking 10 mg/day of RPZ and also took TSUMURA Rikkunshito (六君子湯) Extract Granules 2.5 g t.i.d. for four weeks (n=53).

Arm 2: double-dose group: Participants doubled their RPZ dose to 20 mg/day for four weeks (n=51).

**6. Main outcome measures**

Frequency Scale for Symptoms of GERD (FSSG) score and improvement rate.

**7. Main results**

After allocation, three participants were excluded before administration commenced, making 50 participants in arm 1 and 51 in arm 2. There were no significant differences between participants in both groups before administration in age, gender, body mass index, or endoscopic findings after PPI monotherapy, however, FSSG scores were significantly higher in arm 1 before the trial commenced. The data for 45 participants in arm 1 and 50 in arm 2 were included for analysis after the four-week administration period concluded. FSSG total scores (arm 1,  $P<0.001$ ; arm 2,  $P<0.01$ ) as well as reflux and indigestion subscores improved significantly in both groups after 4 weeks of treatment compared to before administration, while the before/after improvement rates were similar in both groups. Sub-group analysis of male patients with non-erosive reflux disease (NERD) showed significant improvement in arm 1 compared to arm 2, and significant improvement in FSSG scores. Remarkably, the ectomorphic group showed similar trends for BMI.

**8. Conclusions**

Rikkunshito is effective for patients with PPI-resistant GERD (and especially NERD). The effects of combined treatment with RPZ and Rikkunshito are similar to treatment with double the RPZ dosage.

**9. From Kampo medicine perspective**

The researchers did not analyze participants' *sho* (証, patterns), but remarkable and significant effects were observed in ectomorphic males.

**10. Safety assessment in the article**

Not mentioned.

**11. Abstractor's comments**

There is still no clear definition of PPI-resistant GERD and no treatments have yet been established. Against that background, this RCT holds great clinical significance because it compared combined rikkunshito and RPZ with double-dosage RPZ in GERD patients who did not respond to 10 mg/day of RPZ. Participants showed similar rates of improvement; however, the exacerbation rate was lower in the rikkunshito and RPZ group, which indicates the effectiveness of rikkunshito in combination.

**12. Abstractor and date**

Kogure T, 31 December 2012, 31 December 2013.