

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

Oka T. Rikkunshito attenuates milnacipran–induced adverse gastrointestinal symptoms and potentiates its antidepressant effect. *Medical Tribune* 2008; 41: 82 (in Japanese).

**1. Objectives**

To evaluate the effect of rikkunshito (六君子湯) on gastrointestinal adverse reactions induced by milnacipran, an antidepressant.

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

University of Occupational and Environmental Health Hospital, Japan.

**4. Participants**

Forty-four patients with depressive disorder.

**5. Intervention**

Arm 1: milnacipran 100 mg/day (final dose) + TSUMURA Rikkunshito (六君子湯) Extract Granules 7.5 g/day for 8 weeks (n=22).

Arm 2: milnacipran 100 mg/day (final dose) for 8 weeks (n=22).

**6. Main outcome measures**

Gastrointestinal symptoms (assessed by the Gastrointestinal Symptom Rating Scale [GSRS] score) and depressive symptoms (by the Self-rating Depression Scale [SDS] score).

**7. Main results**

Gastrointestinal symptoms induced by milnacipran, especially nausea, were significantly reduced in arm 1 compared to arm 2. Overall gastrointestinal symptoms, reflux symptoms, abdominal pain, and dyspepsia scores were significantly reduced in arm 1 compared to before treatment, but not in arm 2 (scores unchanged). The SDS score after 8-week but not 4-week treatment was significantly lower in arm 1 than arm 2.

**8. Conclusions**

Rikkunshito may suppress gastrointestinal symptoms induced by milnacipran and potentiate its antidepressive effect.

**9. From Kampo medicine perspective**

None.

**10. Safety assessment in the article**

Although the safety of rikkunshito was not addressed, rikkunshito significantly reduced adverse events of milnacipran, particularly nausea.

**11. Abstractor's comments**

This study reports that rikkunshito reduced gastrointestinal symptoms such as nausea, which is the most common adverse event of antidepressant treatment with the serotonin norepinephrine reuptake inhibitor (SNRI) milnacipran. The authors reported a similar study of fluvoxamine (SSRI) in 2007 “Oka T, Tamagawa Y, Hayashida S, et al. Rikkunshi-to attenuates adverse gastrointestinal symptoms induced by fluvoxamine. *Biopsychosoc Medicine* [Internet] 2007 [cited 2008 Dec 31]; 1: 21. [http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2204024 DOI:10.1186/1751-0759-1-21,]”.

The combination of fluvoxamine and rikkunshito did not significantly reduce the SDS score in that study, while milnacipran with rikkunshito did significantly lower the score in this study. However, outcome measures based on subjective symptoms may have been affected by the absence of placebo administration in the control group. As SNRIs are used widely, this study provides evidence that Kampo medicines can be useful in modern medicine.

**12. Abstractor and date**

Motoo Y, 1 June 2010.