

## 21. Others

**Reference**

Yasui T, Yamada M, Uemura H, et al. Changes in circulating cytokine levels in midlife women with psychological symptoms treated with selective serotonin reuptake inhibitors and Japanese traditional medicine. *Maturitas* 2009; 62: 146–52.

**1. Objectives**

To compare the effects of kamishoyosan (加味逍遙散) and paroxetine in improving anxiety and depression as menopausal symptoms.

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

Department of Obstetrics and Gynecology, Tokushima University Hospital, Japan.

**4. Participants**

Seventy-six women with menopausal, psychological symptoms (such as anxiety and mild depression) who were recruited from among patients visiting the outpatient clinic of the Department of Obstetrics and Gynecology between November 2005 and October 2007. Subjects with major depression were excluded.

**5. Intervention**

Arm 1: paroxetine (paroxetine [GlaxoSmithKline] 10 mg/day for 6 months) (n=38).

Arm 2: Kamishoyosan (Tsumura Kamishoyosan Extract Granules 7.5 g/day for 6 months), (n=38).

**6. Main outcome measures**

The main outcome measures were serum levels of cytokines (IL-1 $\beta$ , IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, TNF- $\alpha$ , IFN- $\gamma$ , MCP-1, and MIP-1 $\beta$ ) and climacteric symptoms assessed using Greene's climacteric scale.

**7. Main results**

The psychological, somatic, and vasomotor scores assessed using Greene's climacteric scale were improved in both arms, but improvement was greater in the paroxetine arm. Serum IL-6 levels decreased significantly compared with baseline in both arms, and showed significant positive correlations with Greene's climacteric scores. A significant decrease in IL-8, MIP-1 $\beta$ , and MCP-1 levels was also observed in the paroxetine arm.

**8. Conclusions**

The mechanism of the drug action of both paroxetine and kamishoyosan may involve IL-6, which therefore may be a useful marker of treatment. Though useful in treating menopausal symptoms, kamishoyosan is less effective than paroxetine.

**9. From Kampo medicine perspective**

None.

**10. Safety assessment in the article**

Six of the 38 women in the paroxetine arm dropped out of the study because of the following adverse effects: headache, nausea, and uncomfortable gastrointestinal tract symptoms. One woman in kamishoyosan arm dropped out of the study because of bitter taste in the mouth and diarrhea, and two women dropped out because of no response to the drug.

**11. Abstractor's comments**

Kamishoyosan is often prescribed along with keishibukuryogan (桂枝茯苓丸) for treatment of menopausal symptoms. Although less effective than paroxetine, kamishoyosan was useful. Clinically, kamishoyosan and keishibukuryogan are prescribed based on *Kampo* findings, and the effectiveness of these drugs might be demonstrated if the subjects are treated on the basis of *Kampo* findings. However, it is interesting that improvement in somatic and psychological symptoms was correlated with serum IL-6 level. This correlation suggests a role of IL-6 in the mechanism of kamishoyosan.

**12. Abstractor and date**

Nakata H, 1 June 2010.