9. Cardiovascular Diseases

References

Arakawa K, Saruta T, Abe K, et al. Double-blind placebo-controlled trial of TSUMURA Orengedokuto (TJ-15) for the treatment of accessory symptoms of hypertension*. *Rinsho to Kenkyu* (*Japanese Journal of Clinical and Experimental Study*) 2003; 80: 354-72 (in Japanese). Ichushi Web ID: 2003184342 MOL, MOL-Lib

Arakawa K, Saruta T, Abe K, et al. Improvement of accessory symptoms of hypertension by TSUMURA Orengedokuto Extract, a four herbal drugs containing Kampo-Medicine Granules for ethical use: a double-blind, placebo-controlled study. *Phytomedicine* 2006; 13: 1-10. [CENTRAL ID: CN-00553637, Pubmed ID: 16360926

1. Objectives

To evaluate the efficacy and safety of orengedokuto (黄連解毒湯) in patients with hypertension symptoms.

2. Design

Double-blind, randomized, controlled trial (DB-RCT).

3. Setting

A total of 116 university hospitals and community hospitals, Japan.

4. Participants

A total of 265 patients with hypertension who met the inclusion and exclusion criteria; 204 included and 61 not included for analysis.

5. Intervention

Arm 1: administration of TJ-15 (containing 0.25 g of TSUMURA Orengedokuto (黄連解毒湯) Extract Granules) capsules, 2 cap, t.i.d. (n=103).

Arm 2: administration of placebo capsules, 2 cap, t.i.d. (n=101).

Oral administration before each meal. Duration of treatment: 8 weeks.

6. Main outcome measures

Reduction in blood pressure was evaluated by comparing blood pressure measurements (systolic, diastolic, and mean) obtained after the run-in period and after the treatment period, and the antihypertensive effect was classified into 5 grades. Improvement in five major accessory symptoms – irritability (feeling irritated), anxiety, sleep disorder, hot flushes, and facial flushing – and other subjective symptoms – headache/heavy-headedness, shoulder stiffness, dizziness, and malaise – were graded from –3 to 3.

7. Main results

There was no significant difference in blood pressure decrease, or antihypertensive effect, between the TJ-15 group and placebo group. Significant efficacy against hot flushes and facial flushing was observed in the treatment group. Irritability, anxiety, and sleep disorder were also improved in the treatment group as compared with the placebo group. Scores of the other subjective symptoms improved significantly. There was no significant between-group difference in the overall safety rating.

8. Conclusions

This study demonstrates the efficacy and safety of orengedokuto for the treatment of hypertension symptoms.

9. From Kampo medicine perspective

The inclusion criteria were high blood pressure and presence of hypertension symptoms (irritability, anxiety, sleep disorder, hot flushes, and facial flushing) indicating orengedokuto "*sho* (pattern)". Also 'patients with "*kan-sho*" (寒証, cold/yin pattern) or "*kyo-sho* (虚証, deficiency pattern)" in Kampo medicine' were excluded. Although "*sho*" is not fully equivalent to body-mass index (BMI), patients with thin physique were excluded from this study, resulting in the mean BMI of 24.3. Thus, the focus of this study was on the patients who were most likely to respond to and benefit from orengedokuto.

10. Safety assessment in the article

Adverse effects were observed in eight patients (6.3%) in the placebo group and 15 patients (11.5%) in the TJ-15 group. Nausea (n=2), abnormal laboratory data such as liver dysfunction (elevated liver enzymes) (n=7), and generalized rash (n=1) might be associated with orengedokuto.

11. Abstractor's comments

Orengedokuto, a typical Kampo medicine for hypertension, was reevaluated in this original article. This study targets the symptoms related to stress or hyper-activation of sympathetic nervous system such as anger, stress, anxiety, and fear. In this multicenter double-blind clinical trial, blood pressure tended to decrease, but did not significantly decrease, in response to treatment. However, significant improvement in some accessory symptoms is a milestone. Compared with benzodiazepine anxiolytics in a study of essential hypertension, Orengedokuto seemed to show more efficacy. However, simple comparison cannot be done owing to different criteria used in selecting study participants. This study suggests that treatment based on "*sho*" may be effective. **Abstractor and date**

Namiki T, 15 June 2007, 1 April 2008, 13 March 2009, 1 June 2010, 31 December 2013.