13. Diseases of the Musculoskeletal System and Connective Tissue

Reference

Nishizawa Y, Nishizawa Y, Yoshioka F, et al. Therapeutic effect of boiogitokashuchibushimatsu on gonarthrosis: a 10-year prospective randomized controlled trial with loxoprofen sodium*. *Pharma Medica* 2007; 25: 15-21 (in Japanese). Ichushi Web ID: 2008070613 MOL, MOL-Lib

1. Objectives

To evaluate the efficacy of boiogitokashuchibushimatsu (防已黄耆湯加修治附子末) for gonarthrosis.

2. Design

Randomized controlled trial (RCT).

3. Setting

University hospital (Department of Pathology and Applied Neurobiology, Kyoto Prefectural University of Medicine; Pain Clinic, Department of Anesthesiology, Shiga University of Medical Science; and Graduate School of Pharmaceutical Sciences, Osaka University) and 4 other hospitals, Japan.

4. Participants

Two hundred eleven patients with gonarthrosis.

5. Intervention

Arm 1: administration of boiogitokashuchibushimatsu (防已黄耆湯加修治附子末) (manufacturer unknown) (n=110); age at completion, 81.5±3.4 years; male/female ratio, 8:102.
Arm 2: administration of loxoprofen (n=101); age at completion, 82.0±3.1 years; male/female ratio, 9:92.
Ten-year trial. Capsules were taken with 350 mL of water 30 min before meals.
No more details (e.g. dose, dose frequencies) were indicated in the original paper.

6. Main outcome measures

Exercise capacity (EC), range of motion of knee, various chronic pains (CP), health-related quality of life (Hr-QOL), adiponectin, leptin, and orexin levels, knee circumference, synovial fluid retention as assessed by ultrasound, degree of joint space narrowing as assessed by CT scan, (direct, indirect, total) medical expenses monitored over a 10-year period.

7. Main results

All EC parameters (continuous walking distance, continuous upslope walking distance, number of steps in continuous downslope walking) were larger in arm 1 than in arm 2 (P<0.001). All parameters used to evaluate activities of daily living (ADL) (pain in passive exercise, spontaneous pain, pain on pressure, patella ballottement/soft tissue swelling, local heat, etc.), various CP, and Hr-QOL were significantly improved in arm 1 compared with arm 2 (P<0.001).

8. Conclusions

The treatment significantly improves EC, ADL, CP, and Hr-QOL and lowers total medical expenses.

9. From Kampo medicine perspective

The *sho* (pattern) concept was a criterion for inclusion. Although “gonarthrosis complying with the *sho* for boiogitokabushi” was used as a criterion, the *sho* concept was not defined. The authors appear to consider that all patients with gonarthrosis in the study satisfy the sho for boiogitokabushi. There was no *sho* concept as an exclusion criterion and no subgroup analyses according to *sho*.

10. Safety assessment in the article

A significantly larger number of adverse events occurred in arm 2 (P<0.001 for all items): gastric ulcer (0 event in arm 1 *vs*. 24 events in arm 2), eruption/sleepiness/stomach discomfort/oedema (11 events *vs*. 348 events), and laboratory abnormality (3 events *vs*. 417 events).

11. Abstractor’s comments

The filling of capsules to make the investigational products indistinguishable from each other is necessary for double-blind study of Kampo medicine. However, the dose of loxoprofen is missing from this paper (misprint?). This study assumed that “patients with gonarthrosis satisfy the *sho* for boiogitokashuchibushi.” This assumption should have been verified in a pilot study. However, it is extremely rare that a particular disease corresponds one-on-one to an effective Kampo treatment; the treatment of most diseases needs several Kampo medicines selected according to patient conditions. Furthermore, prolonged administration of drugs (including loxoprofen used as the control drug in this study) causing potentially fatal adverse reactions in the elderly such as gastric mucosal disorder is problematic. Also problematic is the therapeutic use of fixed doses for painful disease. Moreover, duration of the study was too long, given the nature of this disease and the old age of most subjects. Conclusion should be drawn in a shorter term.

12. Abstractor and date

Hoshino E, 15 March 2009, 1 June 2010, 31 December 2013.