

**13. Diseases of the Musculoskeletal System and Connective Tissue****References**

Matsuta K, Gu XP, Ito K, et al. Evaluation of jiinkokato and steroid combination therapy for chronic rheumatoid arthritis. *Kampo Igaku (Kampo Medicine)* 1995;19:50–2 (in Japanese).

**1. Objectives**

To evaluate the efficacy of jiinkokato (滋陰降火湯) for reducing adverse effects of steroids in patients with chronic rheumatoid arthritis mainly by blood cell examination.

**2. Design**

Randomized controlled trial (RCT).

**3. Setting**

Two facilities (Department of Medicine and Physical Therapy, the University of Tokyo Hospital, and Matsuta Internal Medicine Clinic), Japan.

**4. Participants**

Fourteen female patients with chronic rheumatoid arthritis visiting the above facilities between 1992 and 1993 and continuously receiving prednisolone (5–7.5 mg/day) for at least 1 year (mean age, 61 years; range, 38–76 years).

**5. Intervention**

Arm 1: prednisolone 5–7.5 mg/day + TSUMURA Jiinkokato (滋陰降火湯) Extract Granules 2.5 g t.i.d. before meals (n=6).

Arm 2: prednisolone 5–7.5 mg/day (n=8).

**6. Main outcome measures**

Hemoglobin; peripheral hematological parameters, including leukocyte and lymphocyte counts; and C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and albumin/globulin (A/G) ratio as indices of the activity of chronic rheumatoid arthritis, evaluated before and after treatment (treatment period varying from 6 to 28 weeks).

**7. Main results**

There were no changes in any measures in the control group. In contrast, the percentage of neutrophils was significantly reduced to  $64.1 \pm 8.2$  from  $75.9 \pm 9.0$  and the percentage of lymphocytes was significantly increased to  $24.3 \pm 6.8$  from  $17.3 \pm 9.0$  after treatment ( $p < 0.05$ ) with jiinkokato. In two patients, lymphocyte count more than doubled after jiinkokato treatment from less than  $1000/\mu\text{L}$  at baseline. The indices of the activity of chronic rheumatoid arthritis remained unchanged in both arms.

**8. Conclusions**

Jiinkokato is effective for reducing the adverse effects of steroids including increased neutrophils (%) and decreased lymphocytes (%).

**9. From Kampo medicine perspective**

The adverse effects of steroids are considered to represent the state of *yinkyonainetsu* (陰虛内熱, *yin* deficiency with internal heat) according to Kampo (traditional Chinese) medicine, and are an indication for jiinkokato. The hematologic abnormalities noted in steroid-treated patients were improved by jiinkokato, suggesting an immunoregulatory effect.

**10. Safety assessment in the article**

Jiinkokato did not increase the incidences of the following adverse effects of steroids: hypertension, obesity, peptic ulcer, purpura, osteoporosis, diabetes mellitus, and edema.

**11. Abstractor's comments**

Collagen disorders including chronic rheumatoid arthritis are often treated with long-term steroid therapy, which is associated with a reduction in lymphocyte count in some cases, even to  $1000/\mu\text{L}$ , posing a problem for outpatient management. This study showed that the jiinkokato combination decreased neutrophil count and increased lymphocyte count, suggesting that it has efficacy for reducing the adverse effects of steroids. However, possibly because of the small sample size, the measures of chronic rheumatoid arthritis activity were unchanged, and the various adverse effects of steroids were clinically unimproved. A future case series investigation of the efficacy of long-term combination therapy is awaited.

**12. Abstractor and date**

Ushiroyama T, 13 August 2008, 1 June 2010, 31 December 2013.