健常人のTh1/Th2バランスに及ぼす十全大補湯および小柴胡湯の影響

渡辺賢治、金光弼、中田勉、三田一樹、加藤裕之、鳥居塚和生、花輪壽彦

北里研究所東洋医学総合研究所

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Effect of Juzentaiho-to and Shosaiko-to on Th1/Th2 balance

Kenji Watanabe, Guangbi Jin, Tsutomu Nakada, Kazuki Santa, Hiroyuki Kato,
Kazuo Toriizuka, Toshihiko Hanawa

Oriental Medicine Research Center of the Kitasato

Key words Th1/Th2 balance, Juzentaiho-to, Saikokeishi-to

Introduction

It is believed that some auto-immune diseases are caused by excess function of Th1 or Th2. Atopic diseases like atopic dermatitis, bronchial asthma, or allergic rhinitis are typical Th2 diseases. It has been shown that Kampo treatment is effective for these atopic diseases (1,2). The mechanism how Kampo medicines play a role in the treatment of atopic diseases is supposed to be change of the Th1/Th2 balance. We have shown that some Kampo formulas could alter the Th1/Th2 balance in studies using different strains of mice (3,4). In this presentation, we show that how Kampo formulas, Shosaiko-to and Juzentaiho-to affect the Th1/Th2 balance.

Subjects and Methods

Objects and treatment: Three healthy men and 10 wemen (20~38 years old) were administered 7.5 g/day of Shosaiko-to (SST: TJ-9) and ten women (20~25 years old) took 7.5 g/day of Juzentaiho-to (JTT: TJ-48) for 2 weeks.

Mononuclear Cell isolation: Peripheral blood was obtained from these subjects before and after the administration of Kampo. Mononuclear cell (PBMC) were isolated by Ficoll gradient centrifugation.

Mononnuclear cell subpopulation: Cells were incubated with the combination of fluorescein isothiocyanate (FITC)-conjugated anti-human CD3 monoclonal antibody and R-phycoerythrin (PE)-conjugated CD19 monoclonal antibody, FITC-conjugated anti-human CD4 monoclonal antibody and PE-conjugated CD8 monoclonal antibody, or FITC-conjugated anti-human CD4 monoclonal antibody and PE-conjugated CD45RO monoclonal antibody. After incubation, cells were washed 3 times with cold PBS and analyzed using an EPICS Elite flow cytometer (Coulter Cytometry Co, Hialeah, FL, USA).

Cytokjne analysis: PBMC were cultured in RPMI1640 supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 100 IU/ml penicillin and 100 μg/ml of streptomycin. Cells were stimulated with anti-CD3 monoclonal antibody to detect IL-4 and IFN-γ, or LPS to detect IL-12. Supernatant was collected and the cytokine concentrations in the supernatant were determined by ELISA.

Statistics and data analysis: The data were analyzed using Wilcoxon's signed ranks test.

A p value of <0.05 was accepted as statistically significant.

Results

Mononuclear cell subpopulation: In the SST group, none of CD3, CD4, CD8 and CD19 positive cell populations changed. In the JTT group, CD3 positive cells increased that is mainly due to the increase of CD 8 positive cells. In both SST and JTT groups, CD45RO positive memory cells did not changed.

Cytokine analysis: Although IFN-γ and IL-4 secretion by cultured PBMC were increased by both SST and JTT, the ratio of IFN-γ and IL-4 was changed only in the SST group. This result indicated that JTT stimulated the secretion of IFN-γ and IL-4 almost equally and the Th1/Th2 balance was not changed. While, SST stimulated IFN-γ dominantly and the Th1/Th2 balance was shifted from Th2 side to Th1 side. The secretion of IL-12 was increased only in the SST group. IL-12 is the cytokine that stimulates Th1 cells. This data also supported the result that SST changed the Th1/Th2 balance to Th1.

*〒108-8642 東京都港区白金 5-9-1

5-9-1 Shirokane Minato-ku, Tokyo 108-8642, Japan

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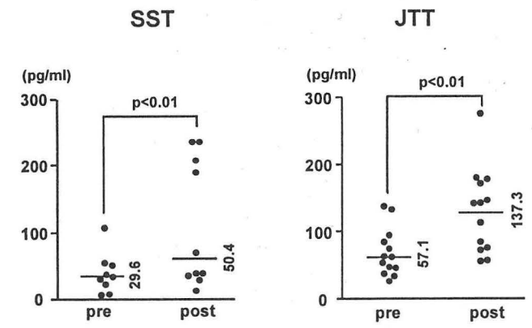

Fig. 1 Effect of Kampo administration on IFN-γ secretion by PBMC. Each Kampo formulation was administered for 2 weeks.
SST: Shosaiko-to, JTT: Juzentaiho-to.

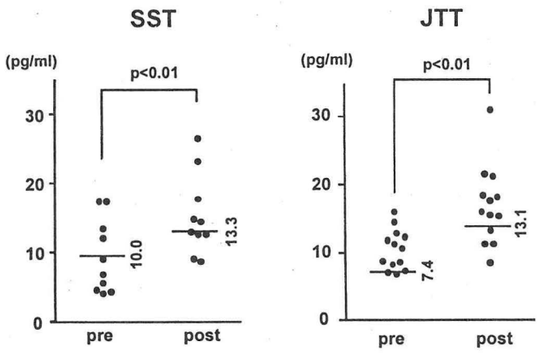

Fig. 2 Effect of Kampo administration on IL-4 secretion by PBMC. Each Kampo formulation was administered for 2 weeks.

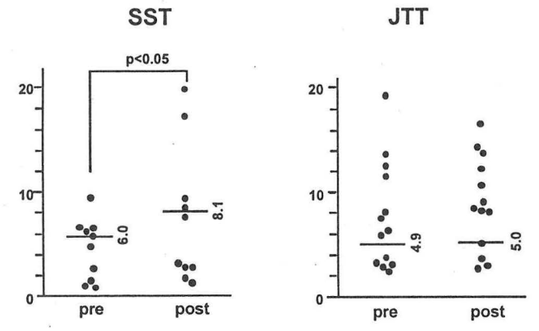

Fig. 3 Effect of Kampo administration on IFN-γ/IL-4 ratio. .

Discussion

The rsults obtained in this study indicated that although both JTT and SST increased the secretion of IFN-γ and IL-4 from PBMC, the response to Kampo formula is different between SST and JTT, i.e. only SST changed the Th1/Th2 balance. However JTT did not change the Th1/Th2 balance in this study, it may change the Th1/Th2 balance if it is administered for longer period, because JTT is usually administered for rather long period of time from a clinical standpoint.

We have shown that Kampo formula improved the clinical symptoms in atopic dermatits patient and the change of the Th1/Th2 balance was observed (5). These data supported the mechanism of Kampo medicine in the treatment of atopic diseases may be the change of Th1 and Th2 related cytokines.

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