

## 21. Others

**References**

Niitsuma T, Fukuda T, Yamamoto S, et al. Effects of saibokuto and other saiko-zai (saiko-drugs) on prednisolone metabolism. *Kampo to Meneki-Arerugi (Kampo and Immuno-allergy)* 1993; 7: 43–52 (in Japanese).

Homma M, Oka K, Ikeshima K, et al. Different effects of traditional Chinese medicines containing similar herbal constituents on prednisolone pharmacokinetics. *Journal of Pharmacy and Pharmacology* 1995; 47: 687–92. CENTRAL ID: CN-00120671, Pubmed ID: 8583374

**1. Objectives**

To evaluate the effects of shosaikoto (小柴胡湯), saibokuto (柴朴湯), and saireito (柴苓湯) on prednisolone metabolism.

**2. Design**

Randomized cross-over controlled trial (RCT-cross over).

**3. Setting**

Department of Clinical Pharmacology, Tokyo University of Pharmacy and Life Science, 3rd Department of Internal Medicine, Tokyo Medical University, Japan.

**4. Participants**

Twenty-two nonsmoking healthy males who took no drug that could affect glucocorticoid metabolism.

**5. Intervention**

Since allocation of patients by administration pattern to these treatment arms is not known, the treatment arms are described in terms of treatment regimen.

**Study 1**

Arm 1: TSUMURA Shosaikoto (小柴胡湯) Extract Granules 2.5 g t.i.d. for 3 days. On the third study day, 10 mg prednisolone was administered orally in combination with the test preparation (n=6).

Arm 2: prednisolone 10 mg (n=6).

Age, 21.8±1.2 years; body weight, 63.8±6.8 kg

**Study 2**

Arm 1: TSUMURA Saibokuto (柴朴湯) Extract Granules 2.5 g t.i.d. for 3 days. On the third study day, 10 mg prednisolone was administered orally in combination with the test preparation (n=9).

Arm 2: prednisolone 10 mg (n=9).

age, 23.5±1.5 years; body weight, 61.3±4.5 kg

**Study 3**

Arm 1: TSUMURA Saireito (柴苓湯) Extract Granules 3.0 g t.i.d. for 3 days (n=7)

Arm 2: prednisolone 10 mg (n=7)

Age, 22.4±1.9 years; body weight, 62.0±7.1 kg

Following a 2-week washout period, subjects were crossed over to the opposite arm.

**6. Main outcome measures**

Areas under the time-blood concentration curve (AUC) of prednisolone and prednisone, measured before and 1, 2, 4, and 6 h after treatment.

**7. Main results**

After the intervention, the AUC of prednisolone was significantly decreased to 0.94–0.78 mgL<sup>-1</sup> in the shosaikoto group ( $P<0.05$ ), significantly increased to 0.92–1.06 mgL<sup>-1</sup> in the saibokuto group, and unchanged in the saireito group. After the intervention, the AUC ratio of prednisolone to prednisone, which reflects the activity of 11β-hydroxysteroid dehydrogenase (11-HSD), an *in vivo* steroid metabolic enzyme, was increased in the shosaikoto group ( $P<0.01$ ), decreased in the saibokuto group ( $P<0.01$ ), and unchanged in the saireito group.

**8. Conclusions**

Different types of saiko drugs affect steroid pharmacokinetics differently. 11-HSD activity is decreased, unaffected, and increased by saibokuto, saireito, and shosaikoto, respectively.

**9. From Kampo medicine perspective**

None.

**10. Safety assessment in the article**

Not mentioned.

**11. Abstractor's comments**

Kampo formulations have been used to stabilize medical conditions treated with steroids, with the aim of decreasing the use of steroids. This valuable study examined the effect of each saiko drug on steroid pharmacokinetics. An RCT in steroid-treated patients, but not healthy subjects as in the present study, would clarify the meaning of the present results.

**12. Abstractor and date**

Tsuruoka K, 26 April 2008, 1 June 2010, 31 December 2013.