21. Others

Reference

Sadakane C, Watanabe J, Fukutake M, et al. Pharmacokinetic profiles of active components after oral administration of a Kampo medicine, shakuyakukanzoto, to healthy adult Japanese volunteers. *Journal of Pharmaceutical Sciences* 2015; 104: 3952-9.

1. Objectives

Comparative analysis of the plasma concentrations of components of shakuyakukanzoto (芍薬甘草湯) after administration of different doses

2. Design

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

3. Setting

A clinic in Tokyo

4. Participants

The inclusion criteria were healthy Japanese adults aged 20–45 with a body mass index (BMI) between 18 and 25. The exclusion criteria were liver, cardiac or vascular diseases; intake of supplements containing components of shakuyakukanzoto or any medicine within 3–7 days before the first dose; allergy, and habitual use of alcohol or nicotine. Twenty subjects were included in the trial.

5. Intervention

Twenty subjects aged 21–42 were assigned randomly to two groups of 10 subjects.

Arm 1: 10 subjects. They were administered shakuyakukanzoto a single oral dose of 2.5 g in the first period. After a 7-day washout period, they were administered shakuyakukanzoto a single oral dose of 5 g in the second period.

Arm 2: 10 subjects. They were administered shakuyakukanzoto a single oral dose of 5 g in the first period. After a 7-day washout period, they were administered shakuyakukanzoto a single oral dose of 2.5 g in the second period.

6. Main outcome measures

The plasma concentrations of 6 active components of shakuyakukanzoto, i.e., albiflorin (ALB), paeoniflorin (PAE), glycycoumarin (GCM), isoliquiritigenin (ILG), glycyrrhetic acid (GA), and glycyrrhetic acid-3-*O*-monoglucuronide (3MGA), were measured by liquid chromatography-mass spectrometry. Based on these concentrations, the pharmacokinetic parameters were calculated, and linearity was assessed.

7. Main results

After oral administration of shakuyakukanzoto, all of the active components were detected in the plasma. ALB, PAE, GCM, and ILG were detected at an early stage. Time to maximum plasma concentration, t_{max}, after administration of 5.0 g were 2.00 hr for ALB, 3.00 hr for PAE, 0.500 hr for GCM, and 0.250 hr for ILG. Elimination half-life, $t_{1/2}$, of ALB (1.81 hr for 2.5 g and 1.76 hr for 5.0 g) and PAE (1.74 hr for 2.5 g and 1.73 hr for 5.0 g) were particularly short. Linearity was observed for the maximum plasma concentrations of GCM, ILG, and GA and for the area under the concentration-time curve of GA.

8. Conclusions

It was demonstrated for the first time in humans that active components of shakuyakukanzoto were absorbed into the blood after oral administration.

9. From Kampo medicine perspective

Not mentioned.

10. Safety assessment in the article

Because it is written that the trial will be stopped if a serious adverse event occurs, and no subject dropped out, it is determined that there were no adverse events. It is argued in the paper that this study provides a basis for elucidating the mechanisms of common adverse events to Kampo medicines such as hypokalemia because the absorption of each component into the blood was confirmed.

11. Abstractor's comments

This is an important trial which proved for the first time in humans that active components of shakuyakukanzoto were absorbed into the blood after oral administration. All 6 components were absorbed into the blood after oral administration of both 2.5 g and 5 g. I expect this study will lead to more clinically relevant studies to identify, for example, the component or components that work against muscle cramp or abdominal pain, which shakuyakukanzoto is known to be effective against.

12. Abstractor and date

Tsuruoka K, 22 April 2017