21. Others

Reference

Inotsume N, Fukushima S, Hayakawa T, et al. Pharmacokinetics of Ephedrine and Pseudoephedrine after oral administration of kakkonto to healthy male volunteers. *Rinsho Yakuri* (*Japanese Journal of Clinical Pharmacology and Therapeutics)* 2009; 40: 79-83. Ichusi Web ID: 2009308892

1. Objectives

To evaluate the pharmacokinetic profiles of serum ephedrine and pseudoephedrine after oral administration of kakkonto (葛根湯), and changes in biokinetics after different administered doses.

2. Design

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

3. Setting

One university, Japan.

4. Participants

Ten healthy male volunteers aged 23-26 years.

5. Intervention

Since allocation of patients to these treatment arms is not mentioned, the treatment arms are described in terms of treatment regimen.

To examine the actual absorption under the conditions of administration after meals, following an overnight fast, kakkonto was given 1 hour after breakfast, and lunch was served 4 hours later. Blood samples were obtained before dosing and at 0.5, 1, 1.5, 2, 3, 4, 6, 8, 10 and 12 hours after drug ingestion. The regimen was repeated in cross-over design after an interval of 2 weeks. Daily dose (7.5 g) of kakkonto contained 14.43 mg of ephedrine and 5.73 mg of pseudoephedrine.

Arm 1: Kanebo (now Kracie) Kakkonto (葛根湯) Extract Granule 2.5 g.

Arm 2: Kanebo (now Kracie) Kakkonto (葛根湯) Extract Granule 3.75 g.

6. Main outcome measures

Indices of the blood level-time curve of ephedrine and pseudoephedrine (maximum concentration [Cmax]), time to maximum serum concentration (tmax), area under the serum concentration-time curve (AUC), mean residence time (MRT), and terminal elimination rate constant (κ).

7. Main results

Serum ephedrine and pseudoephedrine concentrations were measured using a gas chromatograph-mass spectrometer. Standard curves were constructed based on quantitative analysis of deuterium labeled epinephrine and pseudoephedrine.

In Arm 1, the mean values of Cmax (ng/mL), tmax (h), AUC (ng・h/mL), MRT (h), and κ (/h) of ephedrine were 22.0, 3.0, 238.5, 9.8, and 0.1, respectively, and those of pseudoephedrine were 8.1, 3.0, 66.8, 7.4, and 0.2, respectively. The mean Cmax values of ephedrine and pseudoephedrine were 1.50- and 1.58-fold higher in Arm 2 compared with Arm 1, although the tmax did not differ significantly. The mean AUC values of ephedrine and pseudoephedrine in Arm 2 were 1.31- and 1.48- fold higher, respectively, than those in Arm 1, while the mean MRT and κ did not differ significantly.

8. Conclusions

The kinetic behavior of ephedrine and pseudoephedrine are largely linear at the doses examined.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned.

11. Abstractor's comments

This is a basic study evaluating the pharmacokinetics of ephedrine and pseudoephedrine contained in kakkonto in human serum. They were determined using high precision measurements such as gas chromatography, mass spectrometry, and deuterium labeling.

12. Abstractor and date

Fujisawa M, 1 June 2010, 31 December 2013.