21. Others

Reference

Ohnishi M, Hitoshi K, Katoh M, et al. Effect of a Kampo preparation, byakkokaninjinto, on the pharmacokinetics of ciprofloxacin and tetracycline. *Biological & Pharmaceutical Bulletin* 2009; 32: 1080–4. CENTRAL ID: CN-00704915, Pubmed ID: 19483319 J-STAGE

1. Objectives

To evaluate the effects of co-administered byakkokaninjinto (白虎加人参湯) on pharmacokinetics and renal excretion of antibiotics (tetracycline or ciprofloxacin.

2. Design

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

3. Setting

Department of Pharmacy and Pharmacokinetics, Aichi Medical University and Faculty of Pharmacy, Meijo University, Japan.

4. Participants

Twenty healthy male volunteers (aged 23–36, mean 29.3 years).

5. Intervention

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

Study 1

Arm 1: oral ciprofloxacin (Ciproxan tablet) 200 mg alone.

Arm 2: oral ciprofloxacin (Ciproxan tablet) 200 mg + byakkokaninjinto (白虎加人参湯) 3 g.

Each subject took Ciproxan immediately after taking byakkokaninjinto (白虎加人参湯) with 180 mL of water. After a 7-day wash-out period, the treatments were switched.

Study 2

Arm 1: oral tetracycline (Achromycin V capsule) 250 mg alone.

Arm 2: oral tetracycline (Achromycin V capsule) 250 mg + byakkokaninjinto (白虎加人参湯) 3 g.

The dosing and cross-over were performed in the same manner as Study 1.

The number of subjects in each arm is not specified.

6. Main outcome measures

Plasma and urinary concentrations of tetracycline and ciprofloxacin were measured by HPLC.

7. Main results

The peak plasma concentration (C_{max}) and area under the plasma concentration-time curve (AUC) of tetracycline and ciprofloxacin were significantly decreased by co-administration of byakkokaninjinto. The decrease in bioavailability of ciprofloxacin (15%) was smaller compared with that of tetracycline (30%). The co-administration of byakkokaninjinto significantly decreased urinary excretion rate of tetracycline, but not that of ciprofloxacin. Byakkokaninjinto had no effect on renal clearance of either antibiotic.

8. Conclusions

Byakkokaninjinto appears to reduce the absorption of tetracycline and ciprofloxacin.

9. From Kampo medicine perspective

In this study, it was assumed that byakkokaninjinto was used for treating heat exhaustion and febrile disease.

10. Safety assessment in the article

Not mentioned.

11. Abstractor's comments

This highly suggestive study noted that co-administered byakkokaninjinto may reduce the absorption of tetracyclines and new quinolone agents (e.g., ciprofloxacin). The authors stated that this reduction may be due to the formation of chelates with Ca^{2+} contained in byakkokaninjinto. There remain some problems in the study design, such as small number of participants, inclusion of male subjects only, and no description of the number of subjects assigned to each arm. Yet the results of this study, if confirmed, mean that the co-administered byakkokaninjinto may delay the cure of infectious diseases, and therefore will have a strong impact on clinical practice. An RCT of byakkokaninjinto in patients with infectious diseases is desirable, but ethical aspects of such a trial must be considered. Alternatively, retrospective studies, including studies with a case-control design, might be of some help. Further studies on this topic are expected.

12. Abstractor and date

Tsuruoka K, 1 June 2010, 31 December 2013.