2. Cancer (Condition after Cancer Surgery and Unspecified Adverse Drug Reactions of Anti-cancer Drugs)

Reference

Nagao K, Nishimura R, Matsuda M, et al. Clinical evaluation of the combined effect of tegafur and *hozai* (補剤; formulations with tonic effects)*. *Toho Igaku* (*Eastern Medicine*) 1998; 14: 63-71 (in Japanese with English abstract).

1. Objectives

To evaluate the efficacy of hochuekkito (補中益気湯) or ninjin'yoeito (人参養栄湯) for reducing adverse drug reactions and improving quality of life (QOL) in breast cancer patients undergoing postoperative (after curative resection or initial treatment) Sunfral S (800 mg/day).

2. Design

Randomized controlled trial using sealed envelopes for allocation (RCT-envelope).

3. Setting

One hospital, Japan.

4. Participants

Patients with breast cancer receiving the anti-cancer drug Sunfral S (800 mg/day) postoperatively (21 of 26 were evaluated).

5. Intervention

Arm 1: Sunfral S 400 mg/day b.i.d.+ Kanebo Hochuekkito (補中益気湯) Extract Fine Granules 2.5 g t.i.d. for at least 5 months (n=13).
Sunfral S 400 mg/day b.i.d. + Kanebo Ninjin'yoeito (人参養栄湯) Extract Fine Granules 2.5 g t.i.d. for at least 5 months (n=1).

Arm 2: Sunfral S 400 mg/day b.i.d. alone (n=12).

6. Main outcome measures

Adverse drug reactions; white blood cell (WBC), lymphocyte, and red blood cell (RBC) counts; carcinoembryonic antigen (CEA) evaluated before treatment and at 2, 4, and 6 months after treatment; immunological indices including CD2 CD4, CD8, CD16, and NK cell counts, and lymphocyte stimulation index; and duration of administration.

7. Main results

The Kampo medicines did not significantly reduce adverse drug reactions associated with tegafur/uracil (UFT). There were no between-arm differences in WBC, lymphocyte, or RBC counts (statistical analysis not performed). CEA was increased in 0/5 patients in arm 1 and 4/7 patients in arm 2 (not determined in all patients, statistical analysis not performed). Among patients with adverse drugs reactions to Sunfral S, those in arm 1 received Sunfral S for a longer duration.

8. Conclusions

In patients with adverse drug reactions to postoperative Sunfral S (800 mg/day) for breast cancer, hochuekkito was immunostimulatory (according to percent change noted in the lymphocyte stimulation index) and Sunfral S could be administered for a longer period than the control group.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

There were no differences in the incidence or severity of adverse events between arm 1 and arm 2 (statistical analysis not performed).

11. Abstractor's comments

The authors concluded that combination of hochuekkito with the anti-cancer drug (Sunfral S) was immunostimulatory, as indicated by the increase in lymphocyte stimulation index, and thereby facilitated long-term treatment with anti-cancer drugs. This conclusion is however not supported by evidence that the lymphocyte stimulation data reflect the degree of immunostimulation, considering that there were no significant differences in the percent changes in tumor immunity-related markers including lymphocyte surface markers (helper T/suppressor T/NK cell activities). Furthermore, changes in CEA were not evaluated in the total population, and the evaluation depended on an unsound criterion (i.e., change by 1 μg/mL or more). Moreover, arm 1 in this study included more than one Kampo medicine; 13 patients receiving hochuekkito and 1 patient receiving ninjin'yoeito, and thus the amount of data available for statistical analysis was insufficient and a meaningful conclusion cannot be drawn from these findings.

12. Abstractor and date

Hoshino E, 23 April 2009, 6 January 2010, 1 June 2010.