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

Reference

Hibi S, Ina K, Furuta R, et al. Clinical effects of hange-shashin-to on combination therapy of S-1/irinotecan for patients with metastatic gastric and colorectal cancer*. Gan to Kagaku Ryoho (*Japanese Journal of Cancer Chemotherapy*) 2009; 36: 1485–8 (in Japanese with English abstract). CENTRAL ID: CN-00728899, Pubmed ID: 19755817, Ichushi Web ID: 2009352672, MOL, MOL-Lib

1. Objectives

To evaluate the efficacy of hangeshashinto (半夏瀉心湯) for delayed diarrhea induced by irinotecan (CPT-11) in patients with metastatic gastric and colorectal cancer.

2. Design

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

3. Setting

Single facility, Japan.

4. Participants

Twenty patients with inoperable advanced recurrent gastric cancer or colorectal cancer (12 males and 8 females).

5. Intervention

Patients received a course of chemotherapy consisting of 2 weeks on and 2 weeks off oral S-1 (tegafur/gimeracil/oteracil potassium) at 80–120 mg according to body surface area and intravenous irinotecan (CPT-11) at 100–125 mg once every 2 weeks.

Arm 1: Hangeshashinto (半夏瀉心湯) extract 7.5 g/day for 3 days starting on the day of administration of irinotecan (CPT-11) (n=10).

Arm 2: no administration of hangeshashinto (半夏瀉心湯) extract (n=10).

6. Main outcome measures

Anti-tumor effect (RECIST criteria), adverse events (Common Terminology Criteria for Adverse Events v3.0), and quality of life (QOL score developed by Kurihara et al.) evaluated on days 1, 15, and 29.

7. Main results

There was no significant difference in anti-tumor effect between arms. Chemotherapy-associated adverse events were more common in arm 2 than in arm 1 (significance of difference not tested). A decrease in QOL score from day 1 to day 15 was larger in more patients in arm 2 than in arm 1. Overall QOL score was decreased by 15 points or more in 1 patient in arm 1, compared with 4 patients in arm 2, with the mean±standard deviation significantly changed from 79±19 and 87±13 on day 1 to 77±21and 75±23 on day 15 in arm 1 and arm 2, respectively (P<0.05). In particular, QOL in the “social” domain decreased 2 points or more in 7 of 10 patients in arm 2 and 0 of 10 patients in arm 1.

8. Conclusions

Hangeshashinto (半夏瀉心湯) is a useful supportive therapy from the viewpoint of QOL in patients treated for advanced gastric and colorectal cancer with S-1/irinotecan (CPT-11) combination therapy.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned.

11. Abstractor’s comments

Post-marketing surveillance identified gastrointestinal symptoms such as nausea/vomiting (52.5%), anorexia (48.1%), and abdominal pain (12.2%) as frequent adverse drug reactions of CPT-11, besides diarrhea (43%, serious in 10.2% of cases). Hangeshashinto has well known efficacy not only for diarrhea, as reported by Kamataki et al. (1994), but also for nausea/vomiting, anorexia, and epigastric pain. This study demonstrated that hangeshashinto improves QOL. But the study had the following problems: (1) the rationale for the 3-day hangeshashinto administration period after administration of CPT-11 is not indicated. Although the authors seem to assume that the hangeshashinto-*sho* (証, pattern) induced by CPT-11 disappears in 3 days, delayed diarrhea attributable to intestinal mucosal injury by an active metabolite (SN-38) 24 hr after administration, for example, does not disappear in 3 days, warranting consideration of duration of administration in the future; (2) hangeshashinto is effective in only some cases. As QOL score was decreased by 15 points or more in 4 of 10 patients in arm 2 in this study, only these 4 patients are likely to have exhibited hangeshashinto-*sho* (証, pattern). It is recommended that patients be enrolled in the study from the second cycle onward after determining the presence or absence of hangeshashinto-*sho* (証, pattern) and the duration of the *sho* (証, pattern), based on the response to the first cycle of CPT-11.

12. Abstractor and date

Hoshino E, 15 January 2011.