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

References

Hoshino N, Ganeko R, Hida K, et al. Goshajinkigan for reducing chemotherapy-induced peripheral neuropathy: a systematic review and meta-analysis. *International Journal of Clinical Oncology* 2018; 23: 434-42. Pubmed ID: 29270698

1. Objectives

To assess the efficacy and safety of goshajinkigan（牛車腎気丸）for chemotherapy-induced peripheral neuropathy (CIPN)

2. Data source

Scopus, Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, ICHUSHI

3. Selection of study

RCTs (other than cross-over or quasi-RCTs) that compared goshajinkigan with a control for CIPN

4. Data extraction

Titles and abstracts of the studies identified by the literature search were independently screened by two researchers (other than those who performed the literature search). Data were then extracted and entered into the Review Manager software, version 5.3.

5. Main results

Five RCTs were included in the analysis, consisting of 1 study of docetaxel for breast cancer, 1 study of paclitaxel for breast cancer, and 3 studies of FOLFOX (oxaliplatin-based) for colorectal cancer. As a primary endpoint, the efficacy of goshajinkigan was evaluated using the Common Terminology Criteria for Adverse Events (CTCAE) in 4 RCTs, which did not show preventive effect of goshajinkigan against grade ≥2 and ≥3 CIPN compared with the controls (no administration of goshajinkigan). The efficacy was evaluated using the Neurotoxicity Criteria of Debiopharm (DEB-NTC) in 3 RCTs (including 2 RCTs that also used CTCAE), where goshajinkigan showed a tendency to reduce the risk of grade ≥2 and ≥3 CIPN compared with the controls (no administration of goshajinkigan). As a secondary endpoint, 1 RCT evaluated CIPN subjectively on a visual analogue scale (VAS) and reported significant improvement with goshajinkigan. Goshajinkigan had no influence on hematotoxicity in 3 RCTs and tumor response in 2 RCTs. The risk of bias was assessed in the 5 studies. Three RCTs used a computer random number generator. Two RCTs used central registration. Two RCTs included a placebo arm and were reported to be double-blinded. Two RCTs followed all enrolled patients. Of the remaining 3 studies, 2 studies excluded only a few patients. Four studies were registered with the University Hospital Medical Information Network Clinical Trial Registry (UMIN-CTR).

6. Conclusion

Goshajinkigan tended to prevent persistence but not severity of CIPN.

7. From Kampo medicine perspective

None

8. Safety assessment in the article

In five RCTs that reported on adverse events, there were no serious adverse events.

9. Abstractor's comments

This is the first meta-analysis of the efficacy and safety of goshajinkigan for CIPN for which currently no effective treatment exists. CTCAE or DEB-NTC can be used to assess CIPN severity and persistence, with the former being superior for severity assessment and the latter for persistence assessment. This meta-analysis revealed that goshajinkigan tended to reduce the risk of CIPN compared with the controls when the DEB-NTC was used for assessment, but had no significant effect when the CTCAE was used for assessment. However, since the pathogenesis of CIPN can primarily involve either axonopathy (caused by taxanes) or neuronopathy (caused by platinum-based drugs), and since the severity and the time to resolution can differ depending on the pathogenesis, the analysis of CIPN irrespective of pathogenesis may be somewhat impractical. Also, since CIPN can only be measured subjectively, RCTs using objective parameters such as serum biomarkers are desired. Further, these published RCTs had high risk of bias, which should be addressed in the future.

10. Abstractor and date

Motoo Y, 1 June 2020.