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

Reference

Okawa T, Hashimoto S, Sakamoto S, et al. Ninjin-yoei-to in the treatment of leukopenia and symptoms associated with radiotherapy of malignant tumors. *Gan no Rinsho* (*Japanese Journal of Cancer Clinics*) 1995; 41: 41–51 (in Japanese with English abstract). Ichushi Web ID: 1995174288 MOL, MOL-Lib

1. Objectives

To evaluate the improvement in subjective symptoms and leukopenia after ninjin'yoeito (人参養栄湯) administration in patients undergoing radiotherapy for thoracoabdominal tumors.

2. Design

Randomized controlled trial (RCT).

3. Setting

Thirteen university hospitals (Tokyo Women's Medical University [Department of Radiology], Keio University School of Medicine [Department of Radiology], Tohoku University School of Medicine [Department of Radiology], and 10 other universities) and 9 other hospitals, Japan.

4. Participants

One hundred sixteen patients with thoracoabdominal tumors undergoing radiotherapy (lung cancer: 42, esophageal cancer: 19, breast cancer: 9, rectal cancer: 7, cervical cancer: 33, and other cancers: 16).

5. Intervention

Arm 1: administration of Kanebo ninjin'yoeito (人参養栄湯) Extract Fine Granules 2.5 g t.i.d. during radiotherapy (n=63).

Arm 2: radiotherapy only (without ninjin'yoeito [人参養栄湯]) (n=63).

6. Main outcome measures

Subjective symptoms (anorexia, general malaise, diarrhea, coldness, nausea, and vomiting) were evaluated weekly on a 4-point scale. Hematological parameters (white blood cell [WBC], differential WBC, platelet, red blood cell, and reticulocyte counts, hemoglobin, and hematocrit), body weight, and blood pressure were measured weekly. Biochemical values (glutamic-oxaloacetic transaminase [GOT], glutamic-pyruvic transaminase [GPT], albumin, total protein, cholinesterase [Ch-E], blood urea nitrogen [BUN], Cr, Na, K, and Cl) were measured biweekly. Primary physicians evaluated the response of patients based on the above measures on a 4-point scale (marked, moderate, mild, or none).

7. Main results

There were no between-group differences in the mean WBC counts at baseline and at weeks 1–4. The proportion of patients with WBC count >3000 at the end of the treatment (weeks 4–8) was higher in arm 1 (51/56) than in arm 2 (42/60) (P=0.005).

Improvement in subjective symptoms (at least mild response) was observed more frequently in arm 1 (44/56) than in arm 2 (6/60) (P=0.0001).

Improvement in laboratory test results (at least mild response) was observed more frequently in arm 1 (43/56) than in arm 2 (23/60) (P=0.0003).

8. Conclusions

Ninjin'yoeito may prevent subjective symptoms and leukopenia associated with radiotherapy.

9. From Kampo medicine perspective

After the study, a retrospective analysis based on *sho* (証, pattern) was conducted, and *sho* was determined from an assessment of subjective symptoms (anorexia, general malaise, cold hands and feet, and night sweats). However, no correlation between *sho* and effectiveness was found.

10. Safety assessment in the article

Adverse events: 4 patients in arm 1 had, respectively, drug eruption, abdominal discomfort, abdominal pain + diarrhea, and diarrhea.

11. Abstractor's comments

It would be interesting to know whether Kampo medicines can prevent leukopenia associated with radiotherapy. In this study, although the mean WBC counts were similar in both arms, the proportion of patients with WBC counts >3000 was significantly higher in arm 1 than in arm 2 at the end of the treatment (weeks 4–8). The reason should be considered. The WBC count is the only laboratory test result shown. The granulocyte and platelet counts, hemoglobin level, and the biochemical test results are not reported. It was also unclear which subjective symptom was improved. The reliability of this study remains questionable because each result was a composite evaluation by physicians using a 4-point scale and this was an open trial. In the discussion of results, "overall improvement" based on physician's judgment was considered the gold standard. In addition, they just compare "overall improvement" with patient characteristics and test data in the stratified analysis. In this kind of open trial, objectivity is not assured unless the presence and degree of each subjective symptom as well as the test data are recorded sequentially and are compared between groups.

12. Abstractor and date

Hoshino E, 26 April 2009, 1 June 2010, 31 December 2013.