6. Nervous System Diseases (including Alzheimer's Disease)

References

Fukumura N, Yamamoto H, Kitahara M, et al. Hochuekkito reduced the incidence of inflammatory complications in patients with sequelae of cerebrovascular disease in convalescent rehabilitation wards: a randomized multicenter study. *Japanese Journal of Rehabilitation Medicine* 2017; 54: 303-14 (in Japanese with English abstract). Ichushi Web ID: 2017298884, UMIN ID: UMIN000021801 J-STAGE

1. Objectives

To evaluate the efficacy and safety of hochuekkito（補中益気湯）to address reduced activities of daily living (ADL), nutritional status, and immunity in patients undergoing rehabilitation for hemiplegia as a sequela of cerebrovascular disease

2. Design

Randomized controlled trial (RCT)

3. Setting

Four hospitals (departments of rehabilitation)

4. Participants

Thirty-one patients with hemiplegia as a sequela of cerebrovascular disease who were treated between April 2013 and March 2015. Participants had to be 50 years of age, have started their recovery period in a rehabilitation setting within the past 1 week, have a Functional Independence Measure (FIM) total score of ≤40, and be able to orally take medication. Patients were excluded if they had insufficient nutritional intake (<1200 kcal/day), blood C-reactive protein (CRP) ≥10 mg/dL, Physical Disability Certificate Grade ≥2 or Long-term Care Requirement Level ≥3 since before the onset of cerebrovascular disease, taken any Kampo medicine within 4 weeks before participation in this study, had any hepatic, renal, cardiac, hematologic, or metabolic disease that was considered serious, or other conditions not suitable for this study in the opinion of the investigator.

5. Intervention

Arm 1: oral administration of TSUMURA Hochuekkito（補中益気湯）Extract Granules 7.5 g/day (in 2 or 3 divided doses) for 24 weeks, starting at the initiation of rehabilitation (n=11)

Arm 2: no administration of hochuekkito (n=17)

6. Main outcome measures

Primary endpoints were FIM total score, FIM motor subscale score, and FIM cognitive subscale score, and these scores upon admission were compared with those at discharge. Secondary endpoints were albumin, body weight, Body Mass Index (BMI), % ideal body weight, total lymphocyte count, hemoglobin, CRP, and incidence of inflammatory complications.

7. Main results

The analysis excluded 3 patients who did not fulfill the inclusion criteria. The FIM total score significantly improved in both arms (P<0.001), without significant difference between the arms. Albumin significantly increased in both arms (P<0.001 for Arm 1, P=0.01 for Arm 2). CRP significantly decreased after the treatment only in Arm 1 (P=0.04). Other endpoints showed no significant differences. Among the patients with an FIM motor subscale score of ≤20, the total lymphocyte count tended to increase in Arm 1 compared with Arm 2. The incidence of inflammatory complications was 9.1% in Arm 1 and 41.2% in Arm 2, and significantly lower in Arm 1 (P=0.049).

8. Conclusion

Oral administration of hochuekkito was not shown to improve ADL in patients with hemiplegia as a sequela of cerebrovascular disease. Oral administration of hochuekkito significantly reduces occurrence of inflammatory complications.

9. From Kampo medicine perspective

None

10. Safety assessment in the article

Adverse events occurred in 5 patients (8 events) in Arm 1 and 10 patients (14 events) in Arm 2. No adverse reactions to hochuekkito were noted.

11. Abstractor's comments

This article reports an interesting clinical study that evaluated the efficacy and safety of hochuekkito in patients with severe sequelae of cerebral infarction who started their recovery period in a rehabilitation setting. No ADL-improving effects were shown, possibly because of the limited sample size. However, an exploratory analysis showed a significantly reduced incidence of inflammatory complications in the hochuekkito group. Future clinical studies are awaited that have larger sample sizes to re-evaluate the presence or absence of the ADL-improving effect of hochuekkito in the setting of rehabilitation, or that are designed to test new hypotheses, for example using prevention of inflammatory diseases as a primary endpoint.

12. Abstractor and date

Koike H, 1 June 2020.