

4. Metabolism and Endocrine Diseases

References

Takashima T, Ohmori K, Higuchi N, et al. Combination therapy with probucol and daisaikoto (a Kampo medicine) - Effects of daisaikoto on HDL metabolism -. *Domyaku Koka (The Journal of Japan Atherosclerosis Society)* 1993; 21: 47-52 (in Japanese with English abstract).

Yamamoto K. A study of the hepatic triglyceride (TG)-lowering effects and antioxidant capacity of various Kampo preparations *. *Proceedings of the 4th Kampo Treatment Seminar at Kyoto University* 1995: 48-56 (in Japanese).

1. Objectives

To evaluate the efficacy and safety of daisaikoto (大柴胡湯) combined with probucol in patients with hyperlipidemia.

2. Design

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

3. Setting

Ten institutions (1 university hospital, 7 hospitals, and 2 clinics), Japan.

4. Participants

Ninety-six patients with untreated hyperlipidemia (28 to 81 years of age) (33 with type IIa, 26 with type IIb, and 37 with type IV, according to WHO classification).

Patients with total cholesterol ≥ 220 mg/dL and triglyceride ≥ 500 mg/dL were excluded.

5. Intervention

Arm 1: probucol 500 mg/day for 16 weeks (n=35).

Arm 2: TSUMURA Daisaikoto (大柴胡湯) Extract Granules 7.5 g/day for 16 weeks (n=36).

Arm 3: combination of probucol 500 mg/day and TSUMURA Daisaikoto (大柴胡湯) Extract Granules 7.5 g/day for 16 weeks (n=25).

6. Main outcome measures

Blood level of fasting total cholesterol (T-CHO), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C), apoprotein A-I, A-II in the early morning, and B before treatment and at week 4, 8, and 16.

7. Main results

T-CHO and HDL-C decreased significantly in Arm 1 and 3. In Arm 2, T-CHO and TG showed a trend toward decrease, while HDL-C showed no change. Apoprotein A-I decreased in Arm 1, increased in Arm 2, and tended to decrease in Arm 3. There was no change in Apoprotein A-II and B in any group. Analysis according to disease type revealed that 1) for patients with type IIa hyperlipidemia, T-CHO decreased significantly in Arm 1 and 3 and HDL-C did not decrease in Arm 2 and 3; 2) for patients with type IIb and IV hyperlipidemia who had high TG levels, T-CHO decreased significantly in Arm 1 and 3 and tended to decrease in Arm 2 (-8.5% at week 16), while TG decreased significantly in only Arm 3.

8. Conclusions

The combination of daisaikoto and probucol for patients with hyperlipidemia is effective in inhibiting the reduction of HDL-C and reducing TG.

9. From Kampo medicine perspective

None.

10. Safety assessment in the article

Not mentioned.

11. Abstractor's comments

In patients with high T-CHO, probucol monotherapy decreases not only T-CHO but also HDL-C (i.e., "good" cholesterol). In this study, the combination with daisaikoto in these patients suppressed the reduction of HDL-C. In hyperlipidemic patients with high TG, their TG levels were decreased significantly by only the combination therapy. Therefore, the benefit of combination therapy with daisaikoto was shown in both types of hyperlipidemia. In addition to probucol, a number of statins with HDL-C-elevating ability have been developed, lessening the importance of inhibiting the reduction of HDL-C. However, HDL-C-increasing and TG-lowering effects, which are less with statin, are still useful. From this perspective, the combination therapy with statins and daisaikoto may still be significant and worthy of further evaluation.

The article by Yamamoto (1995) also describes a basic study using human cultured hepatocytes to evaluate the reducing effect of daisaikoto on lipid levels.

12. Abstractor and date

Namiki T, 29 December 2008, 6 January 2010, 1 June 2010, 31 December 2013.