COMBINED EFFECT OF RED GINSENG WITH XIAO-CHAI-HU-TANG IN PATIENTS WITH CHRONIC HEPATITIS

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INTRODUCTION

It has been reported from our laboratory that 18 traditional Chinese medicinal plants from 5 traditional formulas and their active principles improved α-naphthyl-isothiocyanate(ANIT)-induced hepatobiliary damage.[1] Xiao-Chai-Hu-Tang(Shosaiko-to) or saikosaponins of bupleurum falcatum L. have been proved to be potent in hepatic damage induced by CCl_4, D-galactosamine, ANIT and cell mediated immunity in several institutions including ours[2-4]. Panax ginseng or ginseng saponins were also reported to suppress CCl_4-induced hepatic damages by Hahn.[5] We found that ginseng saponins accelerated cell division and DNA synthesis in cultured hepatic cells[6], furthermore we found that combined treatment with ginseng saponin and saikosaponin restored ANIT-induced hepatobiliary damage with suppressed DNA synthesis more than either of two[7].

Clinically, shosaiko-to has been reported to be beneficial in patients with chronic hepatitis from many institutions including ours[1]. Five year-following up was also done in our hospital[9]. Mizoguchi reported under our common project that combined treatment with Shosaiko-to and Korean Red Ginseng was more beneficial in their patients with chronic hepatitis of non A-n on B type[9] In this paper, we also report the benefit of the combined treatment of these two in patients with chronic hepatitis on the same line.

OBJECTS AND METHODS

Patients with chronic hepatitis was all out patients of our hospital. Diagnosis of chronic hepatitis was made according to Tokyo Metropolitan diagnostic criteria for specified diseases, selecting patients with chronic hepatitis of over one year duration, in a relatively stable condition and with over 80IU/ℓ of serum GOT or GPT. Korean Red Ginseng powder(Korean Ginseng and Tobacco Corp) and Shosaiko-to(Kotaro) were supplied by Medical Association of Red Ginseng Research, Kobe. The 63 patients were divided into 3 groups, i·e., (1) single Shosaiko-to (S) administered; (2) single Ginseng (G) administered; and (3) combination of both S and G administered. The profile of each patient group was shown in table 1.No difference was observed among three groups. Shosaiko-to and Red Ginseng were administered 2g and 1g, respectively, 3 times a day before each meal for 6 months. Statistical study by student T test was done at the periods of start, 2 months, 3 months and 6 months of administration. Drugs which may effect the present study were prohibited.

Table 1. Profile of the patients with chronic hepatitis

A) Shosaiko-to (S) administered
1) 30 cases(17 men and 13 women)
2) Mean age 54.5 ± 2.2(S.E.) y.o.a.
3) Mean duration 5.6 ± 0.6 years
4) 23 type C; 3 type B+C; and 4 type B
5) Serum GOT 79.1 ± 8.9 IU/l
GPT 112.3 ± 13.2

B) Red Ginseng (G) administered
1) 10 cases (9 men and 1 women)
2) Mean age 57.1 ± 2.7 (S.E) y.o.a.
3) Mean duration 5.8 ± 1 years
4) 9 type C; and 1 type B
5) Serum GOT 70.3 ± 7.9
GPT 98.5 ± 10.0

C) Combination of S and G administered
1) 23 cases (13 men and 10 women)
2) Mean age 53.0 ± 2.3 (S.E) y.o.a.
3) Mean duration 5.2 ± 0.7 years
4) 17 type C; 3 type B+C; and 3 type B
5) Serum GOT 73.8 ± 4.2
GPT 101.1 ± 23.0

RESULTS

1) Single administration with Shosaiko-to(table 2-5) The ratios of serum GOT, GPT and γ-GTP levels o the starting levels in Shosaiko-to administered group were significantly declined as all points. As to serum alkaline phos phatase(ALP) and monoamine oxidase(MAO), the signi ficant decline was seen after 3 or 6 months treatment. Almost all enzyme levels shown here were gradually decreasing in process of time.
2) Single administration with Red Ginseng(table 2-5) The ratios of serum GOT and GPT levels to the start in Red Ginseng administered group were also lowered at all points. As to ALP, γ-GTP and MAO, significant

lowering was observed after 3 or 6 months.

3) Combined administration with both Shosaiko - to and Red Ginseng(table 2 - 5)

The ratios of serum GOT, GPT, ALP, γ - GTP and MAO to the starting point in this group, were all significantly decreased at all points, gradually decreasing up to 6 months.

Differences between single Shosaiko - to treated and combination of both Shosaiko - to and Red Ginseng treated, were significant only at the period of 2 months as to serum GOT, GPT and MAO Red Ginseng may accelerate Shosaiko - to action.

Differences between single Red Ginseng treated and co-

Table 2. Comparison of the effect of Shosaiko - to, Red Ginseng and their combination on serum GOT in patients with chronic hepatitis.

		Serum GOT
Shosaiko - to	(NO.)	Mean ± S.E.
Before	(30)	100
2 months	(26)	86.3 ± 4.1
3	(27)	79.6 ± 5.0
6	(26)	73.9 ± 4.9
Shosaiko - to plus Red Ginseng		
Before	(23)	100
2 months	(19)	72.4 ± 3.5
3	(21)	70.5 ± 4.0
6	(22)	63.9 ± 4.0
Red Ginseng		
Before	(10)	100
2 months	(8)	85.1 ± 3.0
3	(8)	79.3 ± 4.9
6	(8)	75.8 ± 3.8

+) N.S. 0) p<0.1 : 1) P<0.05 : 2) p<0.01 : 3)p<0.001

Table 3. Comparison of the effect of Shosaiko - to, Red Ginseng and their combination on serum GPT in patients with chronic hepatitis.

		Serum GPT
Shosaiko - to	(NO.)	Mean ± S.E.
Before	(29)	100
2 months	(24)	82.7 ± 5.0
3	(27)	79.3 ± 5.3
6	(23)	65.6 ± 4.3
Shosaiko - to plus Red Ginseng		
Before	(23)	100
2 months	(15)	66.7 ± 4.5
3	(21)	67.2 ± 4.3
6	(20)	61.1 ± 4.7
Red Ginseng		
Before	(10)	100
2 months	(9)	83.9 ± 5.5
3	(9)	78.1 ± 2.5
6	(8)	77.8 ± 2.6

+) N.S. 0) p<0.1 : 1) P<0.05 : 2) p<0.01 : 3)p<0.001

mbination of both Shosaiki - to and Red Ginseng treated, were significant in serum GPT at each period and in serum GOT at the periods of 2 and 6 months.

4) Effects on type C and type B

We had only 4 cases of type B in Shosaiko - to administered group and 3 cases in combination of both Shosaiko - to and Red Ginseng administered group. Statistically no significant differences between type C and type B were observed as to effect on serum liver function tests.

Table 4. Comparison of the effect of Shosaiko - to, Red Ginseng and their combination on serum γ - GTP in patients with chronic hepatitis.

		Serum γ - GTP
Shosaiko - to	(NO.)	Mean ± S.E.
Before	(30)	100
2 months	(26)	86.3 ± 4.4
3	(28)	87.0 ± 4.6
6	(22)	69.9 ± 4.2
Shosaiko - to plus Red Ginseng		
Before	(23)	100
2 months	(18)	78.5 ± 4.5
3	(20)	76.2 ± 4.4
6	(20)	69.8 ± 5.3
Red Ginseng		
Before	(10)	100
2 months	(9)	92.6 ± 6.2
3	(10)	78.0 ± 4.9
6	(7)	74.4 ± 7.3

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+) N.S. 0) p<0.1 : 1) P<0.05 : 2) p<0.01 : 3)p<0.001

Table 5. Comparison of the effect of Shosaiko - to, Red Ginseng and their combination on serum MAO in patients with chronic hepatitis.

		Serum MAO
Shosaiko - to	(NO.)	Mean ± S.E.
Before	(28)	100
2 months	(22)	98.1 ± 4.3
3	(21)	92.4 ± 3.9
6	(21)	87.8 ± 3.6
Shosaiko - to plus Red Ginseng		
Before	(21)	100
2 months	(15)	89.3 ± 1.9
3	(18)	83.5 ± 3.9
6	(18)	78.5 ± 4.4
Red Ginseng		
Before	(10)	100
2 months	(8)	88.5 ± 5.0
3	(9)	88.7 ± 5.2
6	(7)	81.3 ± 8.2

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+) N.S. 0) p<0.1 : 1) P<0.05 : 2) p<0.01 : 3)p<0.001

DISCUSSION

A variety of actions of Shosaiko - to and its component medicinal plants, have demonstrated recently. For example, Bupleurum falcatum or saikosaponins has experimentally anti - inflammatory, anti - allergic, immumo - regulatory, anti - atherogenic fatty liver improving, hepatic damage - improving, protein anabolic, pituitary - adrenal - stimulatory actions[10, 11] Panax ginseng also has protein and DNA anabolic, anti - atherogenic, fatty liver improving, hepatic damage - improving, pituitary - adrenal - stimulating actions[11, 12]

Shosaiko - to is one of traditional Chinese formulas, has been prescribed for patients with possible hepatobiliary damage. Shosaiko - to contains Bupleurum falcatum, panax ginseng, Glycyrrhizae(including glycyrrhizin) and other 4 plants.

According to our present clinical data, addition of panax ginseng to Shosaiko - to, might fortify and accelerate each action. Beneficial effect of panax ginseng combination with saikosaponin was shown in ANIT - induced damaged hepatic cells.[7]

CONCLUSION

In this paper, authors endeavoured at first to show experimental basis of combined treatment with Shosaiko - to and Red Ginseng. Then we reported clinical data as to this combined treatment in patients with chronic hepatitis mainly of type C.

Single Shosaiko - to, single Red Ginseng and their combination, improved serum GOT, GPT, γ - GPT, ALP and MAO up to 6 months.

Differences between single Shosaiko - to and the combination were significant as to serum GOT GPT and MAO in the period of 2 months. Differences between single Red Ginseng and the combination were significant in serum GOT and GPT

Combination of Red Ginseng and traditional Chinese formulas might be possibly beneficial.

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REFERENCES

1) Yamamoto, M. et al. : J. Med. Pharm. Soc. WAKAN - YAKU 2 : 386~397, 1985.
2) Abe, H. et al. : Planta Med. 40 : 366~372, 1980.
3) Yamamoto, M. et al. : Proc. Symp. WAKAN - YAKU 16 : 245~248, 1983.
4) Mizoguchi, Y. et al. : Kan - Tan - Sui 6 : 947~951, 1983.
5) Hahn, D.R. : 2. Int'l Ginseng Symp., Seoul. p. 135~140, 1978.
6) Yamamoto, M. et al. : 5 Int'l Ginseng Symp., Seoul, p. 36 ~38, 1988.
7) Yamamoto, M. et al. : J. Med. Pharm. Soc. WAKAN - YAKU, 6 : 336~337, 1989.
8) Yamamoto, M : Progress in Medicine 11 : 531~535, 1991.
9) Mizoguchi, Y. et al. : The Ginseng Review No.11, 653~656, 1991.
10) Yamamoto, M. et al. : Arzniemittel - forschung 25 : 1021 ~1023 : , 25 : 1040~1043, 1975.
11) Yamamoto, M. & Kumagai, A. : Excerpta Medica Int'l Congress Series, No.693 p. 238~247, 1984.
12) Yamamoto, M. et al. : Arzneimittel - forschung 27 : 1169 ~1170 : , 27 : 1404~1405, 1977 : 28 : 2238~2241, 1978.