Korean J. Ginseng Sci
Vol. 7, No. 2 (1983)

Clinical Study on the efficacy of *Panax ginseng* C. A. Meyer on Acute viral (B) Hepatitis – (1)*

Kook Hae Koo and Chung No Joo**
Department of Pathology, College of Medicine, Hanyang University, Seoul
and
Department of Biochemistry, College of Science, Yonsei University, Seoul 120,

(Received October, 6. 1983)

고려인삼이 비루스성 급성간염의 치료효과에 미치는 임상학적 연구 (1)

구 국 회 · 주 충 노
한양대학교 의과대학 병리학교실 · 연세대학교 이과대학 생화학과

(1983년 10월 6일 접수)

Abstract

The effect of ginseng administration on the patients of acute viral (B type) hepatitis has been observed and the results were as follows.

The albumin/globulin ratio of the ginseng administered group has significantly improved 4 weeks after admission while that of control group has not been improved suggesting that the ginseng might be effective in improving the protein metabolism. The thymol turbidity test again gave a similar result.

Recovery of the disorder of bilirubin metabolism was also accelerated in the ginseng administered group compared with control group. The raised bilirubin value of the former returned to the normal value 2 weeks after admission while that of the latter reached to normal 4-5 weeks after admission. However no significant difference of the bilirubin level between ginseng treated and non-treated groups could be observed.

Cholesterol metabolism is also stimulated in ginseng administered group. The lowered cholesterol level of the ginseng group returned to normal 3-4 weeks after admission while that of latter reached to normal 5-6 weeks after admission. The raised S-GOT and S-GPT levels of the ginseng treated group returned to the normal value 3-4 weeks after admission while those of control group returned to normal in 5 weeks after admission suggesting that the ginseng improved impaired liver function.

The improvement of the raised transaminase level seemed to be accelerated by the ginseng administration, however, no significant difference of the transaminase level between the ginseng treated and non-treated group could be observed.

A significant effect of ginseng on the raised alkaline phosphatase level was observed.

* This work was supported by a research grant (1981) of Korea Ginseng and Tobacco Research Institute.
** To whom reprint request should be addressed.

From the above results, it seemed that ginseng might stimulate the improvement of the disturbance of liver function, particularly at the early phase of its development of acute liver disease suggesting that panax ginseng might play a significant role in preventing the disease developing to be chronic.

Introduction

The liver is the largest organ in the body with a variety of metabolic functions, both synthetic and degradative and the liver is known to control the amounts and constituents of the circulating blood. Several observations are pertinent to derangement in liver function when the liver is damaged. Cirrhosis is a general term that includes all forms of chronic diffuse liver disease, which usually leads to death when it is developed.

Recently, acute viral hepatitis, which is a systematic infection affecting predominantly the liver, is spreading over in this country and the number of the patients are estimated approximately as many as 3-4 millions. Paticularly B type viral hepatitis, which is also referred to as serum hepatitis, is known to develope easily to chronic liver diseases unless the disease is treated carefully. Besides, the patients suffering from toxic and drug-induced hepatitis, chronic active hepatitis and liver cirrhosis are increasing.

In the last several years, we were very much interested in the efficacy of panax ginseng, one of the mysterious oriental herbs.

There are several reports regarding to the ginseng effect on liver diseases such as Hopkin's disease[1] and drug induced hepatitis in some experimental animals.[2~5] Furthermore, pharmacological, physiological and biochemical approaches to the ginseng action on the liver have been intensively studied during the last two decades since 1960 and some of the effect of ginseng (particularly the ginseng saponin, one of the major components) have been accumulated. We now know that ginseng saponin stimulate the metabolism of protein, nucleic acid, carbohydrate and lipid in the liver.[6~10]

However, the above observations were limited to experimental animals and a few clinical observations were ever made. In this experiment, it was attempted to observe the effect of panax ginseng on the viral (B-type) hepatitis to see whether the ginseng would accelerate the recovery of the impaired liver functions through blood tests.

Materials and Methods

Among the patients of liver disease admitted to Hanyang University Hospital, Yongdeungpo City Hospital and Haesung Hospital, 67 patients of acute viral (B-type) hepatitis were selected based on clinical feature, pathological tests and radioimmunological assay.

Table 1. Subjects of the patients of acute viral (B) hepatitis

Number of Patients	age / Group	10—19	20—29	30—39	40—49	50—59	over 60	Total
67	Pre-survey	5	7	7	3	1	1	24
(M 45 F 22)	Ginseng	4	7	5	3	1	0	20
	Control	7	8	4	3	1	0	23

The patients were divided into three groups, preliminary survey group, control and ginseng administered groups. Patients of preliminary survey group were treated in usual way and the blood tests was made every week periodically through 8-10 weeks to know the variation of liver function parameters.

Control and ginseng administered groups were under similar conditions of diet and treatments for liver disease. To ginseng administered group, 5g panax ginseng powder (Keumsan white ginseng root powder) were given daily orally.

Radioimmuno assay was made to distinguish B-type viral hepatitis using Abbott laboratory's AUSTRIA II-125 system (HBs-Ag), AUSAB system (HBs-Ag) and CORAB system (HBc Ag).

Blood tests were made everyweek to follow the liver function. It included protein (total and albumin) measurement,[11] thymol turbidity test,[12] bilirubin (total and conjugated) measurement,[13] cholesterol level determination,[14] transaminase (serum-GOT serum-GPT)[15] and alkaline phosphatase[16] activity measurement.

Results and Disscussion

The liver is intimately related with other organs and no single test or procedure which effectively measures the total function of the liver is possible. Many liver function tests are based on a wide variety of biochemical reactions, such that the clinician can select combinations of tests that often measure different aspects of hepatic function.

Since the liver function test represents the liver activities, laboratory findings are not always agree with histological morphology of the impaired liver. However, recently, it was found that some general correlations between histological morphology and laboratory findings from the needle biopsies, surgical biopsies and autopsy materials with reasonably collected liver diseases exist.[17]

Table 2 showed the variation of the blood serum protein levels of the patients after admission. Albumin is known to be synthesized in the liver. During liver injury, changes may occur in the actual synthesis or in its intracellular transport and release. When the liver is damaged, synthesis of albumin is usually affected more than catabolism, but in view of its half-life (17-20 days), several weeks may elapse before the pronounced decrease in serum albumin level occurs. Unlike albumin, not all globulins are synthesized by the

Table 2. Variation of blood serum protein levels of the patients (preliminary group) of acute viral (B) hepatitison time course after admission. The values are given in mean value±standard deviation.

Patients	Protein (g/dl)	Time course (week) after admission					
		0**	1	2	3	4	5
Acute	T	7.1±0.6	6.9±0.7	5.8±0.5$^{(c)}$	7.0±0.4$^{(d)}$	6.5±0.6$^{(c)}$$^{(d)}$	7.2±0.3$^{(c)}$
Viral (B)	A	4.4±0.6	4.1±0.7	3.9±0.5	3.7±0.4$^{(d)}$	3.7±0.6$^{(a)}$	4.0±0.3$^{(d)}$
Hepatitis	G	2.7±0.6	2.8±0.6	2.9±0.5$^{(b)}$	3.3±0.4$^{(d)}$	3.1±0.6$^{(d)}$	3.2±0.3$^{(d)}$
(24)*	A/G	1.7±0.4	1.5±0.5	1.4±0.4	1.2±0.2	1.2±0.4	1.2±0.2
		7	7	8	9	10	
Acute	T	7.1±0.7	7.3±0.5	7.4±0.4	7.2±0.5	7.4±0.3$^{(c)}$	
Viral (B)	A	4.1±0.6	4.3±0.5	4.6±0.4	4.5±0.5	4.8±0.3	
Hepatitis	G	3.0±0.7$^{(a)}$	3.0±0.2$^{(c)}$	2.8±0.4	2.7±0.4	2.6±0.2	
(24)*	A/G	1.4±0.5	1.4±0.2	1.7±0.2	1.7±0.4	1.9±0.2	

T (total protein), A (albumin), G (globulin), A/G (albumin/blobulin ratio), ND (not determined)

* (number of patients), ** (mean ± SD), a ($p<0.05$), b ($p<0.025$), c ($p<0.01$), d ($p<0.001$)

hepatocytes, much of the α-and β-globulins are produced by liver cells, but normally most γ-globulins are synthesized by plasma cells and B lymphocytes in the lymphoid tissue. In addition, infiltrating plasma cells and lymphocytes may be of importance in some form of liver diseases associated with hyperglobulinemia. As shown in Table 2, the albumin level lowered while the globulin level raised significantly 3 weeks after admission, resulting in a significant low albumin-globulin ratio (A/G ratio) of 1.2 compared with the initial value of 1.7 when they were admitted. The A/G ratio was found improved at 8 weeks after admission. Table 3, showed the effect of panax ginseng on the serum protein level of the patients. In control group, A/G ratio was kept steady through 9 weeks in hospital but the ginseng administration stimulated the albumin synthesis significantly and improved the A/G ratio at 5 weeks after admission.

Table 3. The effect of ginseng administration on blood serum protein levels of the patients of acute viral (B type) hepatitis.

Group	Protein g/dl	Time course (week) after admission					
		0**	1	2	3	4	5
Control	T	7.1±0.6	6.7±0.6	6.8±0.8	6.5±0.6(c)	6.8±0.6	7.0±0.5
group	A	4.4±0.6	4.2±0.5	4.0±0.8(b)	3.7±0.6(d)	3.8±0.6(d)	4.0±0.5(c)
(23)*	G	2.7±0.5	2.5±0.5(a)	2.8±0.8	2.8±0.6	3.0±0.6	3.0±0.5
	A/G	1.6±0.4	1.6±0.4	1.5±0.5	1.3±0.4	1.3±0.4(b)	1.4-0.4
Ginseng	T	6.9±0.5	6.7±0.6	7.1±0.6	7.0±0.8	7.3±0.6(a)	7.2±0.6
group	A	4.3±0.4	4.0±0.6	4.3±0.5	4.4±0.8	4.3±0.5	4.7±0.5(a)
(20)*	G	2.6±0.4	2.7±0.5	2.8±0.5	2.6±0.8	2.9±0.6	2.5±0.5
	A/G	1.7±0.3	1.5±0.4	1.5±0.4	1.7±0.5	1.5±0.4	1.9±0.2(a)
			6	7	8	9	
Control	T		7.1±0.5	7.5±0.4(b)	7.3±0.5	7.4±0.6	
group	A		3.8±0.4(b)	4.4±0.4	4.6±0.4	4.6±0.6	
(23)*	G		3.3±0.4(d)	3.1±0.4(b)	2.7±0.4	2.8±0.6	
	A/G		1.2±0.2(d)	1.4±0.2(a)	1.7±0.3	1.7±0.4	
Ginseng	T		7.4±0.4(c)	7.5±0.5(c)	7.4±0.4(c)	7.4±0.4(c)	
group	A		4.8±0.4(a)	4.9±0.4(c)	4.9±0.4(c)	4.9±0.4(c)	
(20)*	G		2.6±0.4	2.6±0.3	2.5±0.4	2.5±0.4	
	A/G		1.9±0.2(a)	1.9±0.2(a)	2.0±0.2(a)	2.0±0.2(a)	p<0.01

The values are given in mean value ± standard deviation.
T: total protein, A: albumin, G: globulin, A/G: albumin/globulin ratio, P: protein, * number of patients.
** (mean ± SD), a ($p<0.05$), b ($p<0.025$), c ($p<0.01$), d ($p<0.001$)

The above rerults suggested that the ginseng may prevent against the acute viral hepatitis developing to be chronic by improving the hyperglobulinemia and stimulating albumin synthesis.

The thymol turbidity test data for acute viral (B type) hepatitis (Fig. 1) supported the above suggestion.

The disorders of bilirubin metabolism can be divided into four catagories, namely, those due to increased pigment production, reduced hepatic uptake of bilirubins, impaired hepatic conjugation and decreased excretion of the conjugated pigments from the liver into bile. Table 4 showed the disturbances of the

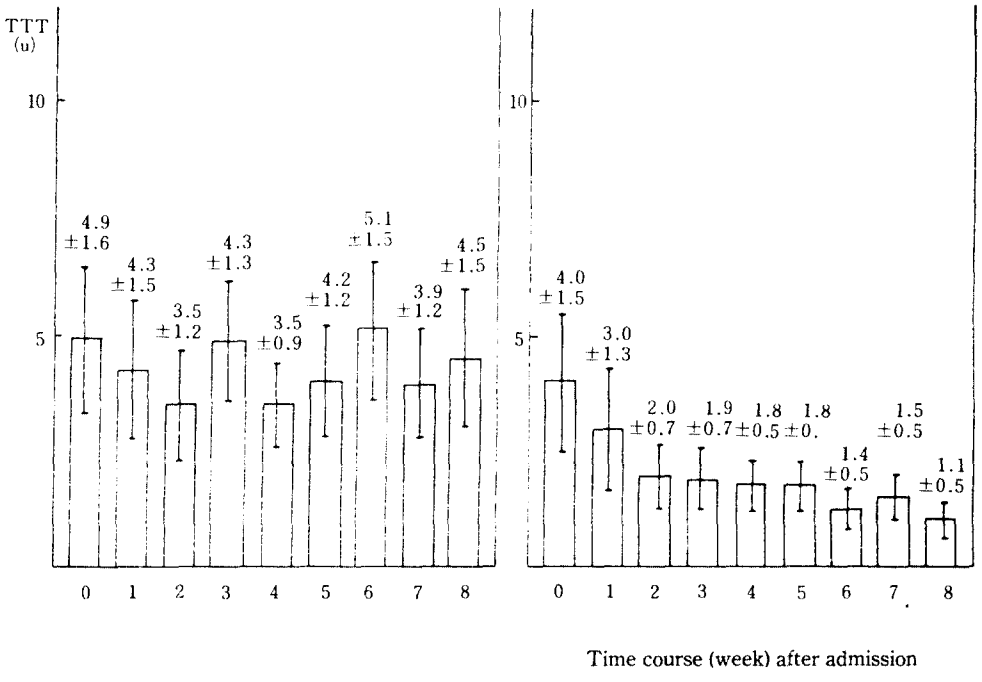

Fig. 1. The effect of ginseng administration on the value of thymol turbidity test of blood serum of patients of acute viral (B type) hepatitis. a: mean ± S.D., b: $p<0.05$, c: $p<0.025$, d: $p<0.01$, e: $p<0.001$.

Table 4. The variation of blood bilirubin levesl of the 24 patients (preliminary group) of acute viral (b) hepatitis the figures in brackets are number of patients.

Bilirubin level (mg/dl)	Time course (week) after admission					
	0	1	2	3	4	5
T	5.7 ± 3.5	2.4 ± 2.5	2.4 ± 3.1	2.2 ± 2.1	1.6 ± 1.2	1.7 ± 1.8
%*	100.0	42.1	42.1	38.6	23.1	27.8
D	4.2 ± 3.0	1.7½22.1	1.8 ± 2.1	1.2 ± 0.8	1.2 ± 0.8	1.3 ± 1.2
I	2.5 ± 2.9	0.7 ± 0.8	0.6 ± 0.4	0.4 ± 0.2	0.4 ÷ 0.3	0.4 ± 0.2
		6	7	8	9	
T		0.9 ± 1.1	1.1 ± 0.9	0.7 ± 0.4	0.5 ± 0.3	
%*		15.8	19.3	12.3	8.8	$p<0.001$
D		0.6 ± 0.8	0.8 ± 0.9	0.5 ± 0.3	0.3 ± 0.1	
I		0.3 ± 0.1	0.3 ± 0.1	0.2 ± 0.1	0.2 – 0.1	

The values are given in mean ± SD
T: total bilirubin, D: Direct bilirubin, I: indirect bilirubin.
* relative % against their first bilirubin level (total) in hospital.

bilirubin metablism of the patients. It can be seen that acute hepatitis caused severe disturbance of bilirubin metabilism but the disturbance was improved to normal in several weeks, and the ginseng accelerated the

Table 5. The variation of cholesterol levels of blood sera of the patients (preliminary group) of acute viral (b) hepatitis.

Cholesterol (mg/dl)	Time Course (week)								
	0	1	2	3	4	5	6	7	8
Cholesterol	178±23 (a)	172±35	168±18	182±22	191±29	198±27 (c)	193±31	197±33 (b)	196±27 (c)
%**	100%	96.6%	94.4%	102.2%	107.3%	111.2%	108.4%	110.7%	110.1%

* 24

The values are given in mean ± SD.
* number of patients
** relative % against the first value in hospital.
(a) mean ± SD, (b) $p<0.05$ (c) $p<0.025$, (d) $p<0.01$

normalization of bilirubin metalism in the patients, but not significantly statistically (Fig. 2).

Severe liver injury often leads to a decrease in total serum cholesterol level including both free and esterified fractions. This may due to decreased cholesterol and cholesterol ester synthesis, decreased apoprotein synthesis or both.

As shown in Tab. 5, a slight hypocholesterolemia could be observed in the early phase of acute viral (B type) hepatitis. Fig. 3 showed the effect of panax ginseng on the decreased cholesterol level of the patients.

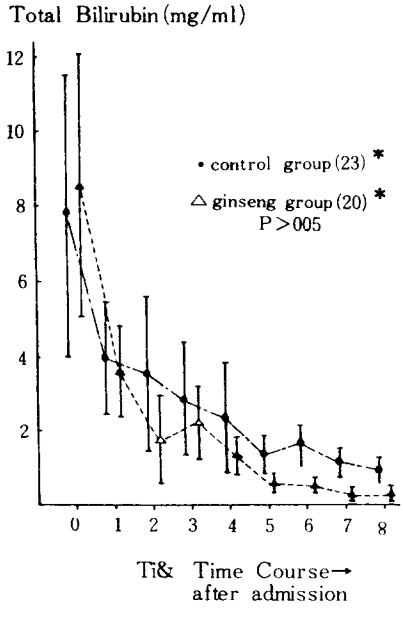

Fig. 2. The effect of ginseng administration on the variation of blood bilitubin levels of the patients of acute viral (B type) hepatitis on time course after admission.
*Number of patients.

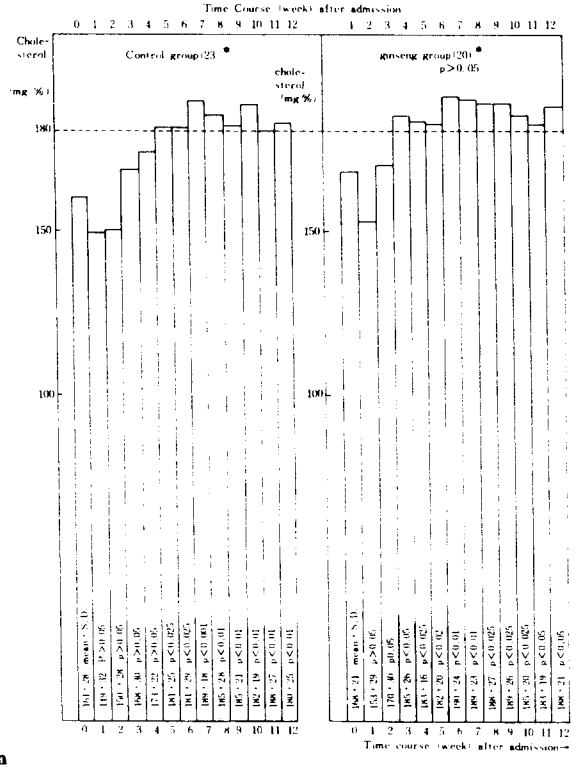

Fig. 3. The effect of ginseng administration on blood serum cholesterol level of the patients of acute viral (B type) hepatitis.
*Number of patients.

Table 6. Variation of blood serum transaminase level of patients (preliminary group) of acute viral (B) hepatifis.

	Trans-aminase	Time course (Week) 0	1	2	3	4	5	6	7	8	9
AVH (24)	S-GOT*	274±342	78±42 (b)	96±38 (b)	68±42 (c)	29-18 (c)	31±12 (c)	46±15 (c)	28±21 (c)	33±15 (c)	29±20 (c)
	S-GPT*	320±417	118±58 (a)	94±49 (b)	83±51 (b)	45±37 (c)	46±25 (c)	27±23 (c)	25±20 (c)	18±10 (c)	20±15 (c)

The values are given in mean±SD, The figures in brackets are the number of patients. (AVH: acute viral (B type) hepatitis)

* S-GOT: serum glutamate oxaloacetate tramsaminase

** S-GPT: serum glutamate pyruvate transaminase

a ($p<0.05$), b ($p<0.025$), c ($p<0.01$), d ($p<0.001$)

It was observed that test group was improved 3-4 weeks after admission while that of control group returned to the normal level much later.

In connection with the many biochemical reactions carried out by the liver, this organ contains thousands of protein catalyst (enzymes). Some are unique to the liver, while many others also found in nonhepatic tissues. The leakage of enzymes out of liver cells into blood stream occurs with liver injury and measurements of non-function plasma enzymes such as S-GOT, S-GPT and alkaline phosphatase are known to be useful test for the liver function.

Table 6, showed the variation of blood serum transaminase (S-GOT, S-GPT) level of the patients of various liver diseases during 9 weeks in hospital. The high value and its wide variation of the patients of acute viral (B type) hepatitis were noticeable, though it turned to normal several weeks after admission in both control and ginseng groups as shown in Fig. 4 and Fig. 5.

Table 7. Variation of serum alkaline phosphatase activity of the patient (preliminary group) of acute viral (B) hepatitis on time course after admission.

Patients	Time course (week) after admission 0	1	2	3	4	5	6	7	8	9
AVH (24)	10.8±5.8	10.1±4.1	11.6±4.9	10.7±5.0	9.8±3.9	9.5±4.7	8.2±3.5	9.8±4.0	7.2±2.9 (a)	6.8±3.0 (b)

The values in K-A* unit are given in mean±SD. The figures in brackets are the number of patients. (* King-Armstrong Unit)

a ($p<0.025$), b ($p<0.01$), c ($p<0.001$)

Table 7, showed the variation of serum alkaline phosphatase level of the patients on time course after admission. The alkaline phosphatase levels of the patients was greatly higher than normal, but the raised alkaline phosphatase level decreased gradually. As shown in Fig. 6, panax ginseng improved the raised alkaline phosphatase level of the patients.

From the above results, it seemed that ginseng would stimulate the protein and cholesterol synthesis, normalization of bilirubine metabolizm, and improving the raised non-function plasma enzyme levels.

Although the elucidation of the metabolism of the ginseng action on the body has to be made, it is generally considered that ginseng is not a drug to cure some specific diseases but rather acts as stimulator

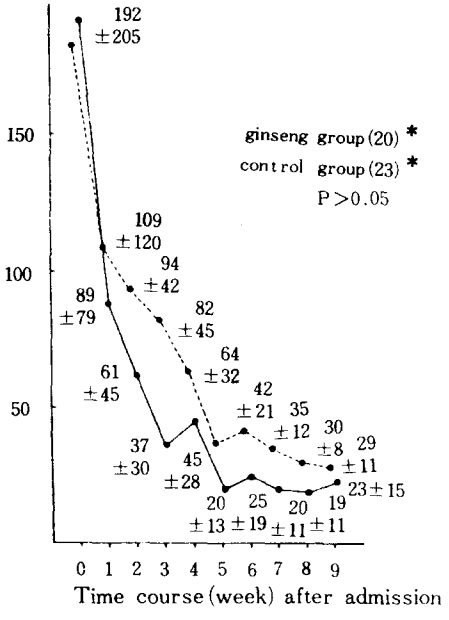

Fig. 4. The effect of ginseng administration on S-GOT level of patients of viral (B) hepatitis. * Number of patients.

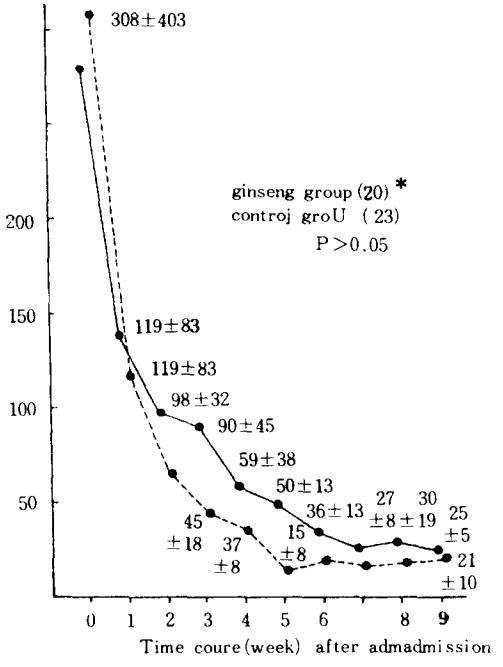

Fig. 5. The effect of ginseng administration on S-GPT of the patient of acute viral (B type) hepatitis on time course after admission. The values are given in mean±S.D. *Number of patients.

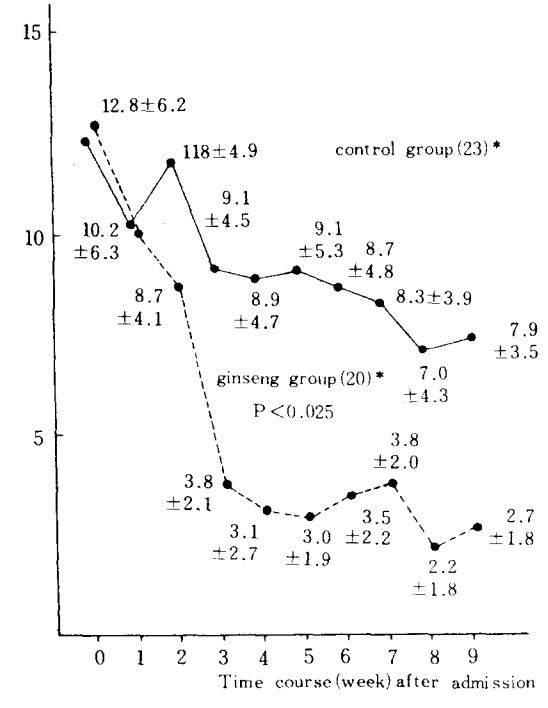

Fig. 6. The effect of ginseng administration on alkaline phaphatase activity in blood serum of the patient of viral (B) hepatitis on time course after admission (* number of patients) The values are given in mean ± S.D.

keeping the body being normal against various stresses. From the view of the above consideration, it seemed that panax ginseng would not specifically effective on such liver disease as acute viral hepatitis, but might improve the impaired function of the liver at the early phase of its development. In other words, the ginseng might prevent against the acute hepatitis developing to be chronic condition.

Acknoledgment

The authors are grateful to Dr. Koo, Ja-Hyun, Dept. of Biochemistry, Hanyang University; Dr. Lee, Tong-Hoo, Hanyang University Hospital; Dr. Hong, Hee, Yongdeungpo City Hospital; Dr. Lim, Yong-Eui, Haesung Hospital and Dr. Choi, Hee-Yoon, Hanyang University Hospital for their full cooperation of this work.

요 약

비루스性 急性肝炎에 대한 高麗人蔘投與(錦山産 白蔘粉末, 5 g/day/patient, 8～10주간) 効果를 觀察한 結果 다음과 같은 血清學的 所見을 얻었다.

對照群의 albumin/globulin比는 有意性있는 改善이 觀察되지 않았으나 人蔘投與群의 경우는 A/G比가 入院 1個月 後부터 改善方向이 나타나고 對照群에 比해 有意性있는 差異가 觀察된 것으로 보아 人蔘이 A/G比 改善에 効果가 있는 것으로 생각된다. Thymol Turbidity test (TTT) 값은 人蔘投與群 에서는 入院 1個月 後부터 低下되었으나 對照群의 경우는 入院期間中 上昇된 TTT값이 지속되었다.

Bilirubin 代謝異常에 대한 개선은 人蔘 投與群에서 그의 개선기간이 對照群에 比해 크게 단축되고 있다. cholesterol 低下 現象의 回復도 對照群은 入院 5～6주 후에 觀察되는데 人蔘投與群은 入院 3～4주후에 관찰되었다.

S-GOT値, S-GPT値의 改善은 對照群에서는 S-GOT, S-GPT 모두 入院 5주후에 改善되었는데 比하여 人蔘投與群에서는 S-GOT値의 改善이 入院 3週後, S-GPT値의 改善이 入院 4週後에 觀察되었고 上昇된 血清 alkaline phosphatase値는 對照群에서는 有意性 있는 改善이 觀察되지 않았으나 人蔘投與群에서는 뚜렷한 改善効加가 觀察되었다.

以上과 같은 肝疾患에 대한 人蔘投與로 因한 영향觀察 成績으로 부터 人蔘은 B형비루스性肝炎 患者의 早期回復에 効果가 있으며 急性肝炎의 만성화를 豫防한다는 點에서 人蔘은 중요한 구실을 할것으로 생각된다.

References

1. Dunayevskiy, G.A. Materialy K. Izucheniyu Zhen-Shenyu in Limonika (2) 189-95 BA **35,** 9046 (1972).
2. Juhn, S.K. *Choesin Uihak,* **5,** 631 (1962).
3. Hahn, D.R. Symp. of gerontology held at Lugano, p. 93 (1976).
4. Hahn, D.R. Proceedings of the 2nd International Ginseng Symposium, (1978).
5. Eui, S.C. Kim, B.Y. Paik, T.H. and Joo, C.N. *Korean, Biochem., J.,* **11,** 1(1978).

6. Oura, H., *Metabolism,* **10,** 467 (1973).
7. Oura, H. Hiai, S., Nabetani, S., Nakagawa, H. Kurota, Y. and Sasaki, N. *Planta Medica,* **28,** 76 (1975).
8. Sakakibara, K., Shibata, Y., Higashi, T., Sanada, S. and Shoji, J., *Chem. Pharm. Bull.,* **23,** 1009 (1975).
9. Joo, C.N., Lee, H.B., and Kim, D.S. *Korean Biochem. J.,* **10,** 71 (1977).
10. C.N. Joo, Proceddings of 2nd Internation Ginseng Symp. held at Seoul (1978).
11. Weichselbaum, T.E. *Amer. J. Clin. Path,* **7,** 40 (1946).
12. Shauk, R.E. and Hoagland, C.W. *J. Biol. Chem.* **162,** 133 (1946).
13. Malley, H.T. and Evelyn, K.A. *J. Biol. Chem.* **119,** (1937).
14. Pearson S. *Analyt. Chem.,* **25,** 813 (1953).
15. Reitman, S. and Frankel, S. *Amer. J. Clin, Path.,* **28,** 56 (1957).
16. King, E.J. and Armstrong, A.R. *Can, M.A. J.,* **31,** 376 (1934).
17. Kim, J.S. and Kim, Y.S. *New Med. J.,* **17,** 218 (1974).