J Korean Med. 2014;35(2):69-78
http://dx.doi.org/10.13048/jkm.14024
pISSN 1010-0695 • eISSN 2288-3339

Case Report

The Effects of *Injincheonggan-tang* on Two Patients with HBeAg-Negative Chronic Hepatitis B : Case Report

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Objectives: This case report was executed to confirm the efficacy and safety of *Injincheonggan-tang* on two patients with HBeAg-negative chronic hepatitis B.
Methods: We reviewed the changes of clinical progress and laboratory records of patients with chronic hepatitis B who did not want to take any antiviral or interferon therapy. One patient has visited the department of internal medicine I of Kyung Hee University Korean Medicine Hospital, from October 2010 and the other, from October 2006. Both of them were prescribed with *Injincheonggan-tang* and laboratory tests were conducted as well.
Results and Conclusions: AST, ALT and HBV DNA which are significant indicators of liver function were controlled in the normal range during the herbal treatment period and subjective clinical symptoms were also improved after taking *Injincheonggan-tang*.

Key Words : Chronic hepatitis B, HBeAg-negative, *Injincheonggan-tang*, Korean medicine, Herbal medicine

Introduction

Chronic infection with hepatitis B virus(HBV) is a major global health problem, affecting more than 400 million people worldwide[1]. The greatest burden of this disease was placed in Asia, where 75% of infected people live, and Africa, homeland to 12% of infected patients[2]. Especially, Korea is a chronic hepatitis B(CHB)-prevalent nation. Despite the hepatitis B surface antigen vaccine, the chief path of this liver infection in Korea is vertical transmission which has a poor prognosis due to uncommon seroconversion and easily develops to liver cirrhosis. For these reasons, the societal and economic burden induced by CHB is considered to be one of the major troublesome medical problems in Korea. Epidemiological and clinical studies showed that about 10% of patients with acute hepatitis B virus infection aggravate to chronic liver disease[3]. It is therefore important to set up delicate therapeutic strategies to prevent them from worsening into chronic liver disease to understand the properties of CHB.

The natural procedures of CHB can be divided into four stages: immune tolerant phase, immune clearance stage(HBeAg(+) chronic hepatitis), inactive carrier state, reactivating stage of HBV replication (HBeAg(-) chronic hepatitis) although patients do not entirely undergo all stages[4]. These four steps do not mean consecutive or gradually proceeding phases.

・Received : 15 April 2014 ・Revised : 24 June 2014 ・Accepted : 24 June 2014
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Among these four phases, we need to pay attention to the reactivating stage of HBV replication(HBeAg(-) CHB) because the annual occurrence of liver cirrhosis has been evaluated to be 2% to 6% for HBeAg(+) and 8% to 10% for HBeAg(-) chronic hepatitis patients[5]. The status of HBeAg(-) CHB is considered to infect silently and attack the liver of chronic hepatitis patients while HBeAg(+) CHB may be checked out more frequently. This makes medical staffs have an intense care for HBeAg(-) chronic hepatitis patients with quiet and active replication of HBV DNA.

Thus, medical treatment which is effective in improving clinical manifestations is required to deal with HBeAg(-) chronic reactive hepatitis patients. This report was aimed to investigate the therapeutic efficacy and safety of *Injincheonggan-tang(IJCGT)* on patients with HBeAg(-) chronic reactive hepatitis.

Case Report

1) Case 1

(1) Name : Hwang ○○

(2) Gender/Age : F/29

(3) O/S : Since 2008

(4) C/C : ① Fatigue ② Dyspepsia

(5) P/H : Chronic hepatitis B (2008. Dx.)

(6) F/H : None specific

(7) The period of treatment : October 2010 to March 2013

(8) P/I : A 29 year-old female with 161cm and 49kg had no clinically serious problem except being diagnosed with Chronic hepatitis B in 2008 and recognizing HBV-carrier in 2001. Since 2008, she had felt general fatigue and had some inconvenience in digesting and visited Seoul National University Bundang Hospital in June 2008. Since then, AST and ALT had soared to 296(U/L) and 496(U/L) intermittently with HBeAg(-) and HBeAb(+). When tested for LFT on October 1st, 2010, AST and ALT were recorded as 175(U/L) and 293(U/L). Due to these increased levels, she was suggested to receive interferon therapy once a day for one year. After she had been given interferon injection twice, she refused to continue the interferon therapeutic option because of the pain and discomfort of the subcutaneous administration. This inconvenience of the interferon therapy made her visit the department of internal medicine I of Kyung Hee University Korean Medicine Hospital on October 18th, 2010. She wanted to take herbal medicine to improve her subjective clinical symptoms such as fatigue and dyspepsia without antiviral therapy.

(9) Image and laboratory results

① Upper Abdomen and kidney sonography in Seoul National University Bundang Hospital (2010. 04. 27) : Slightly coarse liver echotexture. r/o Chronic liver disease.

② Upper Abdomen and kidney sonography in Kyung Hee University Korean Medicine Hospital (2010.10.27) : R/O hepatopathy.

③ Upper Abdomen and kidney sonography in Kyung Hee University Korean Medicine Hospital (2011.05.04 and 2013.03.18) : Unremarkable findings.

④ HBeAg/HBeAb (2010.10.27.~2012.02.11.) : -/ +

⑤ CBC & DC, U/A (2010.10.25.~2013.03.18.): W.N.L

⑥ AFP(~4.0ng/mL) : 28.99(2010.10.27.), 13.13 (2010.11.19.), 1.73(2012.02.11.)

(10) Treatment : *IJCGT* A 1ch#3 adding *Crataegii Fructus*, *Hordei Fructus Germiniatus* and *Amomi Fuctus*

2) Case II

(1) Name : Lee ○○

(2) Gender/Age : M/49

(3) O/S : Since 1988

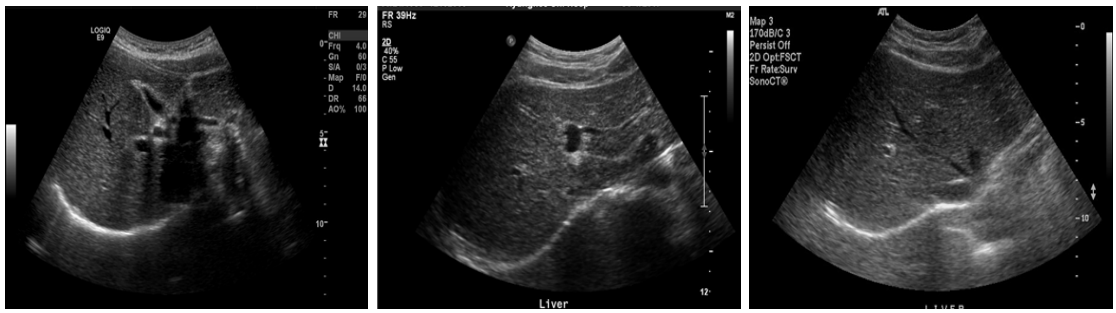
(4) C/C : ① Fatigue ② Rt. side flank discomfort ③ Lt. migraine ④ gum bleeding

(5) P/H : Chronic hepatitis B (1988. Dx.)

(6) F/H : Mother (Liver cirrhosis)

(7) The period of treatment : From October 2006

 http://dx.doi.org/10.13048/jkm.14024



2010.10.27 2011.05.04 2013.03.18

Fig. 1. Upper Abdomen and kidney sonography in Case 1

Table 1. Changes of Liver Function Test and HBV DNA Data in Case 1

	AST(U/L)	ALT(U/L)	HBV titer(IU/mL)	HBV (copies/mL)
2010.10.27	57	125	2,771	16,128
2010.11.19	33	44	718	4,181
2011.02.12	24	23	3,158	18,382
2011.03.26	22	19	10,081	58,671
2011.05.04	20	19	11.963	69.626
2011.12.31	31	43	95,400	555,228
2012.02.11	24	30	66,700	388,194
2013.03.18	35	75	82,600	480,732

(Normal range: AST(~40U/L) ALT(~40U/L) HBV(~ <20 IU/mL, ~< 116 copies/mL))

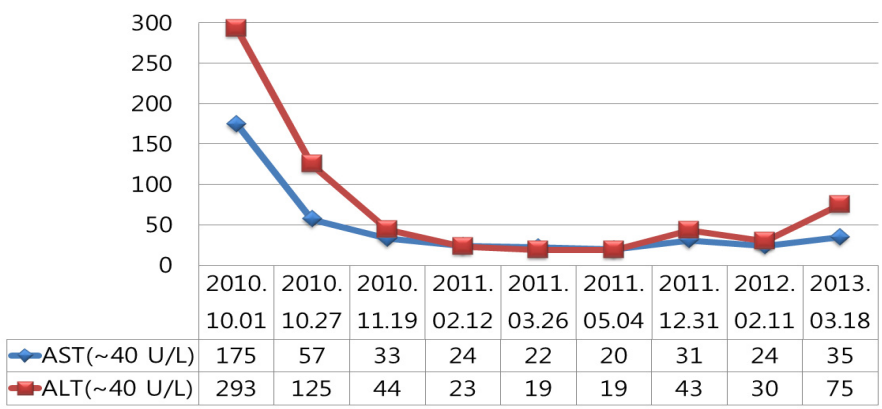


Fig. 2. Transition in serum aminotransferase in Case 1

to March 2013

(8) P/I : A 49 year-old male with 177cm and 62kg had no clinically apparent problem except being informed by medical doctor with Chronic hepatitis B in 1988 and recognizing HBV-carrier in his military service in 1984. It is not certain whether his infection with hepatitis B virus is mother-to-child transmission but he is probably vertically trasmitted due to his mother's medical history as liver cirrhosis. Since 1988, he has felt general fatigue, Rt. side flank discomfort, Lt. migraine, and gum bleeding. In 1995, he was injected with alpha-interferon for 3 months and afterwards he has been prescribed with Legalon and Ursodeoxycholic acid to keep the liver function. He had taken *Chihyeolbogan-hwan* from Gangnam Somang Oriental Medical Clinic for about 1 year in 2005 and lamivudine oral therapy in October 2006. Despite these medical treatments, his clinical presentations still did not go better. When tested for laboratory exam on October 24th, 2006, total bilirubin, HBV-DNA, AST and ALT were estimated as 1.1(mg/dL), 3169(IU/mL), 210(U/L) and 102(U/L), respectively. Abdomen CT was read as "Typical chronic hepatitis changed to early liver cirrhosis, spleen is enlarged without mass, partial nodular, Rt. medial lobe" on that day. Due to above persistent chronic hepatitis B state, he visited the department of internal medicine I of Kyung Hee University Korean Medicine Hospital on 28 October, 2006. He wanted to take herbal treatment to improve his clinical symptoms and laboratory inspection levels related to chronic hepatitis B.

(9) Image and laboratory results

① Abdominal sonography (2007.05.10) : Liver cirrhosis.

② Abdominal sonography (2008.01.25) : Liver cirrhosis with mild splenomegaly. A small low echoic nodule in right dome suggestive of regenerative nodule ; small HCC cannot be excluded. A tiny GB stone

③ Abdomen CT(Dynamic) (2008.09.04) : Cirrhosis of liver mild splenomegaly and coronary collaterals. Two accessory spleen. A small nodule in LLL.

④ Abdomen CT(Dynamic) (2010.03.24) : No interval changes in cirrhosis of liver with splenomegaly, two accessory spleens and others.

⑤ HBeAg/HBeAb (2006.11.28~2013.03.09) : -/ +

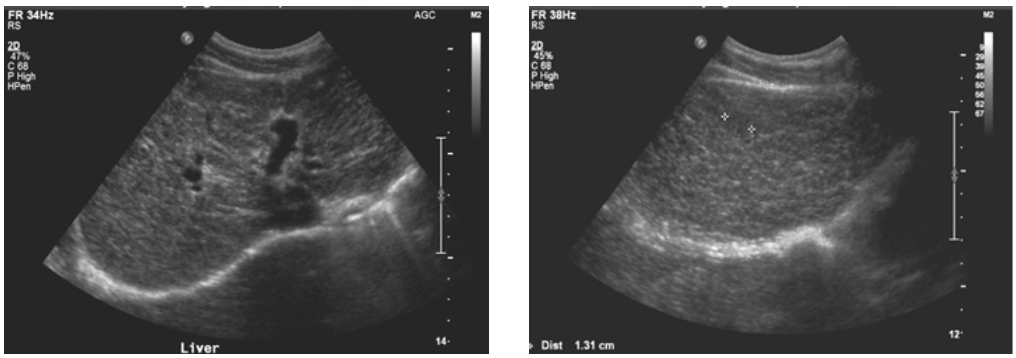
⑥ CBC & DC (2006.11.25~2013.03.09): W.N.L

⑦ AFP(~4.0ng/mL) : 63.8(2006.11.28.), 8.1(2007.01.09.), 4.0(2007.04.30.), 1.6(2007.08.25.), 2.51(2007.10.13.), 1.8(2008.01.12.), 2.2(2008.02.25.), 1.8(2008.09.04.), 1.1(2009.01.10.), 2.92(2010.03.11.), 3.36(2013.03.11.)

Table 2. Herb Composition of *IJCGT A adding Crataegii Fructus, Hordei Fructus Germiniatus and Amomi Fuctus*

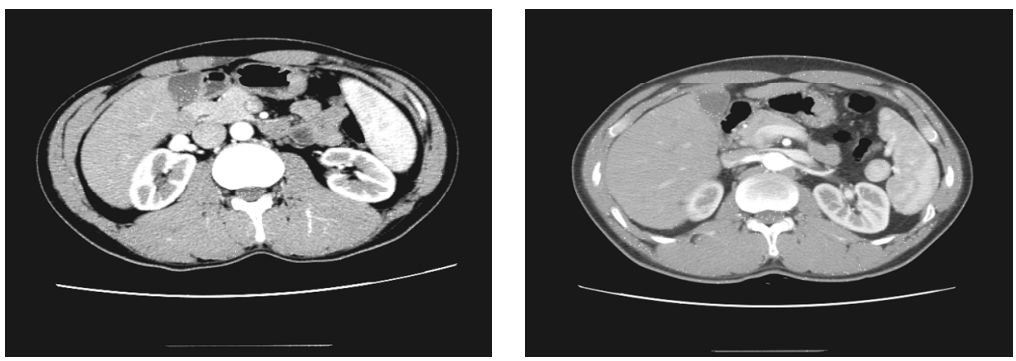
Herb	Scientific name	Amounts(g)
茵蔯蒿	*Artemisiae Capillaris Herba*	50
地榆	*Sanguisorbae Radix*	15
白朮	*Atractylodis Rhizoma Alba*	12
白茯苓	*Hoelen*	12
豬苓	*Drabae Semen*	12
覆盆子	*Rubi Fructus*	12
澤瀉	*Alismatis Rhizoma*	8
蘿卜子	*Raphani Semen*	8
靑皮	*Citrii Unshiu Immaturi Pericarpium*	6
甘草	*Glycyrrhizae Radix*	6
生薑	*Zingiberis Rhizoma Crudus*	12
山査	*Crataegii Fructus*	8
麥芽炒	*Hordei Fructus Germiniatus*	8
砂仁	*Amomi Fuctus*	6

 http://dx.doi.org/10.13048/jkm.14024



2007.04.28 2008.01.25

Fig. 3. Upper Abdomen and kidney sonography in Case 2



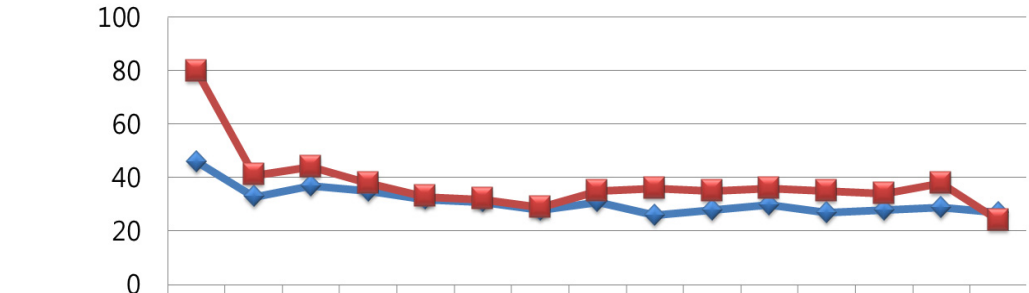
2007.04.28 2008.01.25

Fig. 4. Abdomen CT in Case 2

Table 3. Changes of Liver Function Test and HBV-DNA Data in Case 2

	AST(U/L)	ALT(U/L)	HBV titer(IU/mL)	HBV (copies/mL)
2006.11.27	46	80		
2007.01.08	33	41		
2007.02.26	37	44		
2007.04.30	35	38		
2007.06.28	32	33		
2007.08.27	31	32		
2007.10.13	28	29		
2007.11.24	31	35		
2008.01.12	26	36		
2008.02.23	28	35		
2008.09.04	30	36		
2008.11.22	27	35		
2009.01.10	28	34		
2010.03.10	29	38	13,600	79,152
2013.03.09	27	24	6,070	35,327

(Normal range: AST(~40U/L) ALT(~40U/L) HBV(~ <20 IU/mL, ~< 116 copies/mL))



	2006. 11.27	2007. 01.08	2007. 02.26	2007. 04.30	2007. 06.28	2007. 08.27	2007. 10.13	2007. 11.24	2008. 01.12	2008. 02.23	2008. 09.04	2008. 11.22	2009. 01.10	2010. 03.10	2013. 03.09
AST(~40 U/L)	46	33	37	35	32	31	28	31	26	28	30	27	28	29	27
ALT(~40 U/L)	80	41	44	38	33	32	29	35	36	35	36	35	34	38	24

Fig. 5. Transition in serum aminotransferase in Case 2

Table 4. Herb Composition of *IJCGT B adding Curcumae Radix and Biotae Folium or Salviae Miltiorrhizae Radix*

Herb	Scientific name	Amounts(g)
茵蔯蒿	*Artemisiae Capillaris Herba*	50
地榆炭	*Sanguisorbae Radix*	15
白朮	*Atractylodis Rhizoma Alba*	12
白茯苓	*Hoelen*	12
猪苓	*Drabae Semen*	12
覆盆子	*Rubi Fructus*	12
澤瀉	*Alismatis Rhizoma*	8
蘿卜子	*Raphani Semen*	8
靑皮	*Citrii Unshiu Immaturi Pericarpium*	6
三棱	*Scirpi Rhizoma*	6
莪朮	*Zedoariae Rhizoma*	6
砂仁	*Amomi Fuctus*	6
甘草	*Glycyrrhizae Radix*	6
生薑	*Zingiberis Rhizoma Crudus*	12
鬱金	*Curcumae Radix*	8
側柏炒	*Biotae Folium*	8
丹蔘	*Salviae Miltiorrhizae Radix*	8

(10) Treatment : *IJCGT B* 1ch#3 adding *Curcumae Radix* and *Biotae Folium* or *Salviae Miltiorrhizae Radix*

Treatment results

To diagnose CHB, a series of tests associated with liver function should be examined, and HBsAg, HBsAb, HBcAb, HBeAg, HBeAb and HBV-DNA test are basic laboratory exams. Especially HBV-DNA test shows the amount of the HBV virus actually circulating and replicating in patient's blood and it suggests clinically important meaning for the activity of the CHB disease. In this case, both female and male have been diagnosed with CHB in local medical clinics. This previous diagnosis made HBsAg, HBsAb and HBcAb tests needless to check because we can expect the result of HBsAg(+), HBsAb(-) and HBcAb(+). For this reason, HBeAg, HBeAb and HBV-DNA test in both patients were

 http://dx.doi.org/10.13048/jkm.14024

examined to indicate the state of CHB.

The first patient was diagnosed with CHB in 2008 and recorded HBeAg(-), HBeAb(+) and HBV DNA 16,128(copies/mL) on the beginning of the herbal treatment in 2010. She felt indescribable discomfort in abdominal site with dyspepsia and some persistent fatigue. Her AST and ALT levels had been fluctuated and then boosted to 162(U/L) and 290(U/L) on September 2010. Despite the interferon therapy, she wanted to take herbal decoction to control her CHB. She visited the department of internal medicine I of Kyung Hee University Korean Medicine Hospital on October 18th, 2010. We gave her modulated *IJCGT A* 3 times a day, which was divided 1 dose into 3 packs, and tested her blood laboratory exams.

After taking the herbal medicine for 20 days from October 29th, 2010, her liver function tests showed surprising improvement. AST levels decreased from 57(U/L) to 33(U/L), ALT from 125(U/L) to 44(U/L) and HBV DNA copies from 16,128(copies/mL) to 4,181(copies/mL). Her clinical subjective symptoms such as fatigue and dyspepsia also became better despite of the hardwork doing her business. After about 2 months treatment and 1 month untreatment, she revisited our hospital and her aggravated HBV DNA copies recorded 18,382(copies/mL) probably due to the 1 month untreatment. Although she took modulated *IJCGT A* for 20 days, after that she left untreated for 1 month. In this manner, she voluntarily repeated her herbal treatment and untreatment. Especially, when she came to our clinic after about half a year, her HBV DNA copies skyrocketed from 69,626(copies/mL) to 555,228 (copies/mL) and AST increased from 20(U/L) to 31(U/L) and ALT from 19(U/L) to 43(U/L) but she was none the worse in fatigue and dyspepsia for her aggravated laboratory tests. Her HBV DNA copies again declined to 388,194(copies/mL), AST to 24(U/L) and ALT to 30(U/L) after taking modulated *IJCGT A*. She revisited on march 2013 after about 1 year, and her HBV DNA copies increased to 480,732(copies/mL), AST 35(U/L) and ALT 75(U/L). In this manner, her AST, ALT and HBV DNA have been sensitively responded to *IJCGT* as shown in previous articles[6,7]. Additionally, her AFP decreased from 28.99(ng/mL) on October 27th, 2010 to 13.13 (ng/mL) on November 19th, 2010 and dramatically to 1.73(ng/mL) on February 11th, 2012. Upper abdomen and kidney sonography also showed improvement from "slightly coarse liver echotexture. r/o chronic liver disease" on October 25th, 2010 to "unremarkable findings" on March 18th, 2013. Therefore, we can judge the efficacy of modulated *IJCGT A* on her through the trend of laboratory results and associations between these tests and her visit to our hospital.

In the second case, the male had already been told that he had had chronic hepatitis B and liver cirrhosis in 1988. When tested for liver function 4 days before visiting our hospital, his Total bilirubin, HBV-DNA, AST and ALT were recorded as 1.1(mg/dL), 3169(IU/mL), 210(U/L) and 102(U/L) respectively with HBeAg(-) and HBeAb(+) and the serology called attention to care his progression to HCC or severe liver disease due to his liver cirrhosis diagnosis and family history. He visited the department of internal medicine I of Kyung Hee University Korean Medicine Hospital on October 28th, 2006 with general fatigue, Rt. side flank discomfort, Lt. migraine and gum bleeding. We gave him modulated *IJCGT B* 3 times per day, which was divided 1 dose into 3 packs and tested his blood laboratory exams.

After taking *modulated IJCGT B* steadily since October in 2006 for 1 year, his AST and ALT were improved from 46(U/L) to 28(U/L) and from 80(U/L) to 29(U/L). His clinical presentations such as fatigue, left migraine, uneasy feeling of the left side and gingiva bleeding also became better. After following up the laboratory level without herbal medicine from 2007 to 2008 due to the patient's stability, he restarted to take modified modulated

IJCGT B focused on his heavy feeling in the head from September 2008 to January 2009. He informed us his dull feeling in the head had improved and his AST and ALT also decreased from 30(U/L) and 36(U/L) to 28(U/L) and 34(U/L). On March 10th, 2010, he revisited our clinic because of his fatigue, gingiva bleeding and epistaxis. We gave him modulated *IJCGT B* which we had prescribed from 2006 to 2007 because hemostatic *Cheuckbaek*(側柏) herb was contained in this formula. After 1 month treatment, his bleeding tendency had been improved. Furthermore, his AFP level showed consistently downward pattern from 63.8(ng/mL) on November 28th, 2006 to 3.36(ng/mL) on March 11th, 2013. Abdominal sonography on January 12th, 2008 was recorded as "liver cirrhosis with mild splenomegaly. A small low echoic nodule in right dome → suggestive of regenerative nodule ; small HCC cannot be excluded". Abdomen CT on September 4th, 2008, however, instructed the lower probability of HCC and its reading was following as "Cirrhosis of liver mild splenomegaly and coronary collaterals. Two accessory spleen. A small nodule in LLL". Therefore, we can assume that modulated *IJCGT B* has some efficacy on improving CHB patient's clinical symptoms and laboratory exams and keeping AFP in normal range by preventing from deteriorating into severe hepatitis or liver cirrhosis.

Discussion

HBV is a DNA virus which merges into the host genome. Therefore the entire elimination of the virus from an infected patient is not possible. This impossibility of complete eradication of hepatitis B virus makes the viral infection head toward to a chronic phase. The natural history of chronic hepatitis B infection can be divided into 4 stages largely depending on the age of infection : immune tolerant, HBeAg(+) immune active chronic hepatitis, HBeAg(-) immune active chronic hepatitis, and inactive carrier state[8]. Particularly, the HBeAg(-) immune active chronic hepatitis stage can show the variability of viral replication and clinical symptoms according to the actual number of HBV DNA copies. The HBeAg(-) state in chronic hepatitis infection can indicate not only the suppression of HBV active replication but also the advent of core or precore abnormality that decreases HBeAg production yet viral replication continues in the liver[9]. Comparing with HBeAg(+) chronic hepatitis B infection, therefore, HBeAg(-) chronic hepatitis is usually related to fluctuating pattern of hepatitis and relatively low HBV DNA levels but the longer a person remains in the immune active phase of infection, either HBeAg(+) or (-), the greater the degree of fibrosis and the risk of progressing cirrhosis or HCC. Due to these characteristics of HBeAg(-) CHB, two patients in this case report with increased HBV-DNA copies(>2,000 IU/mL for female and male) in spite of HBeAg(-) state need to be treated with careful inspection not to move from HBeAg(-) to HBeAg(+).

Generally speaking, long-term targets of antiviral therapy for HBeAg(-) CHB are to keep from continuing progression to liver cirrhosis, liver decompensation, and development of HCC and seven therapeutic methods are now accepted by the US Food and Drug Administration(FDA) for the medical care of chronic hepatitis B infection: standard or pegylated interferon- and 5 oral nucleos(t)ide analogues : adefovir, lamivudine, entecavir, tenofovir and telbivudine[8]. Both female and male in this case report were also recommended to take interferon therapy and male had taken Zeffix(lamivudine) from October 25th to 26th, 2006. Interferon therapy, however, gives liver disease patients some discomfort such as pain of subcutaneous injection and side effects like chilling, fever, vomiting and so on. The additional weakness of an antiviral therapy is that it has a tolerance if the same medication is used repeatedly.

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Two patients with CHB in this case report visited our clinic to cure their liver viral infection by herbal medicine. Both of them showed not only surprisingly improved AST, ALT, HBV DNA copies, AFP and Image results but also reduced clinical symptoms after taking herbal medicine. No side effect from herbal treatment was reported and *IJCGT* can touch both the cure of infection and prevention from worsening to more severe state in CHB patients. Especially, the second patient had high risk factors in progression of chronic liver disease. The risk factors related to the development of HCC are gender, age, family history, alcohol, smoking and so on. For example, males have an higher risk of HCC than females about 3~4 times and the hazard of HCC and liver cirrhosis is exponentially augmented over 40 years old. Also, there is an alarmingly higher risk of HCC and liver cirrhosis in people with a family history of liver disease[10]. The second case belonged to the highly risky domain of male gender, over 40 years old with liver disease family history. To this very risky patient, *IJCGT* stabilized AFP level and cared his bleeding, migraine and fatigue. In other words, *IJCGT* can prevent patients with CHB with low or undetectable HBV DNA copies from evolving into HBeAg(+) or increasing in ALT level persistently or episodically.

IJCGT is herbal medicine to treat liver damage related to the infection. It contains *Gagamwieryungtang (GGWRT)*(加減胃苓湯) and *Injinsaryungsan*(*IJSRS*)(茵蔯四苓散) minus *Paeonia lactiflora, Cinnamomum loureirii* and *Pinellia ternata* which eliminates wet-heat(濕熱), excess fluid from patients(利尿) and strengthens the stomach function(健脾). Especially, *IJCGT A* and *IJCGT B* are mainly used for chronic hepatitis and liver cirrhosis. A female patient with CHB appealing dyspepsia and fatigue in the first case was prescribed for *IJCGT A adding Crataegii Fructus*, *Hordei Fructus Germiniatus* and *Amomi Fuctus* which were enriched for the gastro-intestinal function and *IJCGT B* adding *Curcumae Radix* was given to the male in liver cirrhosis and chronic hepatitis which was added *Biotae Folium* in case of bleeding symptoms or *Salviae Miltiorrhizae Radix* in case of heavy feeling in his head.

These two examples of cases will suggest some solutions to various medical issues that may arise in making Korean medicine treatment decisions for patients with chronic hepatitis B. The first issue is the safety of herbal medicine. People commonly think that taking herbal medicine for a long time can damage liver function, however, these patients in this case report had herbal decoction for over at least 1 year and both of them did not display any side-effect. Drug tolerance is the second problem and any resistance to the herbal medicine had not been reported during the period of the persistent use of the decoction. Thirdly, the achievement of medical treatment in CHB is the most important task. Korean medicine treatment has considerable efficacy in CHB patients for stabilizing AST, ALT, AFP, sonographic or CT image and subjective symptoms without inverting HBeAg(-) to HBeAg(+).

The present western medicine has a problem in treating the immune tolerant or inactive carrier states of chronic hepatitis B because there is no obvious role of antiviral therapy. The Korean medicine, in this regard, can suggest the meaningful solution to this problem because it helps the improvement of the serologic exam, clinical symptoms and is safe for longtime use without drug tolerance although we need to do further study regarding virus suppressing effect. Thus our report informed the efficacy of modulated *IJCGT* on CHB and liver cirrhosis patients. For the higher evidence level, we need to show the effectiveness of the herbal medicine on the basis of the more larger sample size and multi-center study. Through these active studies, we will be able to make excellent herbal strategies for the CHB patients.

Reference

1. Lai CL, Ratziu V, Yuen MF, Poynard T. Viral hepatitis B. Lancet. 2003;362:2089-94.
2. Gust ID. Epidemiology of hepatitis B infection in the Western Pacific and South East Asia. Gut. 1996;38(Suppl 2):S18-23.
3. Redeker AG. Viral hepatitis:clinical aspects. Am J Med Sci. 1975;270:9-16.
4. Yim HJ, Anna Suk-Fong Lok. Natural history of chronic hepatitis B virus infection : what we know in 1981 and what we know in 2005. Hepatology. 2006;43:S174.
5. Fattovich G, Stroffolini T, Zagni I, Donato F. Hepatocellular carcinoma in cirrhosis : incidence and risk factors. Gastroenterology. 2004;127 (Suppl 1):S35-S50.
6. Lee JE, Kim CW, Jung YJ, Rhew KY, Kim YC, Lee JH, et al. Two Cases of Injinchunggan-tang Treated Patients with Chronic Hepatitis B Relapsed after Lamivudine Therapy. The Journal of Korean Oriental Internal Medicine. 2005;spr(1):230-39.
7. Woo HJ, Lee JH, Kim SM. The Effect of Inchinchunggantang on inhibition of HBeAg production in HepG2.2.15 Cell line. Collection of dissertations of Korean medicine college of Kyung Hee university. 1998;21(1):171-9
8. Kuo A, Gish R. Chronic Hepatitis B Infection. Clin Liver Dis. 2012;16:347-69.
9. Chu CJ, Keeffe EB, Han SH, Perrillo RP, Min AD, Soldevila-Pico C, et al. Prevalence of HBV Precore/Core Promoter Variants in the United States. Hepatology. 2003;38(3):619-28.
10. McMahon BJ. Natural History of Chronic Hepatitis B Infection. Clin Liver Dis. 2010;14: 381-96.

 http://dx.doi.org/10.13048/jkm.14024