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# A hospital clinic-based survey on traditional Chinese medicine usage among chronic hepatitis B patients

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**Summary**
*Objectives:* To survey the pattern of traditional Chinese medicine usage among chronic hepatitis B patients.
*Design:* Self-administered questionnaire survey.
*Setting:* Hepatitis clinic at a university hospital in Hong Kong.
*Main outcome measures:* Proportion of chronic hepatitis B patients who have ever used traditional Chinese medicine for the treatment of chronic hepatitis B and factors associated with the use.
*Results:* Three hundred and sixty-two patients completed the survey (response rate 93%). One hundred and sixteen (32%) patients reported history of traditional Chinese medicine usage. One hundred and five (91%) patients felt that Chinese medicine had few or no side effects. Most (81%) patients did not inform their physicians on Chinese medicine usage. On multivariate analysis, recent travel to Mainland China, perceived active hepatitis and family members with chronic hepatitis B were independent factors associated with the use of Chinese medicine.
*Conclusions:* Chronic hepatitis B patients commonly use traditional Chinese medicine. As patients seldom inform the physicians about the use of Chinese medicine, doctors should explicitly enquire about this because of potential therapeutic implications.


## Introduction

Chronic hepatitis B virus (HBV) infection affects more than 400 million people worldwide, and is the commonest cause of liver cirrhosis and hepatocellular carcinoma in most Asian countries.[1] Currently,

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interferon-alpha, lamivudine and adefovir dipivoxil have been approved for the treatment of chronic hepatitis B. However, the use of interferon is limited by the inconvenient route of administration and side effects, while the use of anti-viral agents is limited by the need of extended treatment and emergence of drug resistance.[2–4] The overall therapeutic efficacy of these agents is still not satisfactory. For example, among chronic hepatitis B patients with positive hepatitis B e-antigen, 1 year treatment with either lamivudine or adefovir dipivoxil results in hepatitis B e-antigen seroconversion in approximately 15% of cases.[5,6]

Previous studies have demonstrated that many patients are receiving alternative medicine, often without informing their physicians.[7] Traditional Chinese medicine is one form of alternative medicine that is frequently used among Asian patients, and more and more in Western countries. According to a survey conducted in the United States, 2.5% of adults used herbal medicine in the preceding 12 months in 1990, and the figure rose to 12.1% in 1997.[7] The annual spending on herbal products by the general population has been estimated to exceed £40 million per year in the United Kingdom and 5 billion US dollars per year in the United States.[7,8] These surveys in the West have probably combined Western herbal remedies with traditional Chinese medicine and the true picture of traditional Chinese medicine drug usage is uncertain. In our locality, there have been a series of socio-medical surveys concerning the use of traditional Chinese medicine since 1960s but they hardly related to liver diseases.[9–11] Approximately 10% of adults in Hong Kong have consulted traditional Chinese medicine doctors[10,11] and 13.5% have been using traditional Chinese medicine drugs.[11] These phenomena are potentially important in the management of chronic hepatitis B. Firstly, the traditional Chinese medicine may have drug interactions with Western medications, and it is reasonable to assume possible interactions with interferon and/or anti-viral agents.[12–14] Secondly, some traditional Chinese medicine may cause elevations in liver enzymes and may even be hepatotoxic.[15,16] This problem is particularly serious with herbal products which do not have good quality control and assurance. Thirdly, the use of traditional Chinese medicine may affect the health-seeking behavior and the drug compliance. Nevertheless, few studies have investigated the use of traditional Chinese medicine among patients with chronic hepatitis B.

In a study at six liver clinics in the USA, 39% of the attendees reported the use of alternative medicine.[17] However, the study did not report the type of liver disease that the responders suffered from or the use of traditional Chinese medicine. Besides, Asian patients were under-represented in that study. Another study from Taiwan also showed that a third of patients with chronic liver or gastrointestinal diseases used alternative medicine.[18] Only 54% of the responders had chronic liver disease, and the proportion of patients with viral hepatitis was unknown.

As chronic hepatitis B is the commonest cause of liver-related complication in our locality, we set out to survey the proportion of chronic hepatitis B patients who have ever used traditional Chinese medicine, the types of traditional Chinese medicine used, and the factors associated with the use of traditional Chinese medicine in this study.

## Methods

### Patients

All out-patients with chronic hepatitis B attending the liver disease clinics at the Prince of Wales Hospital, Hong Kong during the 4-week period between April 12 and May 9, 2004 were recruited. Approximately 40% of our patients were referred from community-based screening program of asymptomatic subjects while the remaining 60% of patients were referred from family doctors for elevation of liver enzymes or symptomatic hepatitis.[19] Chronic HBV infection was defined as the presence of positive hepatitis B surface antigen for more than 6 months. We invited all Chinese patients aged 18 or above with chronic HBV infection regardless of the hepatitis B e-antigen status, activity of hepatitis or status of liver cirrhosis for this questionnaire survey. Patients with acute hepatitis B or co-infection with hepatitis C virus were excluded.

### Questionnaire

A standardized questionnaire was developed by the authors to investigate the pattern of traditional Chinese medicine usage among chronic hepatitis B patients. Traditional Chinese medicine was defined as any formula containing herbal medication ingredients either prescribed by herbalists or brought over the counter. The clarity of the questions was tested in a pilot study including 12 chronic hepatitis B patients. The questionnaire was divided into three parts. Briefly, Part 1 of the questionnaire contained general questions including age, gender, occupation, marital status, duration of chronic hep-

atitis B since diagnosis, perception or knowledge of severity of liver disease, family history of liver disease and previous and/or current treatment (including traditional Chinese medicine) for the liver disease if there was any. Part 2 of the questionnaire concentrated on the reasons why the patients did or did not use traditional Chinese medicine. The perceived efficacy, adverse effects and expenditure were also asked among those patients who had used traditional Chinese medicine. Part 3 of the questionnaire recorded the specific type and the source (over-the-counter or prescribed by herbalist) of herbal medicine used by the patients.

All patients who fulfilled the inclusion criteria were invited to complete the standardized, anonymous Chinese questionnaire with written informed consent. The questionnaires were completed in waiting area before physician consultation. All patients filled out Part 1 and Part 2 of the questionnaire alone, and assistance was available to any patients with reading difficulties or on patients' request. The investigators (AOSL, CYL, MTS and HYL) would then proceed to directly question those patients who had used traditional Chinese medicine to complete Part 3 of the questionnaire. All the questionnaires were returned on the same day of clinic visit for data entry and analysis.

### Statistical analysis

Data entry was performed by two independent investigators to ensure accuracy. Continuous variables were expressed as mean $\pm$ standard deviation. Continuous variables were compared by Student's *t* test and categorical variables were compared by Pearson Chi-square test. To determine the independent factors associated with traditional Chinese medicine usage, variables with *p* value below 0.1 on univariate analysis were tested by multivariate logistic regression model. All analyses were performed with the Statistical Package for Social Science (SPSS version 11.5, Chicago, IL). All statistical tests were two-sided. Statistical significance was taken as $p < 0.05$.

### Sample size justification

In the pilot study, 5 out of 12 patients had taken traditional Chinese medicine. In this survey, the response distribution of traditional Chinese medicine usage was estimated to be 40%. Our hospital clinic covered approximately one-sixth of the overall population in Hong Kong. As there were approximately 4000 chronic hepatitis B patients followed up in our liver disease clinics every year, the number of chronic hepatitis B patients followed up in all hospital-based clinics in Hong Kong per year was estimated to be 24,000. A survey including 362 patients would be required to determine a 40% response distribution of traditional Chinese medicine usage at 95% confidence interval and 5% margin of error.

## Results

### Patient characteristics

Three hundred and eighty-eight chronic hepatitis B patients attended the liver disease clinics over the 4-week period. Fourteen patients did not return the questionnaires and 11 patients did not consent to the questionnaire survey. One returned questionnaire was invalid as that patient did not indicate the usage of traditional Chinese medicine. In total, 362 (93%) patients had properly completed questionnaires for analysis. The characteristics of studied patients were shown in Table 1. Two hundred and ten (58%) patients had received high school education or above. Two hundred and fifty-seven (72%) patients were in employment while the others were housewives, students, unemployed or retired. One hundred and eighty-six (52%) patients had a monthly salary of 10,000 or higher. One hundred and ten (30%) of patients had traveled to Mainland China in the past year for over a week.

### Pattern of traditional Chinese medicine usage

One hundred and sixteen (32%) patients reported they had ever used traditional Chinese medicine, and 58 (50%) of them were actively using traditional Chinese medicine at the time of the study. Among them, 66 (57%) of patients received traditional Chinese medicine from herbalists, 28 (24%) patients bought it over the counter, and 22 (19%) patients obtained the medicine from both sources. Eighty-two patients had used decoctions of herbs while 67 patients had used patent products (29 patients had used both). Seventy-six (67%) patients spent less than US$65 per month on traditional Chinese medicine, 20 (18%) patients spent US$65 to US$130 while 18 (16%) patients spent more than US$130 per month (2 patients had missing information).

Forty-eight (42%) patients rated traditional Chinese medicine as very effective or effective in the treatment of chronic hepatitis B, 47 (42%) patients found the effectiveness fair while only 18 (16%) patients thought that traditional Chinese

**Table 1** Characteristics of patient in the survey.

| Characteristics | Result | Evaluable patients (*n*, %) |
|---|---|---|
| Age (years) | 44 ± 13 | 360 (99.4%) |
| Male gender (*n*, %) | 239 (66.0%) | 362 (100%) |
| Married (*n*, %) | 277 (76.5%) | 362 (100%) |
| Education level | | 361 (99.7%) |
| Junior secondary or below | 151 (41.8%) | |
| High school | 107 (29.6%) | |
| Tertiary education or above | 103 (28.5%) | |
| Working status | | 358 (98.9%) |
| Professionals | 27 (7.5%) | |
| White collar group | 139 (38.8%) | |
| Blue collar group | 91 (25.4%) | |
| Non-working | 101 (28.2%) | |
| Monthly income (HK$) | | 358 (98.9%) |
| <5000/month | 107 (29.9%) | |
| 5,000—10,000/month | 65 (18.2%) | |
| 10,000—20,000/month | 96 (26.8%) | |
| >20,000/month | 90 (25.1%) | |
| Travel to mainland China in the past year | | 361 (99.7%) |
| Never | 107 (29.6%) | |
| Less than 1 week | 144 (39.9%) | |
| 1 week to 1 month | 60 (16.6%) | |
| Over 1 month | 30 (13.8%) | |
| Duration of chronic hepatitis B (years) | 11.6 ± 8.2 | 361 (99.7%) |
| Perception of active disease | | 362 (100%) |
| Yes | 94 (26.0%) | |
| No or don't know | 268 (74.0%) | |
| Knowledge of liver cirrhosis | | 362 (100%) |
| Yes | 86 (23.8%) | |
| No or don't know | 276 (76.2%) | |
| Family member/friends with chronic hepatitis B | | 362 (100%) |
| Yes | 220 (60.8%) | |
| No | 142 (39.2%) | |
| Family member/friends with hepatocellular carcinoma | | 362 (100%) |
| Yes | 88 (24.3%) | |
| No | 274 (75.7%) | |
| Previous use of Western medication | | 362 (100%) |
| Yes | 106 (29.3%) | |
| No | 256 (70.7%) | |

medicine had little or no effect (3 patients had missing information). On the other hand, 105 (91%) patients felt that traditional Chinese medicine had few or no side effects, 9 patients found the side effects were moderate and only 1 patient experienced severe side effects (1 patients had missing information). Only 58 (50%) patients had informed their physicians regarding the use of traditional Chinese medicine. Most (81%) patients who did not inform their physician on traditional Chinese medicine usage did not think this information was important.

Sixty (52%) patients obtained information on traditional Chinese medicine from relatives or friends, while 35 (30%) patients obtained the information from herbalists. Minority of patients obtained the information from various sources including the internet, advertisements, recommendation from other patients or their physicians.

Forty-four (38%) out of 116 patients who preferred taking traditional Chinese medicine were recommended by relatives or friends. Twenty-five (22%) patients took traditional Chinese medicine because they thought it was better than Western

**Table 2a** Commonly used herbal ingredients by 116 chronic hepatitis B patients.

| Herbal components (Chinese name) | Percentage |
|---|---|
| *Abrus cantoniensis* Hance (雞骨草 ) | 53 |
| *Ganoderma lucidum* (靈芝 ) | 28 |
| *Atractylodes macrocephala* (白朮 ) | 28 |
| *Poria cocos* (茯苓 ) | 24 |
| *Schisandra chinensis* (五味子 ) | 21 |
| *Salvia miltiorrhiza* (丹參 ) | 18 |
| *Ligustrum lucidum* (女貞子 ) | 13 |
| *Cordyceps sinensis* (冬蟲夏草 ) | 10 |

The list includes herbal components used by more than 10% of the responders.

**Table 2b** List of all the identifiable herbal components used by 10% or less patients in alphabetical order.

| Herbal components (Chinese names) |
|---|
| *Amomum villosum* (砂仁/春砂仁/陽春砂 ) |
| *Artemisia capillaries* (茵陳蒿/綿茵陳 ) |
| *Astragalus mongholicus* (黃耆/北蓍 ) |
| *Bupleurum falcatum* (柴胡 )) |
| *Carapax Amydae* (鱉甲 ) |
| *Carapax Testudinis* (龜板 ) |
| *Citrus medica* var. *sarcodactylis* (佛手 ) |
| *Codonopsis pilosula* (黨參 ) |
| *Desmodium styracifolium* (金錢草 ) |
| *Glycyrrhiza uralensis* (甘草 ) |
| *Hedyotis diffusa* (白花蛇舌草 ) |
| *Isatis tinctoria* (板藍根 ) |
| *Lobelia chinensis* (半邊蓮 ) |
| *Lycium chinense* (枸杞子 ) |
| *Phyllanthus urinaria* (珍珠草/葉下珠 ) |
| *Plectranthus striatus* (溪黃草 ) |
| *Polygonum cuspidatum* (虎杖 ) |
| *Polygonum multiflorum* (何首烏 ) |
| *Prunella vulgaris* (夏枯草 ) |
| *Scutellaria barbata* (半枝蓮 ) |
| *Siphonostegia chinensis* (土茵陳 ) |

medicine. Nineteen (16%) patients took traditional Chinese medicine because they did not get any prescription from their physicians in the hospital clinic. Other reasons for using traditional Chinese medicine included personal preference, concern about the adverse effect of Western medication and influence by the mass media.

In contrast, among 246 patients who did not use traditional Chinese medicine, 88 (36%) patients felt that they did not require any treatment and 66 (27%) patients did not believe in the efficacy of traditional Chinese medicine or were worried about the safety of the medication. Other reasons for not using traditional Chinese medicine included inconvenient preparation (25 patients, 10%), advice from physician or relatives (21 patients, 9%) and other miscellaneous reasons. One hundred and forty (57%) patients have heard of the potential benefit of traditional Chinese medicine in treating chronic hepatitis B.

Tables 2a—2c illustrate the identifiable herbal ingredients used by more than 10% of the responders (Table 2a), herbal ingredients used by less than 10% of responders (Table 2b) and the names of the patent products (Table 2c). Eight-three (72%) of patients could identify the major ingredient of the herbs. Fifty-five (47%) patients were on herbs with more than one ingredient. The most frequently used herbal ingredients were *Abrus cantoniensis*, followed by *Ganoderma lucidum* and *Atractylodes macrocephala*.

## Factors associated with the use of traditional Chinese medicine

In addition to the demographic characteristics, factors that might reflect the perception of liver disease were also analyzed in relation to traditional Chinese medication usage. On univariate analysis, several factors were found associated with the use of traditional Chinese medicine, namely male gender, higher monthly salary, recent travel to Mainland China, longer duration since the diagnosis of chronic hepatitis B, perceived active liver disease activity, knowledge of presence of liver cirrhosis, family members or friends with chronic hepatitis B and previous use of Western medicine (Table 3). Other factors including age, marital status, education, employment status and family history of hepatocellular carcinoma had no association with traditional Chinese medicine usage. On multivariate analysis, recent travel to Mainland China, perceived active disease activity and family members or friends with chronic hepatitis B were independent factors associated with the use of traditional Chinese medicine (Table 4).

**Table 2c** List of all the identifiable patent drugs used by 116 chronic hepatitis B patients.

| Patent drugs | Chinese names |
|---|---|
| 329 Treatcam | 三二九保肝丸 |
| KY88 Liver Livo | KY88 九保肝丸 |
| Wu Zhi Capsules | (四川)五脂膠囊 |
| Zhangzhou Pien Tsz Huang | 福建片仔癀(漳州) |
| Ta Huang Zhe Chong Wan | 大黃蟅蟲丸 |
| Wan Ying Jian Gan Wan | 金源牌萬應健肝丸 |

**Table 3** Comparison of chronic hepatitis B patients who used traditional Chinese medicine and those who did not.

| Characteristics | Patients using traditional Chinese medicine ($n = 116$) | Patients not using traditional Chinese medicine ($n = 246$) | $p$ value |
|---|---|---|---|
| Male gender | 86 (74%) | 153 (62%) | 0.03 |
| Age | $44 \pm 11$ | $44 \pm 13$ | 0.97 |
| Married | 89 (77%) | 188 (76%) | 1.00 |
| High school education or above | 71 (62%) | 139 (57%) | 0.35 |
| Working group | 90 (78%) | 167 (69%) | 0.06 |
| Monthly salary above HK$10,000 | 68 (60%) | 118 (48%) | 0.05 |
| Travel to Mainland China over 1 week in the past year | 48 (42%) | 62 (25%) | 0.001 |
| Duration of diagnosis of chronic hepatitis B (years) | $14 \pm 9$ | $11 \pm 7$ | 0.001 |
| Perceived active liver disease | 46 (40%) | 48 (20%) | <0.001 |
| Knowledge of liver cirrhosis | 36 (31%) | 50 (20%) | 0.03 |
| Family members or friends with chronic hepatitis B | 84 (72%) | 136 (55%) | 0.002 |
| Family members or friends with hepatocellular carcinoma | 33 (28%) | 55 (22%) | 0.21 |
| History of treatment by Western medicine | 47 (41%) | 59 (24%) | 0.001 |

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as number (percentage).

**Table 4** Multivariate analysis of factors associated with the use of traditional Chinese medicine among chronic hepatitis B patients.

| Factors | Adjusted odds ratio | 95% confidence interval | $p$ value |
|---|---|---|---|
| Perceived active liver disease | 2.07 | 1.21–3.55 | 0.008 |
| Family members of friends with chronic hepatitis B | 2.00 | 1.17–3.42 | 0.01 |
| Travel to Mainland China over 1 week in the past year | 1.88 | 1.13–3.16 | 0.02 |

## Discussion

The health-seeking behavior of Hong Kong people is heavily influenced by both the Western and the Chinese culture. Using traditional Chinese medicine to promote health is a deep-rooted practice in Hong Kong.[9] In this study, one third of patients with chronic hepatitis B have used traditional Chinese medicine. This figure is similar to that of previous surveys on patients with other chronic illnesses.[7,20,21] The users of traditional Chinese medicine believed that it had moderate to good therapeutic benefit but little or no side effects. This might explain why a quarter of the patients who used traditional Chinese medicine never consulted the herbalists before taking those agents in this survey. Two recently updated systematic reviews of Chinese medicinal herbs for chronic hepatitis B suggested that several herbal formulae and ingredients including Jianpi Wenshen recipe, Fuzheng Jiedu Tang, *Polyporus umbellatus* and *Phyllanthus* species may have antiviral activity.[22,23] However, the methodological quality of the trials is generally low and the evidence is weak.[22–24] Nonetheless, these patients were willing to spend substantial sums on such preparations. The expense was not low as compared to that of Western medicine (monthly cost of lamivudine is approximately US$100). Probably as a result of the close family bonding in Chinese families, influence by relatives appeared to be important in patients' decision on use of traditional Chinese Medicine.

In this study, perception of having active hepatitis, having relatives or friends with chronic hepatitis B and recent travel to Mainland China are independently associated with the use of traditional Chinese medicine. These factors in turn may reflect the health-seeking behavior of patients in Hong Kong. Some patients might be told by the herbalists or friends to have active liver disease, as indicated by the relatively high proportion of patients who received information on traditional Chinese medicine from the herbalist (30%), took traditional Chinese medicine because no Western medicine was prescribed (16%), and did not reveal the usage of traditional Chinese medicine to their physicians (50%). As the syndrome of liver disease in traditional Chinese medicine is not exactly

the same as that of Western medicine, some of these patients may not have abnormal liver biochemistry or liver cirrhosis. Patients who have family members or friends with chronic hepatitis B may have a higher awareness of the disease and therefore a higher tendency to seek treatment. However, knowing family members or friends with hepatocellular carcinoma does not increase the use of traditional Chinese medicine, suggesting that patients tend to view traditional Chinese medicine as health enhancers instead of preventive treatment against liver-related complications. Patients who had recently traveled to China may represent those who have closer relationship with China and thus tend to use traditional Chinese medicine, and this phenomenon is probably not related to the education levels or the social classes of patients.

The most commonly used herbal ingredients, *Abrus cantoniensis*, *Ganoderma lucidum* and *Atractylodes macrocephala*, are not specifically anti-viral agents. These are herbs that have been used as to improve the immune function and maintain normal physiological activities of the internal organs. So far, there is no clinical trial addressing the efficacy and safety of these herbal ingredients in the treatment of chronic hepatitis B.[23,24] However, several preliminary animal experiments demonstrated possible hepatoprotective effects. A Japanese study suggested that Kaikasaponin III and Soyasaponin I, triterpenoidal saponins isolated from *Abrus cantoniensis*, may have anti-hepatotoxic activity in rats concomitantly exposed to $CCl_4$.[25] Studies in China and Korea also showed the hepatoprotective role of *Ganodrma lucidum* extracts against *Mycobacterium bovis* bacillus Calmette-Guerin-induced immune liver injury in mice and $CCl_4$-induced liver injury in rats, respectively.[26,27]

Our study has several limitations. First, as all patients in this survey were recruited from a single hospital based clinic, the characteristics of patients may not accurately reflect those of patients in other parts of Hong Kong. Most patients attending the clinic belong to the lower or middle social classes as evidenced by their lower education level, nature of occupation and the relatively low income. The behavior of these patients cannot be extrapolated to the more wealthy patient population in the private health sector. This bias is partially compensated by the good reputation of the university hospital as well as the wide diversity of patient referrals received by the clinic. Second, as most patients with chronic hepatitis B are asymptomatic, patients attending hospital clinic follow-up represent those who are more health conscious and have more confidence in Western medicine. It is possible that the use of traditional Chinese medicine is more popular in the general public. Third, because of the anonymous nature of the questionnaire, we cannot assess the relationship between the use of traditional Chinese medicine and the clinical disease severity. However, an anonymous questionnaire is less likely to introduce bias as some patients may not want to disclose the use of traditional Chinese medicine to their physicians. In fact, half of the responders who used traditional Chinese medicine did not inform their physicians about this matter. Fourth, the exact nature of the herbal ingredients was derived from memory of the patients. Different parts of the herb may have different values but this information could not be obtained in this survey. The herbal ingredients claimed to be used by patients might be adulterants or erroneous substitutes which possibly cause adverse event or even herbal poisoning.[28,29] So far, there have not been such reports among the commonly used herbal ingredients in this survey.

In conclusion, traditional Chinese medicine is commonly used among Chinese patients with chronic hepatitis B in Hong Kong. This health-seeking behavior may be influenced by the herbalists, family members, friends as well as by the traditional Chinese culture. As physicians are not informed of traditional Chinese medicine usage in approximately half of the patients in this survey, it is important for physicians to inquire specifically on the use of these products. Knowledge of the commonly used herbal ingredients by the physicians is also important for patient care. Patients use traditional Chinese medicine probably more for health enhancement rather than as evidence-based treatment. Future well-designed, randomized clinical trials are warranted to evaluate the efficacy and safety of the commonly used herbal ingredients in the treatment of chronic hepatitis B.

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