

RESEARCH ARTICLE

## Use of alternative product in patients with chronic viral hepatitis

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### ABSTRACT

**Objectives:** Some of the patients with chronic hepatitis use both alternative product and/or antiviral treatment. These herbal products sometimes lead to clinical deterioration. In this study we aimed to determine the purpose of alternative product utilization and rate among the chronic hepatitis B (CHB) and C (CHC) patients.

**Methods:** This prospective cohort study included 200 consecutive adult patients with chronic hepatitis B and C at the Department of Infectious Diseases, Ondokuz Mayıs University, between 1 March 2012 and 30 July 2012. At enrollment, clinical information, demographics, laboratory variables and knowledge about alternative products were recorded.

**Results:** Of the patients 150 had CHB, 50 had CHC. 54% of patients were male. Use of alternative products was 26%. Antiviral treatment rate was 48.5% for all patients. The most used alternative products were artichoke extract and honey. 67.3% of patients were using single alternative product whereas the others were using two or more alternative products. 46.2% of patients who use alternative product provided information about the alternative product usage, but the others did not.

**Conclusions:** Majority of patients used alternative products. More than half of these patients did not give information to their physicians about their use of alternative medicine. Use of alternative product should be asked in all patients with chronic hepatitis.

Herbal product usage was detected in majority of patients and also approximately half of these patients did not give information to their doctors about taking alternative medicine. In conclusion, it is necessary to take detailed information about herbal product usage in patients with chronic hepatitis. *J Microbiol Infect Dis 2014; 4(3): 102-106*

**Key words:** Chronic hepatitis B and C, alternative medicine

## Kronik viral hepatitli hastalarda alternatif ürün kullanımı

### ÖZET

**Amaç:** Kronik hepatitli hastalar antiviral ilaç tedavisiyle beraber alternatif ürünleride kullanabilirler. Alternatif ürünler bazen klinik kötüleşmeye yol açabilir. Bu çalışmada kronik hepatit B (KHB) ve kronik hepatit C (KHC)'li hastaların alternatif ürün kullanımını ve sıklıklarını belirlemeyi amaçladık.

**Yöntemler:** Bu prospektif kohort çalışmaya Ondokuz Mayıs Üniversitesi Enfeksiyon Hastalıkları Klinik Mikrobiyoloji polikliniğinde 1 Mart-30 Temmuz 2012 tarihleri arasında kronik hepatit B ve C tanısı ile izlenen 200 yetişkin hasta dahil edildi. Hastaların klinik bilgileri, demografik, laboratuvar değerleri ve alternatif ürün kullanma bilgileri kaydedildi.

**Bulgular:** Hastalarımızın 150'inde KHB ve 50'inde KHC enfeksiyonu olup % 54'ü erkekti. Alternatif ürün kullanım oranı % 26 idi. Bütün hastalarda antiviral tedavi kullanım oranı % 48,5'idi. En sık kullanılan alternatif ürünler enginar ve baldı. Hastaların % 67,3'ü sadece bal kullanırken, diğerleri iki veya daha fazla alternatif ürün kullanıyordu. Alternatif ürün kullanan hastaların sadece % 46,2'si ilk sorgulamada ürün kullanımı hakkında bilgiyi verirken diğerleri vermedi.

**Sonuç:** Çalışmaya alınan hastaların çoğunluğunda alternatif ürün kullanımı belirlenirken hastaların yarısı alternatif ürün kullandıkları hakkında doktoruna bilgi vermedi. Sonuç olarak kronik hepatitli her hastada alternatif ürün kullanımı detaylı şekilde sorgulanmalıdır.

**Anahtar kelimeler:** Kronik hepatit B ve C, alternatif ürün

## INTRODUCTION

Chronic viral hepatitis is a disease that can cause cirrhosis, hepatocellular carcinoma and sometimes death. Due to its characteristic chronic nature, therapeutic challenges and the complexity of the management of complications, and because of relatively long duration of treatment and higher costs, patients may be referred to alternative treatment methods. According to World Health Organization (WHO) report 70-80% of the world population could be referred to herbal products in practices of basic health services.<sup>1,2</sup>

Today, scientific developments based on evidence for the diagnosis and treatment of diseases made people live longer and thus the number of people with chronic diseases increased. Phytotherapy, which is an alternative medical practice, described as using plants in various forms for therapeutic purposes. Plants have been used extensively in the worldwide and the origin of phytotherapy goes back to ancient times. Deficient scientific research about herbal medicines, legal flaws, insufficient control mechanism, tremendous information pool and the broadcasting by visual and printed tools have become important in terms of complementary and alternative medicine (CAM) to consider public health.<sup>3</sup>

This study was conducted on patients with chronic viral hepatitis who were admitted to our clinic for treatment and follow up, and the frequency and duration of CAM use, informative sources patients preference, and the awareness of their personal physicians about using such an alternative therapy were predicted.

## METHODS

This cross-sectional study was held on patients who admitted to Department of Infectious Diseases, Ondokuz Mayıs University School of Medicine between March 1, 2012 and July 30, 2012. A total of 200 patients with chronic hepatitis B and C who were under or completed antiviral treatment during follow-up period and patients with inactive hepatitis B on follow-up without treatment were included in this study. The uniquely questionnaire developed for this study included questions such as the patients' demographic characteristics, information level about chronic hepatitis and the use of herbal medicine. Patients were interviewed personally and the questionnaires were completed with the consent of patients. Patients younger than 18 years old

were excluded from the study. Descriptive statistics have been expressed as an arithmetic mean  $\pm$  standard deviation and percentage in discrete variables. This study was approved by the Institutional Review Board.

## RESULTS

Of the 200 patients included in the study, 54% were male, 46% were female. 75% of the patients had chronic hepatitis B (CHB) and 25% had chronic hepatitis C (CHC). CAM use rate was detected 26% of patients. 67.3% of patients used only alternative products, while the number of patients who used two or more products was 32.7%. The most commonly used alternative products were artichoke (44.2%), honey (28.8%) and parsley extract (15.4%) respectively. The most popular CAM products are presented in Table 1.

**Table 1.** Alternative products used by patients

Name of product	Number of patient (%)
Artichoke	23 (44.2)
Honey	15 (28.8)
Parsley	8 (15.3)
Ready preparate + artichoke	6 (11.5)
Lavender	3 (5.7)
Ginger + pomegranate juice	3 (5.7)
Urtica urens + parsley	3 (5.7)
Green tea	3 (5.7)
Broccoli	2 (3.8)
Thistle	2 (3.8)
Taraxacum	2 (3.8)
Curcuma+pomegranate juice	2 (3.8)
Others (Aquamarine juice, Celery, Grape molasses)	5 (9.6)

Considering the education level of patients, 7.7% were found to be illiterate, 42.3% primary school graduates, 32.6% secondary and high school graduates and 17.3 % college graduates respectively. No statistically significant difference was found between education level and alternative product usage. 53.8% of the patients revealed that they informed their physicians about the product they used, whereas the other 46.2% not. 75% of patients using complementary and alternative products were reportedly satisfactory with conventional non-medical alternative treatment. 34.6% of patients indicat-

ed radio and television broadcasts as their source of information and 34.6% stated their source as the internet. In addition, other sources of information were the recommendations of people with similar diseases, neighbors, relatives and friends.

Considering the frequency of using alternative herbal products, 50% of patients reported that they used them every day, 26.9% used these products irregularly, 19.2% 2-3 times a week and 3.8% used once a month respectively. The length of usage time was as follows: in 38.5% 1-3 months, in 25% 4-12 months, in 17.3% less than 1 month and in 17.3% more than one year respectively. On the other hand, 7.5% of patients reported no use of antiviral treatment but only herbal products. Of the patients, 50.5% underwent medical treatment and 18.5% received both antiviral treatments and CAM and 23.5% did not receive any. It was found that, 39.2% of patients had performed no systematic investigation about the usage of herbal products.

No statistically significant difference was found considering prior and after treatment PCR HBV DNA, PCR HCV RNA values and ALT levels in patients using only CAM ( $p=0.160$ ,  $p=0.230$ ). Conversely, a significant difference was found between the pre and post treatment PCR HBV DNA and PCR HCV RNA, ALT values of the chronic viral hepatitis B and C patients who had antiviral treatment ( $p=0.001$ ).

Of patients 75% under follow-up with the treatment of chronic viral hepatitis and using CAM, reported that they believed in the therapeutic effect of alternative products due to broadcasts (13.5%), recommendations of patients (36.5%) and decreased confidence in medical treatment (3%).

## DISCUSSION

Patients with hepatitis carry some risks about using herbal products. Herbal products can cause hepatotoxicity in people who does not have hepatitis before. Major herbal products that cause toxic hepatitis are xiao-chai-hu-tang, basil, teucrium polium, briar patch, senna, mistletoe, scutellaria laterifolia, gentian, comfrey (includes pyrrolizidine alkaloid) and herbal teas. Recently, well defined acute hepatitis-like disorder resulting from use of 'jin bu huan' has been reported. High doses of vitamin A can cause liver damage. In addition, it has been reported that pyrrolizidine alkaloids in Chinese herbal mixtures can cause veno-occlusive liver disease.<sup>4</sup> In our study, 26% of 200 patients with chronic hepatitis reportedly used alternative products.

White et al. reported in a study with 76 patients with chronic viral hepatitis C, 28% of patients used vitamin or mineral supplement, 24% used herbal products which were similar rates in our study and 18% were reported to seek other natural treatment methods such as acupuncture.<sup>5</sup> They reported mostly used herbal products as milk-thistle (56%), evening primrose oil (17%) and glucosamine supplement (11%) respectively. Considering patients using herbs, 72% used only one product, whereas 17% used two and 11% used three different products concurrently. Sources of herbs were pharmacy in 83%, and market in 17%. In patients using CAM, 68% gained information about how to use from supermarkets, 16% from the internet, 8% from books, 4% from alternative medicine specialists and 4% from physicians. None of patients who used CAM were reported to have side effects. They found that, 83% of people reached CAM by pharmacies and supermarkets. Most frequently used triple herbal products were milk-thistle, evening primrose oil and glucosamine supplement. Our study revealed that, broadcasting by radio and television had a major impact in 69.2% of patients in reaching herbal products. Most of the products used were artichoke, honey and parsley respectively.

In another study, Ferruci et al.<sup>6</sup> found that, 248 of 1040 patients with chronic hepatitis used at least one CAM method. Of patients, 188 preferred vitamin and food supplements, 175 preferred herbal products and 16 preferred homoeopathy whereas 86 patients used multiple CAM treatment modalities. Most widely used herbal products were milk-thistle (43.8%), St. Aaron's beard (10.7%), echinacea (8.9%) and valerian (4.5%) respectively. They revealed that, CAM use was found to be significantly higher in patients with a story of hepatitis C and alcohol, hepatitis B and only alcohol when compared with patients who had non-alcoholic hepatosteatosis and steatorrhoeic hepatitis. CAM use and demographic characteristics were found to have a significant relationship with parameters such as male gender, young age, level of education, level of income and hospitalization. This study was similar to our findings in that the patients had a rate of 23.8% CAM use which was very close to our results. However, unlike our study, Ferruci et al.<sup>6</sup> found a significant relationship between CAM use and demographic characteristics, male gender, young age, level of education, level of income and hospitalization. We did not find any significant difference in patients who used these products in terms of age, gender and level of education. In addition,

no hepatotoxicity due to the products was found. Although, the products patients used were not agents reported as hepatotoxic, we observed unexplained liver enzyme increases in 3 patients undergoing antiviral treatment and in patients who had positive response parameters.

Seeff et al.<sup>7</sup> reported that 235 of 1145 patients with chronic hepatitis C used herbal products in the past while 269 of them were using herbal products during the follow-up. Majority of patients reported usage of more than 60 herbs in various combinations. These were mainly silymarin (72%), green tea (13.7%) and garlic (10.7%) in 269 patients. They indicated no significant difference between patients who used silymarin and those who did not ( $p=0.08$ ). Conversely, serum ALT levels were found to be significantly higher in users of silymarin than those of non users ( $p=0.04$ ). They concluded that, in patients with hepatic injuries, silymarin use arised from the belief that it had a protective effect in liver damage caused by *Amanita phalloides* toxicity. Silymarin demonstrated no antiviral activity against chronic hepatitis C virus.<sup>6</sup> Although, both studies showed different CAM choices considering herbal products, no significant relationship was found between herbal products and PCR HCV RNA and ALT. In addition, aforementioned study was largely directed about the efficacy of silymarin, on the other hand, in our study, the rate of using alternative products in 200 consecutive patients with chronic viral hepatitis was 26%. Of patients, 53.8% stated that, they informed their physicians about herbal product use whereas 46.2% did not. All patients in our study used herbs for the aim of treatment.

In another study from China, 80% of patients with chronic hepatitis were reported to demand traditional Chinese medical products as well as interferon and nucleoside analogs. An internet based review study in China found that, the most used herbal product was Mongolian milk vetch root.<sup>8</sup> In our study, majority of patients used only one product while some patients used multiple concurrently. A questionnaire of 310 patients applied by family physician recently in Ankara revealed that, 84.5% of patients were interested in herbal treatment and they used such treatment in the past. Of these patients, 21.6% used herbal products for a healthier life and as a vitamin supplement while 40% used for the treatment. This study also revealed that, 62.9% of patients gained information about herbal medicine through media and 42.6% from friends and neighbours.<sup>9</sup> Similarly, we found that, majority of patients stated that, they had information from the

internet (34.6%), radio-television (34.6%), relatives-neighbors (25%) while only 3.8% indicated similar patients as their source of information.

Why do so many patients need to divert standard treatment modalities? Factors such as the difficulties in the treatment may have directed patients to different alternative methods. The well-known chronic course of the disease, prolonged treatment duration and the side effects of interferons used in hepatitis C may have led to psychiatric problems.<sup>10</sup>

Some studies from the United States revealed that, patients using herbal products were in generally female, highly educated and over 60 years.<sup>10,11</sup> We did not find any statistically significant difference between patients in terms of age, gender and level of education. We found that, of patients 39.2% had performed no systematic investigation about the usage of herbal products, exhibiting that people still rely on chit chat rather than scientific data. In addition, majority of patients did not inform their physicians about usage and these yielded unfavorable results such as side effects or drug interaction. Therefore, physicians should ask about the use of such CAM methods. Besides, it should also be remembered that, patients who use herbal products can hinder their principal treatment.

Some herbs can have positive psychological effects such as elimination of exhaustion and cause a general feeling of well-being. However, it should be kept in mind that these substances can interact with the patient's medication and lead to alteration in drug levels.<sup>12,13</sup>

In conclusion, the use of alternative medical products in patients with chronic hepatitis represents a challenge for public health. Patients who do not inform their personal physicians about the use of herbal products, uncontrolled sales, benefit-oriented advertisements lacking scientific basis and people's recommendations make this situation more complicated. Health authorities, physicians and broadcast staff are all responsible to lead people and patients in a true scientific manner.

### Completing interest

The authors declare that they have no competing interest.

### REFERENCES

1. Traditional Medicine. <http://www.who.int/mediacentre/factsheets/fs134/en/> Accessed October 1,2012.
2. Sansen O, Caliskan D. Fitoterapi: Bitkilerle tedaviye dikkat. *Sted* 2005; 14:182-187.

3. Gürün MS. Bitkisel tıp. ANKEM Derg 2004; 18:133-136.
4. Dienstag JL, Isselbacher KJ. Toxic and Drug-induced Hepatitis. Principles of Internal Medicine, 16th edn. McGraw-Hill: Kasper DL, 2005;1843-1844.
5. White CP, Hirsch G, Patel S, et al. Complementary and alternative medicine use by patients chronically infected with hepatitis C virus. *Can J Gastroenterol* 2007;21:589-595.
6. Ferrucci LM, Bell BP, Dhotre KB, et al. Complementary and alternative medicine use in Chronic Liver Disease Patients. *J Clin Gastroenterol* 2010;44:40-45.
7. Seeff LB, Curto TM, Szabo G, et al. Herbal product use by persons enrolled in the hepatitis C antiviral long-term treatment against cirrhosis trial. *Hepatology* 2008;47:605-612.
8. Zhang L, Wang G, Hou W, et al. Contemporary clinical research of traditional Chinese medicines for chronic hepatitis B in China: an analytical review. *Hepatology* 2010;51:690-698.
9. Gamsizkan Z, Yücel A, Kartal M. Using of herbal product. *Journal of Clinical and Analytical Medicine* 2012;3:300-302.
10. Schaefer M, Capuron L, Friebe A, et al. Hepatitis C infection, antiviral treatment and mental health: a European expert consensus statement. *J Hepatol* 2012;57:1379-1390.
11. Bardia A, Nisly NL, Zimmerman MB, et al. Use of herbs among adults based on evidence-based indications: findings from the National Health Interview Survey. *Mayo Clin Proc* 2007;82:561-566.
12. Kennedy J. Herb and supplement use in the US Population. *Clin Therap* 2005;27:1847-1858.
13. Meisel C, Johne A, Roots I. Fatal intracerebral mass bleeding associated with *G. biloba* and ibuprofen. *Atherosclerosis* 2003;167:367.