

Case Report:

Effect of Bee Stings on the Viral Clearance in Chronic Hepatitis-C Virus

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Abstract

A 47 year old male patient suffered from chronic hepatitis C virus (CHC) infection since 1999 came to Bee Venom Research Center (BVR) at El-Arish City in June 2006 asking to be one of volunteers in Bee Venom Therapy (BVT) courses. He was treated with traditional interferon (IFN) and ribavirin (RBV) for 12 months since May 2000 to May 2001. After completion of his treatment course, quantitative Polymerase chain reaction (PCR) for Hepatitis C virus Ribonucleic acid (HCV-RNA) was done and the result was negative. In June, quantitative PCR for HCV-RNA was repeated and the result was positive. He was involved in BVT course for three months starting from July 2006 to the end of September 2006. At the end of BVT course quantitative PCR for HCV-RNA was done and the result was negative. Since September 2006 until now repeated quantitative PCR for HCV-RNA were negative.

Key Words: Chronic HCV infection – Bee venom – HCV-RNA.

Introduction

APPROXIMATELY 200 million people are chronically infected with hepatitis C (HCV). Infection with HCV is curable by therapy, with the current standard treatment based on the combination of Pegylated interferon- α (pegIFN- α 2a) and RBV [1]. Egypt has the largest epidemic of HCV in the world, about 14.7% of the current population in Egypt had been infected with this virus, and 9.8% continue to have HCV-RNA. The issue of treatment for those that develop HCV related liver disease is essentially a medical care crisis for the country [2].

HCV infection is curable by therapy. Cure of infection is characterized by the sustained virological response (SVR), defined as undetectable HCV-RNA in peripheral blood by means of sensitive

molecular biology-based techniques. Treatment of chronic hepatitis C based on the combination of a pegIFN- α 2a and RBV. This combination cures approximately 80% of infections in patients infected with HCV genotypes 2 or 3, but only 40%-50% in patients infected with genotypes 1 or 4 [3].

Many patients try conventional medicine and herbal medicine all over the world particularly in poor countries [4].

The appearance of wide ranges of conventional/traditional mode of therapies appeared in our community is due to the great demand and pressure of the population to find out an acceptable treatment for the CHC.

Case presentation:

In June 2006, a 47 year old male patient was diagnosed to be a CHC. The patient came to BVR center at El-Arish City asking to be one of volunteers in BVT courses. His story with the disease was started by nonspecific complaints as indigestion, flatulence and right hypochondrial pain in 1999. His treating doctor ordered for HCV antibodies (HCV Ab) test that was positive then followed by quantitative PCR for HCV-RNA which was positive too. He was treated by regular IFN and RBV for 12 months starting from May 2000 to May 2001 and achieved SVR until December 2001. In June 2002,

Abbreviations:

| | |
|---------|---------------------------------------|
| BV | : Bee venom. |
| BVT | : Bee venom therapy. |
| CHC | : Chronic HCV infection. |
| HCV Ab | : HCV antibodies. |
| HCV | : hepatitis C. |
| HCV-RNA | : Hepatitis C virus Ribonucleic acid. |
| IFN | : Interferon. |
| RBV | : Ribavirin. |
| SVR | : Sustained virological response. |

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quantitative PCR for HCV-RNA was repeated and it returned positive (Table 1). Since the former date he was under symptomatic treatment only until he heard about the BVR center and came to BVR center. He was involved in BVT course for 6 months with a 3 months intervals starting from 26th of July 2006 and he was followed-up until the end of 2013:

The following was done for him:

- Detailed medical history.
- Full clinical examination.
- Skin test to prove that the patient isn't allergic to bee venom.
- Venom sting program which extended for 6 months [5]:

1st week: One sting between the two scapulae alternating daily with one sting at the level of L5 toward its end.

2nd week: Two stings daily on the back at the level of the 12th rib toward its end.

3rd week (Until the end of the 6th month): One sting between the two scapulae alternating daily with one sting at the level of L5 and two stings on the back at the level of the 12th rib.

Two Doctors in the BVT Research Center apply the bee sting program for the patients under supervision of the center's executive director. The service at the BVT Research Center is free charged.

During BVT courses repeated quantitative PCR for HCV-RNA was done and all the results were negative (Table 2).

Table (1): Viral load of the patient during IFN and RBV course.

| Dates of PCR for HCV-RNA | Viral load |
|--------------------------|---------------------------|
| 20/11/1999 | Positive (0.17 MEq/ml) |
| 7/11/2000 | Negative |
| 25/3/2001 | Negative (<0.2 MEq/ml) |
| 6/6/2001 | Negative (<600 Iu/ml) |
| 27/12/2001 | Negative (<2500 copy/ml) |
| 26/6/2002 | Positive (2800 copies/ml) |

Table (2): Viral load of the patient during BVT course.

| Dates of PCR for HCV-RNA | Viral load | ALT | AST |
|--------------------------|-----------------------|-----|-----|
| 12/9/2006 | Negative (<100 Iu/mL) | 24 | 29 |
| 14/12/2006 | Negative (<100 Iu/mL) | 30 | 39 |
| 6/11/2007 | Negative (<100 Iu/mL) | 23 | 40 |
| 5/4/2009 | Negative (<100 Iu/mL) | 10 | 11 |
| 22/6/2010 | Negative (<100 Iu/mL) | 25 | 27 |
| 4/11/2011 | Negative (<100 Iu/mL) | 52 | 40 |
| 15/3/2012 | Negative (<100 Iu/mL) | 18 | 12 |
| 31/12/2013 | Negative (<15 Iu/ml) | 30 | 22 |

Discussion

Hepatitis C virus (HCV) infection represents a major public health problem, with more than 170 million people infected worldwide [2]. El-Zanaty and Way, reported that Egypt has the largest epidemic of HCV in the world. Their results suggested that about 14.7% of the current population in Egypt had been infected with this virus and 9.8% continue to have HCV-RNA [6].

Current standard treatment of CHC consists of the combination of pegIFN- a2a and RBV, administered for 24-72 weeks. However, only 40%-50% of individuals infected with HCV genotypes 1 or 4 obtain a SVR compared with 80% of patients infected with genotypes 2 or 3 who obtain SVR. Moreover, pegIFN- a2a and RBV therapy is often associated with important adverse effects such as depression and anemia [7].

As pegylated interferon is expensive, standard interferon is still the main therapy for HCV treatment in underdeveloped countries. On the other hand, studies showed that pegIFN- a2a and RBV therapy had severe side effects like hematological complications. Herbal medicines (laccase, proanthocyanidin, Rhodiolakirilowii) are also being in use as a natural and alternative way for treatment of HCV [8].

Many patients try conventional medicine and herbal medicine all over the world particularly in poor countries. Laccase are largely used as herbal medicine that is extracted from oyster mushroom (*Pleurotus ostreatus*). Studies showed that laccase is proficient in inhibiting the HCV replication rate [4]; however the mechanism of action of this medicine is not known.

As Hepatitis C virus infects the liver and this infection requires two or more decades to extend into substantial disease, a nutritional supplement might facilitate to decrease or stop disease development [9]. More recent studies regarding herbal treatment provoked a hope for HCV patient that is based on a chemical known as proanthocyanidin, extracted from blueberry leaves. It had been reported that proanthocyanidin can stop HCV replication in infected patients [9]. According to another study rhizomes of the Chinese medicinal herb *Rhodiolakirilowii* may also act as possible inhibitor of HCV [10]. Many patients try herbal medicine and conventional medicine all over the world particularly in poor countries.

BV is a unique weapon in the animal kingdom. BV apparatus has a prime role of defense to the

bee colony. BV is an efficient and complex mixture of substances designed to protect bees against a broad diversity of predators from other arthropods to vertebrates. BV from the venom gland located in the abdominal cavity contains several biologically active peptides, including melittin (a major component of BV), apamin, adolapin, mast cell degranulating peptide and enzymes (phospholipase A2 (PLA2), and hyaluronidase) as well as non-peptide components, such as histamine, dopamine and norepinephrine [11].

The therapeutic application of BV has been used in traditional medicine to treat diseases, such as arthritis, rheumatism, pain, cancerous tumors, and skin diseases. BV has been reported to have anti-arthritis effects in several arthritis models. Melittin, a major peptide component of BV, has anti-inflammatory and anti-arthritis properties, and its inhibitory activity on nuclear factor kappa (NF- κ B) may be essential for the effects of BV [12].

Measuring the rate of viral clearance from serum is helpful in predicting the likelihood of a response to therapy, for determining the optimal duration of therapy and as a stopping rule for patients with CHC. Accordingly, there has been intense interest in tailoring treatment regimens for individual patients using viral kinetics [13].

In 2009 a study evaluated the antiviral activity of honey bee venom on West Nile virus (RNA virus model); they found that virus infectivity titer showed non-significant change in case of evaluation of bee venom treated and non-treated virus [14].

This agrees with the results of a study conducted in 2009. They studied a three groups of patients (Group 1 included patients treated with bee stings (n=28), group 2 included patients treated with interferon (n=5) and group 3 included patients treated with conventional liver support drugs and bee stings (n=7), no patient reached the sustained viral response (for example, negative PCR results or below the detectable level) and the viral load showed no significant difference between the three groups [5].

In contrary to the results of the previous 2 studies, Abdel-Sabour and Hegazi, applied an integrated natural therapeutic approach on a sixteen patients aged from 30 to 55 years suffering from liver dysfunction with variable causes: Two patients positive for hepatitis B virus (HBV) (one also schistosemiasis positive), 8 HCV positive patients (four schistosemiasis positive) and 4 patients suffering from schistosemiasis only. The remaining

two patients had no definite detectable causes. All patients were subjected to full clinical examination, dental examination, abdominal sonography, laboratory assessment including: albumin, prothrombin concentration, gamma glutamyl transferase, alanine transaminase, aspartate transaminase, alpha-fetoprotein, complete blood count, anti-schistosomal antibody, viral markers and lastly quantitative PCR for positive marker cases. The main outlines of therapy included: Dental cleanse, bowel cleanse with diet regulations, colon cleanse, parasitic cleanse, blood and liver cleanse, bioelectric therapy and Apitherapy. The course of treatment was 6 months and more 6 months for follow-up. Symptoms of liver dysfunction as fatigue, apathy, digestive disorders improved markedly even ascites and lower limb edema. Also, laboratory liver functions returns to normal limits without reversal during the follow up period. The 2 patients who were positive for HBV recovered completely (PCR negative). Hepatitis C (8 cases) patients, 5 of them recovered completely (negative PCR), while other 3 cases (combined HCV and schistosemiasis) showed decrease in viral load [15].

In a study done by Badr et al., only one patient became avireamic (1/9, 11.1%) at the end of the BVT. The only responder patient had a low baseline viral load was (2000IU/ml) and responded to treatment at week 36 [16].

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