Normalization Of Liver Enzyme Levels In A Patient With Chronic Hepatitis C Virus Infection Treated By Ribavirin Placed Into The Field Of Unusual Properties Of Low Level Laser Radiation: Case Report And Review Of Literature.

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Citation

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Abstract

Chronic hepatitis C is a major cause of chronic liver disease globally, and the natural history of progression may lead to cirrhosis with liver failure, hepatocellular carcinoma, and premature liver-related death. We present the case of a 24-year-old Asian man with chronic hepatitis C virus infection 1 genotype treated by ribavirin placed into the field formed by low level laser radiation and transmitted through the light-guide. The administrated therapy resulted in stabilization of the pathological processes accompanied by the normalization of serum alanine-aminotransaminase and gamma-glutamyltransferase levels, improvement of patient's condition and his quality of life. No side effects in applying the aforementioned method were observed.

INTRODUCTION

The current treatment of chronic hepatitis C (HCV) is peginterferon alfa-2a or alfa-2b plus ribavirin, which had a sustained virological response after 48 weeks of combination therapy in pivotal trials in approximately 42% to 52% of patients with a genotype 1 infection[1-3]. The primary goal of treatment of chronic HCV is to prevent late liver-related morbidity and mortality; however treatment of HCV has traditionally been difficult because of high rates of treatment discontinuation due to the side effects of pegintereferon therapy[4]. Ribavirin is an oral nucleoside analog, which is well tolerated and appears to decrease HCV infectivity in a dose-dependent manner, but its mode of action is not completely understood[5]. Monotherapy with ribavirin is associated with an end-of-treatment biochemical response and improvement in histology, which result in normalization or near normalization of serum aminotransferase levels, but it is ineffective in eliminating HCV RNA[6,7]. In this paper, we present a case of chronic HCV infection treated by ribavirin, placed into the field formed by low-level laser radiation transmitted through the light-guide, that has resulted in long-lasting normalization of serum aminotransferase levels. To the best of our knowledge, this is the first case report of treatment of a patient with chronic HCV infection by this method.

CASE REPORT

In September 2005, a 24-year-old, single Asian man, BMI-17.9, presented to the Outpatient Department of the Institute of Virology with complaints of lethargy, fatigue, periodical pain in the epigastrium, nausea and heartburn. His medical history included a single blood transfusion episode in his early childhood and the surgical intervention caused by a foot wound in 2001. In January 2005, the patient started complaining of the aforementioned symptoms, and the examination found a high level of alanine aminotransferase (ALT). The patient tested positive for HCV RNA (qualitative). In March 2005, the therapy with pegylated interferon alfa (PEG-INF) and ribavirin was started. The drugs were administered according to the standard protocol. However, due to complaints of weakness so severe he couldn't serve himself, headache and 6 kg weight loss associated with the treatment, the patient refused further therapy after one month and till September 2005 did not receive any treatment. The ALT level remained high during this period of time. At the time of his first visit, the physical examination revealed enlargement of the liver by 2.5 cm; however, his vital signs were normal. Investigations revealed the patient was positive for HCVAb, which were detected using the first-generation enzyme-linked immune-sorbent assay (ELISA); HBs Ag, HDVAb, HIVAb were negative.

Quantitative plasma HCV RNA assay was detected by polymerase chain reaction (PCR) in real time (product of Interlab-Service, the Institute for Epidemiology, Moscow, Russia). (All investigations were carried out in the Reference laboratory of the Health Ministry, Tashkent, Uzbekistan). ALT level was 227 IU/L (5.4ULN-upper limit of norm), gamma-glutamiltransferase (GGT) level was 80 IU/L (1.6ULN). The results of thyroid function tests (serum T3, T4 and TTG) were normal. Results of serum Fe and alpha-fetoprotein tests were normal. The patient refused a liver biopsy for disease confirmation. The patient was offered to begin therapy with ribavirin, which would be put into a "device for remote transfer of information from medicine to patient's body"[8].The detailed explanation of the nature of the exposure was given to the patient, who signed informed consent to participate in the study. The Ethics Committee of Health Ministry of Republic Uzbekistan has approved our investigation.

The treatment began on 11.09.2005. Having reviewed the available literature, we decided to pioneer the protocol of application of ribavirin placed into "the device for remote transfer of information from medicine to patient's body" to be applied once a day for a period of 10 days. Such a protocol, in our opinion, provides the least exposure and allows us to carefully trace the patient's condition during the course of therapy. The table below demonstrates some laboratory tests results.

Figure 1

Table. Some Laboratory Test Results: Baseline and on the Stages of Therapy.

	15.01.2005	21.05.2005	Pre-treatment baseline	Treatment 8 weeks	Treatment 12 weeks	Treatment 18 weeks
WBC (10^9/l)		6,2			4	5
HGB(g/l)		134			130	156
RBC(10^{12}/l)		4,5			4,2	5
HCT(%)						
ESR(mm/h)		4			10	6
Lymph(%)		32	38		47	39
ALP(IU/L)		186.8	89	229,2	197,1	238,5
ALT (IU/L)	203.8	386	227	21,7	49,9	463
AST(IU/L)	100	268	121	63,8	34,4	266
GGT(IU/L		115.9	80	77,8	33,4	63.2
Albumen(g/l)		41	41	44	39	40
Total bilirubin (mmol/l)	14,6	10,2	15,9	25,5	19,6	14,5
HBsAg		NEG				
HIV Ab		NEG				
HBC RNA PCR (copies/ml)	POS	POS	$5.6 \cdot 10^2$			

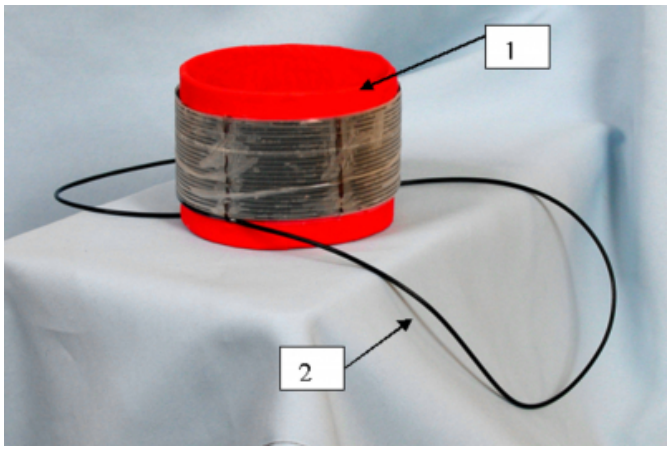
Figure 2

	Treatment 40 weeks	Treatment 74 weeks	Follow up 2y.11m.	Follow up 3y.11m.	Treatment 4y.5 m	Follow up 5y 3m	Follow up 6y
WBC (10^9/l)	4,5	5,5		5	5,9	6,2	5,8
HGB(g/l)	150	145		137	140	145	146
RBC(10^{12}/l)	4	4,5		4,3	4,4	4,6	4,4
HCT(%)				43,4	43,5	45,4	43,3
ESR(mm/h)	7	10		2	6	11	10
Lymph(%)	34	39		56,4	44,4	42	37,4
ALP(IU/L)	106,7	115,3	432	327	99	95	99
ALT (IU/L)	102,1	62,5	38	23	52	64	47
AST(IU/L)	66,5	39,6	40	24	52	40	28
GGT(IU/L	28	25,2	22	18	35	25	23
Albumen(g/l)	40	40,1	42	46	46	52	50
Total bilirubin (mmol/l)	25,2	20,5	11,5	19,7	13,6	18,5	12,7
HBsAg							
HIV Ab							
HBC RNA PCR (copies/ml)	NEG		NEG	$1.8 \cdot 10^3$	$3.4 \cdot 10^3$		$3.9 \cdot 10^4$

The patient therapy included the following stages: first we examined our patient with traditional methods. Then the patient was examined with electro-acupuncture diagnosis according to Voll (EAV) to determine the functional status of organs and body systems, as well as to scrutinize meridians, where we detected the presence of the hepatitis C virus[9]. To identify the virus we used the nozod of hepatitis C virus[10]. In the next stage we made the decision on administration of the actual therapy, i.e. which organs and in what sequence they would be treated. After that, he laid down on a couch in supine position. Ribavirin was placed into the internal space of the cylinder, which was positioned on the patient's body over the area of the sick organ projection or above the pathological focus. Then the cylinder was closed with a cover, and the laser device was switched on. The duration of the procedure ranged from 5 to 25 minutes. After the procedure was completed, the laser device was disconnected and, 4-5 minutes later, the device was ready again to repeat the exposure. The patient did not sense when the device was switched on or off and was not given any notice about it. Fig.1 shows the device applied in our patient's therapy. It includes the hollow cylinder made from non-conductive material (in our case, dense cardboard) around the outer surface of which runs a spiral of light-conducting fiber connected to the light source. As a light source, we used a red low-level laser with wavelength ? = 650 nm and with power P= 15 mW (Fig.2). The efficiency of the therapy was estimated by ALT and GGT enzymes, evaluated during the course of the therapy. HCV RNA detection was performed at the screening visit and then at the different stages of therapy. Safety assessments included physical examination, recording the adverse events, and chemical and hematological tests.

Figure 3

Figure.1. The device for therapy of patients includes



1- the hollow cylinder made from non-conductive substance

2- a spiral of light-conducting fiber connected to the light source

Figure 4

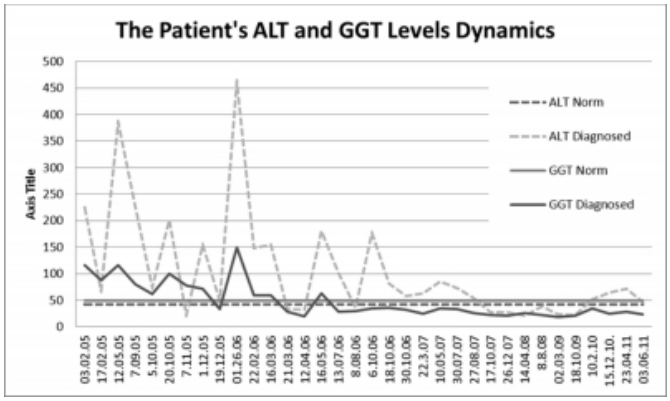
Figure.2. Light source – the red low-level laser named "Sogdiana"

During the course of therapy (September 2005 - October 2011) the patient was exposed to the above described procedure 47 times; that is equivalent to 47 days of administration of ribavirin according to the routine (oral) practice of its application. This scheme of management is explained by several intervals in the course of therapy when we needed to observe the patient's condition and during the pauses in the treatment that occurred when, according to laboratory tests, we observed remission in our patient's condition. Vitamins B, C, and E were also prescribed to the patient; no other therapy was used.

On the patient's first visit, the presence of hepatitis C virus, as revealed by EAV, was noted on the following meridians: the gall bladder, spleen-pancreas, liver, pericardium meridian and the lymphoid meridian (Voll). Accordingly, we focused the therapy on the following organs: the liver, spleen, and chest lymphatic channel. Therapy was carried out according to the scheme described above. At the following visit, according to EAV data, the procedure was carried out on the following organs: the liver, gall bladder and bone marrow. Thus, at each subsequent visit of the patient, we selected the organs and body systems to be exposed to the effect of ribavirin, placed into the "device for remote transfer information from medicine into the patient's body." On the whole, during the course of therapy the following organs and body systems were treated: the liver, gall bladder and hepatic ducts, spleen, pancreas, chest lymphatic channel, small intestine, kidneys, and bone marrow. The table shows that application of ribavirin in the presented technology does not affect blood indices while it is known that the main adverse effect of ribavirin is hematologic complication. A single side effect of our exposure was development of insignificant weakness observed for 24 hours after the procedure, which resolved independently without any special therapy for our patient.

Figure 5

Figure 3. The Dynamics of ALT and GGT Levels in our Patient on Baseline and on the Stage of Therapy.



The diagram depicts the dynamics of ALT and GGT levels in our patient. The first signs of ALT level normalization were observed in week 12 of the therapy. In week 18, some exacerbation of the activity of pathological processes was observed as the ALT levels raised to 42ULN, though the enzyme level dropped to normal values in week 24 of therapy. Later on, there were two ALT level rises to 4.2 ULN, each followed by a drop to normal values by August

2007 (in two years after the therapy start). From August 2007 till February 2010 the ALT level was within the normal values. During this period, the patient presented no complaints and received no therapy. In February 2010, the patient showed an increase in ALT level to 1.7ULN, which normalized after a single exposure by the device with ribavirin placed inside it. Due to the therapy, the GGT level for the first time returned to normal values in therapy week 12. Later on, a small rise of GGT level to 1.3ULN occurred, which coincided with the next exacerbation of the pathological process and the ALT level rise to 4.2ULN in therapy week 32. However, since then no other increase in enzyme level has been observed in our patient. The virus load dynamics in the patient's blood also have changed because of therapy. For instance, the initial low virus load reached undetectable levels by 13.07.2006 (therapy week 40) and later the virus was undetected in the patient's blood till 20.01.2009 (3 years and 4 months of observation). Against the background of complaints of pyrosis, decreased appetite, and slight weakness presented in January 2009, the virus was registered in the patient's blood again. However, the ALT and GGT levels remained within the normal values. The therapy with ribavirin placed in the device started again, and by 10.02.2011 the virus load in the patient's blood had decreased by half; however, the ALT level was slightly raised to 1.7ULN, but later on returned to normal. Up to the present, our patient has no complaints and adheres to a healthy lifestyle. The patient is still under the physician's observation.

DISCUSSION

Assessment of the disease severity of patients with chronic HCV infection includes evaluation of ALT and GGT levels as markers of liver inflammation. ALT is concentrated in the liver tissue and, as a predominantly cytosolic enzyme, leaks readily into circulation upon hepatocellular injury. Consequently, serum ALT is widely used in monitoring patients with chronic hepatitis C[11]. Fluctuations of serum ALT activity in an individual with chronic hepatitis C, even within the normal range, are generally indicative of disease activity. Patients who subsequently develop ALT "flares" have greater histological damage at baseline, and, in general, accelerated fibrosis progression and more severe liver histological activity.[12,13] The study of the ALT decay dynamics under high-dose daily IFN treatment of HCV indicates that there is a clear association between the kinetics of viral load decay and the kinetics of ALT decay[14]. Cancer genesis processes are also known to be more expressed in patients with chronic viral hepatitis C, while long-lasting increase of ALT level promotes faster development of liver cancer[15]. A low or normal level of ALT is a guarantee of the decrease of frequency of HCV complications, in particular hepatocellular carcinoma[16]. GGT determination has lesser importance in patients with HCV. However, in diseases of the liver and bile-excreting passages, GGT hyperactivity in patients' sera is invariably found that necessitates monitoring in order to control antivirus therapies.

Electro-acupuncture diagnosis according to Voll (EAV), which is based on the examination of the electrical conductivity of acupuncture points on the skin surface, is considered to be the method of evaluation of the functional status of the organs and body systems[9]. According to Traditional Chinese Medicine Theory, acupuncture points are located along meridians (connected points across the anatomy structures, which relate to a specific organ or other part of the body)[17]. Nozodes, which are used in EAV to make an ethological diagnosis, are the homoeopathic medicines extracted from sterilized pathogenic substances, secretions and destroyed germs. Many nozodes come from pathogenic products, vaccines, bacteria and viruses[10]. A lot of research has shown a high correlation between the EAV findings and those obtained by traditional diagnostic methods[18,19]. The data about the presence of HCV in different organs and systems in our patient's body collected by us during the EAV coincide with the literature data about the extra-hepatic replication of HCV.[20,22] However, the attitude to EAV in various parts of the world is different. For instance, in Russia the EAV method is officially allowed in medical practice, whereas the U.S. Food and Drug Administration does not recognize Voll's method as a diagnostic one.[23,24]

In the recent decade, low-level laser (LLL) therapy has been used widely. Throughout the world, LLL is used to treat various diseases accompanied by painful syndromes: back pain, carpal tunnel syndrome, arthritis pain, fibromyalgia and other injuries[25]. The recent literature has given some information about new and still poorly understood LLL radiation properties. The first data on discovery of a non-physical component of LLL radiation, regarding its effect on some characteristics of pure water (the value of specific conductance) were given in the reports of Kvartalnov V and Anosow V.[26,27] As the result of 40 years of research conducted in the Novosibirsk Medical Institute and the

Institute of Clinical Experimental Medicine of the Russian Academy of Medical Sciences, a light-guided laser device has been designed, i.e. the source of the non-physical component of LLL radiation[28]. The light source in this device is a low-level helium-neon red laser[8]. According to the description, "the device for remote transfer of information from medication to human body" contains a medication and a hollow closed cylinder from electrically non-conductive material with a cover. On its outer surface and around the cylinder a light-guide connected to a light source is wound in a spiral. The medication is placed inside the cylinder. The authors of the device suggest placing the cylinder on the patient's body above the ill organ or the pathological focus. The researchers studied properties of the device both in vitro as well and in vivo [29]. To decrease sugar levels in the blood of patients with diabetes mellitus type 2, the scientists conducted the following investigations: the information from insulin was transferred onto the patient's liver projection, which resulted in a decrease of sugar level in the patient's blood. When studying the possibility of heart rhythm restoration in patients with rhythm disorders, the information from an adrenaline solution was transferred onto the projection of the patient's heart. To assess the effect, the ECG was analyzed before and after exposure, and the R-R interval and reliability of its changes were determined. The value of the parameter was used as the control of a response to the remote effects of adrenaline. The experiment results showed a reliable decrease in R-R interval that according to the researchers, confirms the rendered effect of remote transfer of the information from adrenaline to a human body.

In our research, we did not change the scheme offered by the Russian scientists and also used the cylinder inside which ribavirin was placed. According to the data obtained by the Russian scientists, when the spiral light-guide is twisted from the right to the left, the effect of strengthening mitosis in the cells exposed to the unusual properties of laser radiation was observed, whereas the light-guide spiral twisting from the left to the right leads to strengthening of synthesis of protein and carbohydrates[28]. In view of the data obtained by the Russian scientists, we used the device with the lévogyre light-guide.

In the onset of the disease, our patient was treated according to the traditional scheme of CHCV therapy. However, due to the expressed side effects, he refused further treatment. Since the patient had long-stable hyperenzymemia, he was offered the choice to begin therapy with ribavirin, though not applied in the orally, as is traditional, but using the device for transferring the properties of medical products. This therapy has led to long and stable normalization of hepatic enzymes ALT and GGT and thus, in our opinion, has shown the produced effect of remote transfer of the information from ribavirin to the patient's body. The advantages of this effect are in its safety, the absence of adverse effects, and the affordability of the therapy. Uzbekistan has high rates of chronic hepatitis C, therefore, these facts are of a special value.[30.] CHCV infection cannot be successfully treated without the use of antiviral drugs and, consequently, the method of usage of antiviral drugs described by us, in our opinion, considerably expands the possibilities of antiviral therapies.

CONCLUSION

Thus, our research has demonstrated that pharmaceutical properties of ribavirin were remotely transferred into the patient's body using "the device for remote transfer of information from medicine to patient's body." Application of the developed method of exposure has led to normalization of ALT and GGT levels, improved patient's quality of life and, thus, contributed to prevention of development of severe complications of chronic hepatitis C virus infection in our patient.

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