

Preliminary Results of Ozone Therapy as a Possible Treatment for Patients with Chronic Hepatitis C

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Abstract:

Background: Medical ozone is more bactericidal, fungicidal, and virucidal than any other natural substance. Some studies proved that ozone infused into donated blood samples can kill viruses 100% of the time. Ozone, because of its special biologic properties, has theoretical and practical attributes to make it a potent hepatitis C virus (HCV) inactivator, which suggests an important role in the therapy for hepatitis C.

Aim: The study aim is to evaluate the role of ozone therapy in decreasing HCV ribonucleic acid (HCV RNA) load and its effect on the liver enzymes among patients with chronic hepatitis C.

Methods: This study included 52 patients with chronic hepatitis C (positive polymerase chain reaction [PCR] for HCV RNA and raised serum alanine transaminase [ALT] for more than 6 months). All patients were subjected to meticulous history taking and clinical examination. Complete blood count, liver function tests, and abdominal ultrasonography were requested for all patients. The ozone group included 40 patients who received major autohemotherapy, minor autohemotherapy, and rectal ozone insufflation. The other 12 patients (conventional group) received silymarin and/or multivitamins.

Results: There were significant improvements of most of the presenting symptoms of the patients in the ozone group in comparison to the conventional group. ALT and aspartate transaminase (AST) levels normalized in 57.5% and 60% in the ozone group, respectively, in comparison to 16.7% and 8% in the conventional group, respectively. Polymerase chain reaction (PCR) for HCV RNA was negative among 25% and 44.4% after 30 and 60 sessions of ozone therapy, respectively, in comparison to 8% among the conventional group.

Conclusions: Ozone therapy significantly improves the clinical symptoms associated with chronic hepatitis C and is associated with normalized ALT and AST levels among a significant number of patients. Ozone therapy is associated with disappearance of HCV RNA from the serum (-ve PCR for HCV RNA) in 25%–45% of patients with chronic hepatitis C.

Introduction

MEDICAL OZONE is more bactericidal, fungicidal, and virucidal than any other natural substance, including hydrogen peroxide. In fact, studies proved that ozone infused into donated blood samples can kill viruses 100% of the time. It does not do damage to healthy cells.^{1,2} On the basis of oxidative destruction of ozone upon bacteria, viruses, and fungi, it is ideal for treating infected wounds, intestinal infections, vaginal infection, and topical skin diseases caused by fungus.³ Low-concentration ozone treatments (5–40 $\mu\text{g}/\text{mL}$) are used to stimulate the immune system and increase the antioxidant

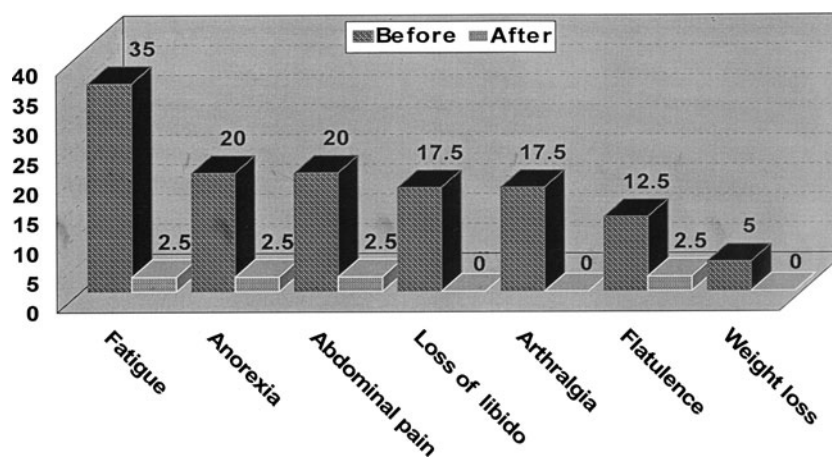
enzymes in the body.^{4,5} Higher concentration ozone (40–100 $\mu\text{g}/\text{mL}$) is a powerful germicidal substance.^{3,5} Some viruses are much more susceptible to ozone's action than others. It has been found that lipid-enveloped viruses are the most sensitive.⁶ The possible mechanisms of antiviral action of ozone are denaturation of virions through direct contact with ozone, peplomer alteration, lipid and protein peroxide formation,⁵ activation of humoral and cell-mediated immunity, host-specific autovaccine creation,⁷ and anti-oxidant enzymes enhancement.⁸

The aim of this study is to evaluate the possible role of ozone therapy in treatment of patients with chronic hepatitis C.

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FIG. 1. Clinical symptoms of patients with chronic hepatitis C before and after ozone therapy.



Patients and Methods

Study design

A prospective case-control design was used.

Setting

The patients were selected from those attending the outpatient clinic of the hepatitis viruses and ozone unit, Department of Tropical Medicine and Gastroenterology, Assiut University Hospital.

Inclusion criteria

The inclusion criteria for the study were the following:

1. Positive hepatitis C virus antibody (HCV-Ab).
2. Raised serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) for more than 6 months.
3. Positive polymerase chain reaction (PCR) for HCV RNA.

Exclusion criteria

The exclusion criteria for the study were the following:

1. Positive hepatitis B surface antigen.
2. Liver cirrhosis and/or hepatocellular carcinoma.
3. Glucose-6-phosphate dehydrogenase deficiency.
4. Thyrotoxicosis.

Patient groups

Ozone group. This group included 40 patients who received major autohemotherapy, minor autohemotherapy, and rectal ozone insufflation.

1. Major autohemotherapy: 150 mL of blood were withdrawn from the patient, mixed with a dose of ozone/oxygen mixture of a predetermined concentration, and then returned via the same intravenous catheter 3 times weekly. The concentration was initially 25% and gradually elevated every five sessions by 5% until the maximum concentration of 60% was reached with the volume fixed at 125 mL.⁹
2. Rectal ozone insufflation: After a rectal enema, a catheter is inserted into the colon and gas from the ozone machine is gradually introduced, using a concentration of 40% and a volume of 300 mL given at the first session only.¹⁰
3. Minor autohemotherapy: 10 mL of an ozone/oxygen mixture with a concentration of 20 $\mu\text{g}/\text{mL}$ is added to 3–5 mL of the patient's own blood and after thorough mixing and shaking, is re-injected intramuscularly.¹⁰ It was given at the first session only.

Control group (conventional group). This group included 12 patients who received silymarin and/or multivitamins.

FIG. 2. Clinical symptoms of patients with chronic hepatitis C before and after conventional treatment.

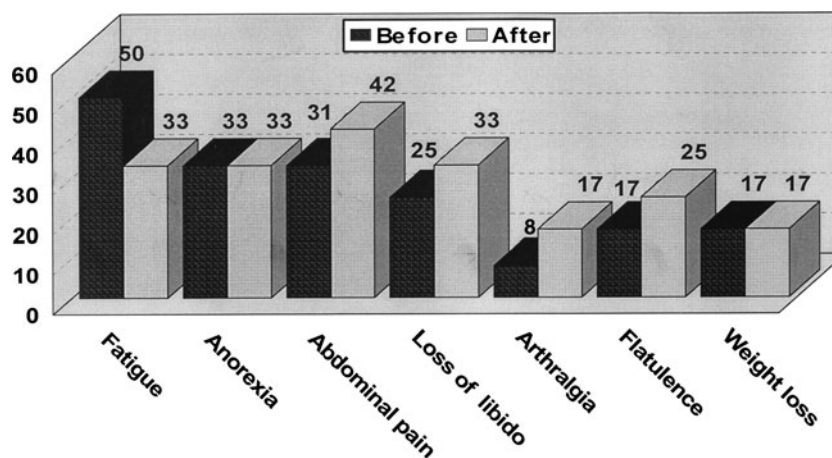


TABLE 1. CHANGES IN ALANINE TRANSAMINASE (ALT) LEVEL IN PATIENTS WITH HEPATITIS C VIRUS BEFORE AND AFTER OZONE OR CONVENTIONAL THERAPY

ALT level	Ozone group (n = 40)			Conventional group (n = 12)			p-Value
	Before	After		Before	After		
		Normal (n = 23)	Raised (n = 17)		Normal (n = 2)	Raised (n = 10)	
< Double the normal	20	15 (75%)	5 (25%)	5	1 (20%)	4 (80%)	0.040
> Double the normal	20	8 (40%)	12 (60%)	7	1 (14%)	6 (86%)	0.224
Total	40	23 (57.5%)	17 (42.5%)	12	2 (16.7%)	10 (83.3%)	

All patients were subjected to the following:

1. History taking and clinical examination.
2. Abdominal ultrasonography monthly.
3. Complete blood count, and liver function tests monthly.
4. Quantitative PCR for HCV RNA before the start of treatment, after 30 sessions and after 60 sessions of ozone therapy.
5. Quantitative PCR for HCV RNA before the start after 10 weeks and 20 weeks of treatment for the control group (the same schedule as the ozone group).

HCV RNA detection and quantitation was performed using COBAS AMPLICOR HCV monitor test version 2 described by Michael and Alexandra.¹¹ HCV viremia of $0.6-100 \times 10^3$ is considered low, $100-800 \times 10^3$ is considered moderate, and more than 800×10^3 is considered high.¹¹

Statistical analysis was done using mean and standard deviation. Student's *t* test is used for comparison between groups. *P* value < 0.5 is considered significant.

Results

Ozone therapy was evaluated in 40 patients diagnosed to have chronic HCV infection; they were given ozone for 30 sessions and 18 (45%) of them had 60 sessions of ozone therapy. In addition, 12 patients on conventional treatment for 5 months were taken as a control group.

Following 30 sessions of ozone therapy, there was significant improvement of most of the presenting symptoms in comparison to those who received conventional therapy ($p < 0.5$) as shown in Figures 1 and 2. The levels of ALT and AST normalized in 57.5% and 60%, respectively, following ozone therapy in comparison to 16.7% and 8%, respectively, after conventional therapy with a significant difference (Tables 1 and 2). Following 30 sessions of ozone therapy, 10 of 40 patients (25%) showed negative PCR for HCV RNA

with a significant difference ($p = 0.001$), while 1 patient (8.3%) in the conventional group became negative PCR for HCV RNA; however, the difference is not statistically significant ($p = 0.331$; Tables 3 and 4). On the other hand, among 18 patients who are still positive after 30 sessions of ozone therapy, 8 (44.4%) became negative PCR for HCV RNA while 1 patient in the conventional group is still negative, and the difference is significant ($p = 0.040$; Table 5). For confirmation of the safety of ozone therapy, evaluation of the blood count monthly revealed no changes in the various blood elements and no evidence of hemolysis with no significant changes in the bilirubin levels before and after ozone therapy.

Discussion

Hepatitis C (HCV) is a global disease with an expanding incidence and prevalence base of massive public health importance. It represents a supremely challenging problem in view of its adaptability and its pathogenic capacity. The unique strategies that HCV utilizes to parasitize its host make it a formidable enemy, and therapeutic interventions need considerable honing to counter its progress. The natural history of HCV infection is still largely unclear, and the current treatment options for patients are limited. Chronic infection can lead to liver cirrhosis, hepatocellular carcinoma, and death. There is no vaccine for HCV, and the only available treatment, a combination of α -interferon and ribavirin, is effective in only a minority of patients,¹² with an eradication rate and long-term disease remission in approximately 40% of patients. This treatment is required for 24 or 48 weeks and requires parenteral therapy, is costly, and has frequent side-effects. Thus, the benefits and risks of therapy should be weighed carefully in each patient.¹³

Standard interferons have been chemically modified using polyethylglycerol to improve antiviral efficacy. Higher

TABLE 2. CHANGES IN ASPARTATE TRANSAMINASE (AST) LEVEL IN 40 PATIENTS WITH HEPATITIS C VIRUS BEFORE AND AFTER 30 SESSIONS OF OZONE THERAPY

AST level	Ozone group (n = 40)			Conventional group (n = 12)			p-Value
	Before	After		Before	After		
		Normal (n = 24)	Raised (n = 16)		Normal (n = 1)	Raised (n = 11)	
< Double the normal	20	16 (80%)	4 (20%)	5	1 (20%)	4 (80%)	0.023
> Double the normal	20	8 (40%)	12 (60%)	7	0 (0.0%)	7 (100%)	0.057
Total	40	24 (60%)	16 (40%)	12	1 (8%)	11 (92%)	

TABLE 3. CHANGES IN THE LEVEL OF VIREMIA OF HEPATITIS C VIRUS AFTER 30 SESSIONS OF OZONE THERAPY

Level of viraemia	High	Moderate	Weak	Total	p-Value
Before ozone	15 (37.5%)	13 (32.5%)	12 (30%)	40 (100%)	
After 30 ozone sessions					0.001
High	3 (20%)	0 (0.0%)	1 (8.3%)	4 (10%)	
Moderate	7 (46.6%)	5 (38.5%)	2 (16.7%)	14 (35%)	
Weak	1 (6.7%)	6 (46.1%)	5 (41.7%)	12 (30%)	
Negative	4 (26.7%)	2 (15.4%)	4 (33.3%)	10 (25%)	

sustained virologic response rates in patients with chronic hepatitis C have been reported for the pegylated forms of interferons compared with standard interferons both in monotherapy as well as in combination therapy with ribavirin.¹⁴ In these trials, patients were treated for 48 weeks. In patients chronically infected with genotypes 2 or 3, the treatment duration can be reduced from 48 to 24 weeks without compromising antiviral efficacy.¹⁵

Ozone, because of its special biologic properties, has theoretical and practical attributes to make it a potent HCV inactivator, which suggest an important role in therapy for hepatitis C, either as a monotherapy, or as an adjunct to standard treatment regimens.¹³

Ozone therapy is claimed to be useful in treatment against hepatitis, improving the patient's health and the healing time of the disease. Few clinical studies are available in treatment of viral hepatitis.¹⁶ This study was designed in view of these facts about ozone therapy, its possible antiviral efficacy, and the drawbacks associated with the currently available treatment regimens.

This current study demonstrated that ozone therapy using a combination of major autohemotherapy, minor autohemotherapy, and rectal ozone insufflation resulted in improvement of most of the presenting symptoms in about 90% of patients with chronic HCV infection after 30 sessions of ozone therapy, with no recurrence or appearance of new complaints until the end of treatment. On the other hand, the improvement of the presenting symptoms after conventional treatment (silymarin and/or multivitamins) was not significant. These results agree with the results of Mawsouf et al., who found that ozone therapy in 95% of patients with chronic active hepatitis C showed marked improvement of the general condition, improvement of the quality of life, and some of them returned to work after they were staying at home.¹⁷ Tanamly et al.¹⁸ compared the efficacy of silymarin and placebo among patients with chronic hepatitis C re-

garding the presenting symptoms and found no significant differences between the two groups of patients. The majority of the presenting symptoms showed no significant improvement.¹⁸ ALT activities may be useful in monitoring HCV infection but are insensitive in predicting disease progression to cirrhosis. ALT activities may be normal or fluctuate in those with HCV infection, and a single normal value does not exclude active infection, progressive liver disease, or cirrhosis.¹⁹ In the current study, AST and ALT levels became normalized among 60% and 57.5% of cases after 30 sessions ozone therapy, respectively. On the other hand, AST and ALT levels were normalized among 8% and 16.7%, respectively, among patients who received conventional therapy and the differences were statistically significant. The percentage of ALT normalization after ozone therapy was comparable to that after daily interferon therapy for 1 year (58%), as reported by Ferenci et al.²⁰ These results are better than those reported by Mawsouf et al.,¹⁷ who found that after 8 weeks of ozone therapy, the elevated enzyme levels returned to normal in 20% and 23.33% of cases for the ALT and AST, respectively.

Preliminary research has shown that reduction of viral load in hepatitis C by means of ozone therapy can significantly normalize hepatic enzymes and improve measures of general patient health. Volunteers who received ozone therapy according to the major autohemotherapy protocol showed a viral load reduction on the order of 99.9%, along with a normalization of liver enzyme levels.²¹

In the treatment of patients with chronic hepatitis C, Yamamoto reported a positive effect on 4 patients. After two to five ozone sessions in the form of major autohemotherapy, a decrease in hepatitis C virus RNA load could be measured. The individual values decreased by about a half of serum viral load.²² Viebahn recommended continuing this regimen for at least 3–6 months in order to obtain permanent clinical success.²³

TABLE 4. CHANGES IN THE LEVELS OF VIREMIA OF HEPATITIS C VIRUS AFTER 30 SESSIONS OF OZONE THERAPY AND CONVENTIONAL TREATMENT

Level of viremia	Before treatment		After treatment	
	Ozone (n = 40)	Conventional (n = 12)	Ozone (n = 40)	Conventional (n = 12)
High	15 (37.5%)	3 (25%)	4 (10%)	3 (25%)
Moderate	13 (32.5%)	5 (41.6%)	14 (35%)	3 (25%)
Weak	12 (30%)	4 (33.3%)	12 (30%)	5 (41.6%)
Negative	0 (0.0%)	0 (0.0%)	10 (25%)	1 (8.3%)
p-Value	0.714		0.331	

TABLE 5. CHANGES IN THE LEVELS OF VIREMIA OF HEPATITIS C VIRUS AFTER 60 SESSIONS OF OZONE THERAPY AND CONVENTIONAL TREATMENT

Level of viremia	Before treatment		After treatment	
	Ozone (n = 18)	Conventional (n = 12)	Ozone (n = 18)	Conventional (n = 12)
High	4 (22.2%)	3 (25%)	0 (0.0%)	3 (25%)
Moderate	11 (61.1%)	5 (41.6%)	2 (11.2%)	3 (25%)
Weak	3 (16.7%)	4 (33.3%)	8 (44.4%)	5 (41.6%)
Negative	0 (0.0%)	0 (0.0%)	8 (44.4%)	1 (8.3%)
p-Value			0.040	

In this study it was found that, following 30 sessions of ozone therapy the disappearance of serum HCV RNA has been reported in 25% of patients at the end of such treatment. This percentage was increased to 44.4% in 18 patients who received 60 sessions of ozone therapy. On the other hand, the results of the conventional group showed only 1 case that became negative out of 12 cases after treatment (8.3%). These results are better than those reported by Mawsouf et al.,¹⁷ who found that after 8 weeks of ozone therapy (24 sessions), the viral load decreased in 91.67% of cases that reached zero level in 20% of cases. Following 24 weeks of ozone therapy (72 sessions), there was further decrease of the viral load that reached 95% of cases, with a zero level in 36.67% of cases.¹⁸ The results of this study can also be compared with results of Tanamly et al.,¹⁸ (2004) who demonstrated that reverse transcriptase-PCR persisted in 67/69 (97.1%) of the silymarin group and in 69/72 (95.8%) given multivitamins.

Conclusions

These preliminary results for evaluation of ozone therapy in chronic hepatitis C showed that it has an effect on improvement of many presenting complaints, and is associated with reduction of ALT and AST levels. In addition, there was reduction of viremia and disappearance of HCV RNA in 25% of patients after 30 sessions of ozone and in 44.4% of patients after 60 sessions. These can be considered promising results; however, further evaluation and larger controlled trials are needed.

At present, many questions remained unanswered: Are these effects due to actual elimination of the virus or are they due to reduction of the level of viremia to a level undetected by conventional PCR? What are the long-term sustained virological effects? And what are the relapse rates? Thus, further large and more prolonged controlled studies are needed.

Disclosure Statement

No competing financial interests exist.

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