

Original paper

Behavioral Patterns Towards Ozone Therapy for Hepatitis C Infection

Khaled Mahmoud Abd Elaziz

Department of Community, Occupational, and Environmental Medicine, Faculty of Medicine, Ain Shams University

Samya Hassan El-Saati

Faculty of Women for Arts, Science and Education, Ain Shams University

Magdi Habachi

Ain Shams University

Mikhail Habachi

Ain Shams University

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Abstract

During the last decade, Viral Hepatitis C (HCV) has emerged as a new biological threat. Studies were performed in Egypt, between 1999 and 2008 to evaluate the role of ozone therapy for HCV. Whether the disease was in early or late stage, ozone therapy was found to be an effective, safe and, less expensive method in treating hepatitis "C" patients, used alone or in combination with drug therapy. Our study aims to investigate attitudes among physicians and patients towards the disease conditions, predisposing factors and, different therapeutic approaches including ozone therapy for HCV. Using two interview questionnaires, first for physicians (n=42) and the second for patients (n=50), managing HCV cases, via face to face structured interviews at the site of treatment reception in Cairo and Alexandria. Sites were grouped into three categories: (1) Ministry of Health governmental organizations and university hospitals (2) Army Facilities (3) Private clinics and centers. Snowball sampling method for ozone therapy, and conventional therapists interviewed after obtaining permission from the director of each establishment visited. Negative attitudes towards ozone therapy were observed among our study sample physicians with significant differences when distributed by place of study and physician's specialty. In our study sample 38.1% of physicians believe that ozone therapy is not scientific evidence-based medicine. Moreover, 54.8% assumed that ozone is an illegal and unapproved therapy for HCV. (93.1%) of the patients interviewed in governmental organization clinics and university hospitals never received ozone. 62.5% interviewed in private and army clinics had ozone therapy, and they all had positive attitudes towards ozone therapy for HCV. More research is needed to elucidate the debate concerning ozone therapies..

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Autor para correspondencia:: Khaled Mahmoud Abd Elaziz, Department of Community, Occupational, and Environmental Medicine, Faculty of Medicine, Ain Shams University

Introduction

During the last decade, Hepatitis C Viral (HCV) infection has emerged as a new biological threat (**Howard, et al., 2012**). Studies were performed in Egypt, between 1999 and 2008 to evaluate the role of ozone therapy for HCV. Ozone therapy was found to be an effective, safe and, less expensive method in Hepatitis “C” patients, used alone or in combination with drug therapy and, weather the condition is early or late (**Mawsouf et al., 2016**).

The published Egyptian Demographic Health Survey (EDHS) in 2009, estimated an overall anti-HCV antibody prevalence of 14.7% (**Miller et al. 2010**). Egypt Health Issues Survey (EHIS) in 2015, reported that the collected blood samples for testing at the Central Public Health Laboratory of the Ministry of Health and Population (MOHP), individuals age 1-59, for hepatitis testing, the number of individuals with an active hepatitis C infection was estimated based on the projected population age 1-59 years as of July 1, 2014 (**CAPMAS 2015**).

The quantitative real time Polymerase Chain Reaction (PCR) used at the Central Public Health Laboratory for the detection of HCV RNA, which is indicative of active (current) infection, estimated 3.5 million Egyptians, were found to have an active infection. Six percent had a positive result on the hepatitis C antibody test, indicating that they had been exposed to the virus. The high level of HCV infection has been attributed in part to the use of inadequately sterilized needles during mass campaigns undertaken to treat schistosomiasis during the 1960s through the early 1980s (**Pybus et al., 2000**). Hepatitis C superseded schistosomiasis as a result of iatrogenic and biological factors, unsafe injection practices (non-sterile needles) (**Frank et al., 2000**). A large body of literature on the epidemiology of HCV transmission in Egypt is identifying ongoing iatrogenic exposures as the major driver for HCV transmission and, short comings in infection control and standard procedures (**Miller et al., 2010**).

The Economic and Social Justice Unit of the Egyptian Initiative for Personal Rights claims that poverty in Egypt with, 26% of the population live with less than USD 1.6 per day (the national poverty line) and, concludes that hepatitis C is a socioeconomic condition, hitting the poorest segments of the population. (**Gomaa et al. 2017**). Hepatitis C virus is known as an RNA virus that replicates in the cytoplasm of liver cells, but is not directly cytopathic. Cytopathic effect or, cytopathogenic effect, CPE refers to structural changes in host cells that are caused by viral invasion. The infecting virus causes lysis of the host cell or when the cell dies without lysis due to an inability to reproduce (**Chen & Morgan, 2006**).

The virus has a high ability for replication ranging between 10^{10} and 10^{12} virion per day (**Neumann et al., 1998**). There are six genotypes of HCV (**Boyer et al., 2002**), HCV genotype 4 (G-4) is the most common in Egypt representing more than 90% of the cases (**Kamal, 2007**). The virus also has more than fifty subtypes (**Chen & Morgan, 2006**). HCV genome mutate frequently because of the weak error proofreading by the viral RNA polymerase in addition to rapid viral replication (**Bukh et al., 1995**). Study from Egypt showed late relapse rates of 9% (**El-Raziky et al., 2006**).

Numerous subtypes and frequent mutations have made difficulties in discovering vaccine for HCV till now. The standard treatment of HCV genotype 4 (HCV- G4) patients was a combination of pegylated interferon (PEG-INF) and ribavirin (RBV) for 48 weeks (**Abdel-Razek et al., 2015**). The efficacy of this combination to treat HCV-G4 patient was small. A worldwide study containing 7163 HCV patient treated by PEG-IFN/RBV showed only 41% SVR (**Pearlman et al., 2011**). Also, between 2007 and 2014 the National Program for Control of HCV in Egypt (NCCVH) has treated about 350,000 patients with this combination (**Waked et al. 2014**) and the result showed SVR between 45% and 55% (**Esmat, 2013**). Then, direct acting antivirals (DAAs), targeting specific sites in HCV replication complex, a breakthrough in the efficacy of HCV treatment was introduced. Sustained virologic response (SVR) has been labeled as the evidence supporting, clinically meaningful end point of successful antiviral therapy (**Pearlman et al., 2011**).

The National Committee for Control of Viral Hepatitis (NCCVH) in May 2015 has adopted one IFN-based regimen and two IFN- free regimens for treatment of HCV-G4 patients in Egypt. The IFN- based regimen was composed of SOF+PEG/RBV for 12 wks. The second regimen was for patient ineligible for interferon where the first option was sofosbuvir (SOF) + simeprevir (SIM) for 12 weeks., while the second option was SOF+RBV for 24 weeks (**Hézode et al., 2016**). The inclusion criteria according to May 2015 guideline include all HCV RNA positive patients between 18 and 70 years, either naive patients or treatment experienced patients without restriction to their fibrosis stage (**Abdel-Razek et al., 2015**).

Considering the price of these regimens, the WHO's Global hepatitis report, 2017 demonstrates that in Egypt, generic competition has reduced the price of a 3-month cure for hepatitis C, from US\$ 900 in 2015, to less than US\$ 200 in 2016. Improving access to hepatitis C cure received a boost at the end of March 2017, when WHO prequalified the generic active pharmaceutical ingredient of sofosbuvir, enabling more production of affordable hepatitis medicines (**WHO, 2017**).

Alternative treatments for HCV besides instituting lifestyle changes that prolong liver health, approaches for helping the liver damage from Hepatitis C fall under the domain of Complementary and Alternative Medicine (CAM). CAM includes use of natural health products such as vitamins, homeopathic remedies, traditional therapies and herbal medicines (**Sinclair, 2001**). CAM was defined as “those treatments and health care practices that are not an integral part of conventional western medicine, not taught in medical schools, and not generally used in hospitals” (**NCCAM, 2012**).

Ozone therapy purports to increase the amount of oxygen in the body. Ozone introduced to the blood stream directly i.e. intra venous, or indirectly through a procedure called AutoHaemoTherapy (AHT) (**Sagai et al. 2011**), but also through the ear, rectum and vagina by insufflations, by funneling, bagging and sauna (**Altman, 2008**) Studies indicate that ozone therapy cures many infections, including hepatitis (**McCabe, 2008**). For HCV/ozone treatment protocol adopted in Egypt, was blood *ozonation*, a process whereby: A portion of blood is withdrawn from the patient with HCV; an ozone/oxygen mixture is added to the withdrawn blood; the ozone/oxygen-rich blood is then returned to the patient; Researchers have confirmed that lipid-enveloped viruses are the most sensitive to ozone. As a lipid-enveloped virus, HCV stands to be one of the pathogens most easily affected by ozone therapy (**Mawsouf et al. 2008**) (**Zaky et al. 2011**).

Their studies have shown that ozone therapy can significantly normalize hepatic enzymes and improve measures of general patient health. AHT protocols have showed a viral load reduction on the order of 99.9%, along with a normalization of liver enzyme levels. (**Bocci et al. 1994**) 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 liver enzymes levels. (**Zaky et al. 2011**) The World Federation of Ozone Therapy in 2015 Review the Evidence Based Ozone Therapy with over 1300 references. In 2012 the Spanish Association for ozone therapy identified more than 26,000 health professionals practicing ozone in different parts of the world. The information about the properties of ozone, their mechanisms of action, forms and methods of application as well as instructions to correctly apply this valuable therapy following the recommendations of the authors, experts in research and clinical practice of ozone is available (**Noci et al., 2015**).

Our study aimed to investigate attitudes among HCV physicians and patients towards different therapeutic approaches including ozone therapy.

Subjects and methods:

A descriptive cross sectional survey study, in which, face to face, structured interviews were conducted between 2012-2014. Using two sets of interviewing questionnaires shaped to include: Physicians and Patients; delivering and receiving HCV therapy; either conventional and/or, ozone therapy. Each questionnaire had groups of questions to record;

- 1- Personal Data and social background: Personal and general information about age, gender, education level.
- 2- Information recorded about their prescriptions and tests done during treatment. HCV history, ways of transmission, predisposing factors and sources of infection, tests, and therapies considered.
- 3- Attitudes; positive and/or negative regarding the different approaches in disease management, as for considering; Resting in bed, herbal, nutritional, natural, spiritual and ozone therapies.
- 4- Behavioral Patterns and attitudes towards the disease transmission, detection, available therapies: antiviral, surgical, herbal and natural including ozone.
- 5- Possible explanations for, conventional and alternative therapies, attitudes towards government decision to ban ozone and, possible motives. Questions were formulated as simple (yes) and (no) answers. Unanswered questions, (may be) or, (I don't know) answers were recorded and grouped in items for statistical analysis and comparison.

Sites visited were: El Demerdash University Hospital, The Interferon Institute at Heliopolis Hospital, Cleopatra Private Hospital, The Ozone Clinic at Mostafa Kamel Army Hospital, Navy Ras El Tin hospital, Hyperbaric Navy Medical Center, Military Rehabilitation center in Agouza, private clinics and centers.

Sites of study were grouped in three categories: (1) Ministry of Health governmental organization and university hospitals (MoH/Gov.Org) (2) Army Facility (3) Private clinics and centers.

DATA MANAGEMENT: The developed questionnaires reviewed and the collected data entered onto spread sheets, using the Microsoft Excel® software program, then imported to the Statistic Package for Social Sciences (SPSS). Groups were assessed for differences in variables using the chi-squared test. The conventional 0.05 level of statistical significance was used to determine differences between the groups.

INCLUSION CRITERIA FOR PATIENTS: Adult patients (older than 18 years old), with confirmed diagnosis of HCV, at the site of treatment reception and, able to respond to questionnaires.

EXCLUSION CRITERIA FOR PATIENTS with late stage liver complications.

SAMPLING CONSIDERATION: Snowball sampling method used for ozone therapy, and for conventional therapies, permission from the director of each establishment visited was obtained before interviewed subjects on Volunteerism bases after obtaining authorization from the director of each establishment visited. The collected data were entered onto spread sheets, using the Microsoft Excel® software program, then imported to the Statistic Program for Social Science (SPSS), Groups were assessed for differences in variables using the chi-squared test. The conventional 0.05 level of statistical significance was used to determine differences between the groups.

LIMITATION OF THE STUDY: Snowball sampling for ozone therapy is not in favour for generalization of the study results.

RESULTS:

FIRST: PHYSICIANS SAMPLE:

Table 1: Demographic distribution of studied physicians:

Demographic characteristics	No (42)	%
Gender:		
Male	25	59.5
Female	17	40.5
Age (years):		
≤ 50	27	64.3
> 50	15	35.7

Table 2: Comparison between place of study and acceptance of use of ozone among physicians:

Place of study	Acceptance of ozone		X ²	P
	Yes	No		
MoH, Gov.org and, Uni.Hosp. N=22	No. % 4 18.2	No. % 18 81.8	9.5	0.002
Private and Army Facility N=20	13 65.0	7 35.0		

The study sample physicians interviewed in governmental ministry of health organization and university hospitals represented 52.4% and, the remaining 47.6% were interviewed in private and Army Facilities (AF). Males were more than females, 59.5% and, 40.5% respectively.

Comparison between place of study and acceptance of ozone among physicians showed significant statistical difference ($X^2=9.5$) ($p<0.05$).

Table 3: Comparison between physician specialty and acceptance of ozone:

physician specialty	acceptance of ozone			
	Yes No. %	No No. %	X^2	P
Hepatology /liver and internal diseases specialists (N= 18)			11.2	0.001
	2 11.1	16 88.9		
Others (N= 24)	15 62.5	9 37.5		

Physician specialty recorded as chosen by participants. Hepatologists and/or liver and internal diseases specialists represented 42.9% of the sample physicians. Comparing liver doctors and other specialties regarding acceptance of ozone therapy showed highly significant statistical difference ($X^2=11.2$) ($p<0.01$).

Table 4: Distribution of the physician sample according to their attitudes towards recommendations and prescriptions):

physician sample	Prescription patterns			
	Yes		No	
	No.	%	No.	%
PCR for diagnosis	37	88.1	5	11.9
Surgical Biopsy	36	85.7	6	14.3
Liver Function Tests	38	90.5	4	9.5
Antiviral Drugs	34	81.0	8	19.0
Herbal Supplements	10	23.8	32	76.2
Bed Resting	24	57.1	18	42.9
Nutrition support	30	71.4	12	28.6
Surgical Liver Transplant	27	64.3	15	35.7
Ozone Therapy	17	40.5	25	59.5

88.1% (N=37) of physicians had positive attitudes towards using and recommending PCR for diagnosis, 85.7% (N=38) surgical biopsies and, 90.5% (N=38) responded having positive attitudes towards liver function tests. 81.0% (N=34) of physicians recommended for the use of antiviral drugs. Positive attitudes towards herbal supplements were present in 23.8% (N=10) of physicians. 57.1% consider bed- resting their patients and , 71.4% (N=30) favor special diet and nutrition support. 64.3% (N=27) had positive attitudes towards surgical liver transplants and 40.5% (N=17) had positive attitudes towards ozone therapy for HCV.

Table 5: Distribution of the physician sample according to their attitudes towards ways of contamination, and HCV predisposing factors:

Predisposing factor	Attitude			
	Positive		Negative	
	No.	%	No.	%
Parenteral exposure via blood or blood products	40	95.2	2	4.8
Barbers and Hairdressers	39	92.9	3	7.1
Dentists	40	95.2	2	4.8
Antiviral Drugs	34	81.0	8	19.0
Blood manipulation	26	61.9	16	38.1
Sexual transmission	26	61.9	16	38.1
Bad Hygiene	25	59.5	17	40.5
Treatment Planned according to patients income level	29	69.0	13	31.0

Regarding the patients personal hygiene as a background for infection with HCV, 40.5% of physicians excluded the possibility that poor hygiene may be a predisposing factor for infection. 66.7% (n=28) of physicians responded that HCV is a disease affecting both equally rich and poor, 11.9% described HCV as a disease of rich people and 19.0% as poor men disease.

Table 6- Distribution of the physician sample according to their attitudes towards different therapies:

Different Therapies	Attitudes			
	Positive		Negative	
	No.	%	No.	%
herbal supplements	12	28.6	30	71.4
ozone therapy	19	45.2	23	54.8

Table 7- Distribution of the physician sample according to their interpretations for the reasons behind banning the ozone prescriptions for HCV:

Possible reasons for banning ozone	Yes No. %	No No. %
Ozone is not effective therapy	28 66.7	14 33.3
Ozone is not scientific evidence medicine	16 38.1	26 61.9
Ozone Conflicts Pharmacological Industry interests	29 69.0	13 31.0

SECOND: PATIENTS SAMPLE:**Table 8:** Demographic distribution of studied group's patients:

Demographic distribution	No (n=50)	%
Gender: Male	34	68.0
Female	16	32.0
Age: (Years) ≤ 50	18	36.0
> 50	32	64.0

Patients interviewed in governmental organization represented 58.0% and, the remaining 42.0% were interviewed in private and army clinics. 74% of the patients study sample received treatment in governmental organization/ministry of health hospitals and university hospitals, 48% in private clinics, and 16 % in army hospitals.

Table 9: Comparison between place of study and acceptance of ozone among patients:

place of study	Ozone acceptance		Total No. %		
	Yes No. %	No No. %			
MoH, Gov.Org N= 29	2 6.9	27 93.1	23 100	X^2 22.6	P 0.00
Private and Army N= 2	15 71.4	6 28.6	21 100		

93.1% of the patients interviewed in governmental organization clinics and university hospitals never received ozone. While, 62.5% interviewed in private and army clinics had ozone therapy. Comparison between place of study and acceptance of ozone among patients showed highly significant statistical difference. $X^2=22.6$, $p<0.001$.

Table 10: Comparison between patient's level of education and acceptance of ozone among patients:

level of education			Total (N=50)	X^2 6.2	P 0.17
	Yes No. %	No No. %			
Highly educated	12 52.2	47.8	23 100		
Others	5 18.5	22 81.5	27 100		

Acceptance of ozone therapy showed no significant difference among highly educated patients compared to others. ($X^2=6.2$) ($p>0.05$).

Table 11: Distribution of the study sample patients according to the ozone therapy modalities received and their attitudes towards cost of treatment and perceived effectiveness :

Ozone Therapy Received	Yes		NO OZONE	
	No.	%	No.	%
	20	40.0	30	60.0
Intra Venous/Auto-haemotherapy	17	34.0		
Ozone Insufflations	17	34.0		
Ozone after/with Antiviral drugs	12	24.0		
Only treated with ozone	9	18.0		
Is Ozone treatment expensive?	10	20.0		
Positive attitude towards ozone	20	40.0		

Forty percent (N=20) of the patients sample received ozone therapy. 34% had ozone intravenous / AHT, and equally, 34% had insufflations. Twelve patients received ozone after/with antiviral drugs. Nine patients received ozone exclusively. Half of them expressed that ozone was expensive and represented a budget burden and all of them had positive attitudes towards the therapy.

Distribution of the study sample patients according to ozone therapy reception showed no significant difference between mean age groups, genders, age of infection, and level of education.

OTHER FINDINGS: Presence of records: 14 out of 42 interviewed sample physicians had a negative response to record keeping. While half of the interviewed patients had HCV history of more than 3 years, 34% discovered the infection by routine examination and, 64% had symptoms of disease. 60% of the patients study sample did not receive antiviral therapies. 25% of patients who had ozone therapy also had antiviral therapies. Half of the patients treated with ozone had it intravenously, and another half had rectal insufflations. Half of the total sample patients considered ozone therapy as expensive and represented a burden on their budget. Regardless the therapies they follow almost half of the patients sample believed that drug industry had interests in banning ozone, 2% think that money interests are not involved in medical and health care administration and research. The majority of patients (96%) consider PCR a diagnostic tool, 32% accepts surgical biopsy for diagnosis, 70% consider antiviral therapy and, 12% considered liver transplant if possible. Regarding acceptance of herbal and natural therapies, 64% of the sample patients showed positive attitudes.

Discussion & conclusion

Attitudes toward therapeutic measures: Negative attitudes towards Alternative and Complementary Medicine (CAM) were observed among our study sample physicians. 71.4% of our study sample physicians refuse herbal, ozone and diet therapies for HCV, controversially, 64.0% of patients had positive attitudes. In our study sample physicians 38.1% believe that ozone is not scientific evidence based medicine and controversially 35.1% believe that it was banned because it conflicts drug industry and corporations interests. Moreover, 54.8% assumed that ozone is illegal and unapproved therapy for HCV.

Studies exploring the prevalence and patterns of knowledge about, referrals to, training in, and practice of complementary and alternative medical therapies and their perceived effectiveness are undertaken. Physicians in the province of Ontario, Canada, as an example for comparison revealed that 72% reported referring patients for alternative medicine therapies, and 20% had training in and 20% practiced some form of alternative medicine (**Ko and Berbrayer, 2000**). Sixty-four percent of our study sample patients showed positive attitudes towards herbal and alternative therapies, while only 23 % of our study sample physicians did. In a study to evaluate the attitudes of physicians at an academic medical center toward complementary and alternative medicine (CAM) therapies and the physicians' knowledge base regarding common CAM therapies, in Rochester, MN, USA.

Most physicians agreed that they should have knowledge about the most prominent CAM treatments and that the spiritual beliefs and practices of patients are important for their healing. Although 67% agreed that some CAM therapies hold promise for the treatment of symptoms, conditions and diseases, 70% of the physicians stated that the current practice of CAM therapies in the United States represents a threat to the health of the public (**Dietlind et al., 2006**).

In a study involving liver disease and CAM, up to 39% of patients attending liver disease clinics admitted to using some form of CAM at least once during the preceding month. The average use of CAM in liver disease patients was reported to be 41% (range 33% to 75%) in a study involving six different institutions (**Seeff et al. 2001**).

A study in Florida (**Giese, 2000**) showed 43% of patients who used CAM used it for liver disease. One study that specifically surveyed clinic patients (**Bruguera et al., 2004**) found that of 37% of patients that had used or were using CAM, 20% were using the CAM therapy because of chronic hepatitis and 17% were using it for other reasons. The use of CAM for liver disease may actually be higher outside western populations; a study looking at CAM use in Taiwanese patients found as many as 66% of patients used CAM (**Yang et al., 2002**).

The liver depends for 80% of its blood supply on other organ systems (**Charbon et al., 1989**). So, bed rest is favourable for the nutrition and function of the liver by modifying its blood supply (**Yong-Song et al., 2013**).

In our present study 57.1 % of physicians recommended bed rest and, 71.4% considered proper nutrition while managing HCV. Sixty four percent (n=32) of our study patients considered bed rest and good nutrition as positive factors for a cure. 21.4% (N=9) of our study physicians had negative attitudes towards bed rest. And five (11.9%) physicians claimed negative attitudes towards nutritional support. *HCV being a viral infection, only antiviral drugs will control it they claimed*. So explained by the 78.6% (N=7) of the sample physicians had positive attitudes toward; antiviral drugs and the 64% (N=27) in favor of surgical liver transplants.

Liver transplant activity in the Arab world until 2013 was evaluated and arranged according to date of the first transplant revealed that Egypt since 1991, had 56% (2,140 living donor and deceased donor liver transplantation) of the total of 3,804, in 11 countries members of the Arab League States (**Khalaf et al., 2014**). Saudi ranked second with 1,338 (35%) liver transplant operations. Compared to physicians, patients showed less acceptance towards surgical interventions; 68% (N=34), and towards antiviral drugs 34% (N=17). The relevance of these findings reveal that the increasing demand and scarce supply of organs in the Arab World, is more a physician concern than a patient concern.

These facts generate concern related to organ trafficking and transplant tourism (**Khalaf et al., 2014**). **Attitudes toward Disease transmission:** The risks of transmission of hepatitis C during sexual relations or from a mother to her child at birth or when breastfeeding are low, and few Egyptian Health Issues Survey (EHIS) responded mentioning those as possible ways to contract hepatitis C. Around 1 in 5 women and 1 in 7 men thought incorrectly that casual physical contact with an infected person was a way in which hepatitis C is transmitted (**El-Zanati et al., 2015**).

In our study physicians 38.1% (n=16) affirmed the possibility of sexual transmission and, 38.1% (n=16) denied. From the total physicians sample (n=42), regarding behavioral related risk factors for HCV transmission and possible ways of infection; the majority of interviewed physicians reported positive answers regarding the parenteral nature of the infection, via contaminated blood or, blood products (n=40) (95.2%), at the barbers and hairdressers (92.9%) and/or at dentists (95.2%). Drugs (81.0%), blood manipulation (61.9%), and sexual transmission, (61.9%). These attitudes are in accordance with studies of risk factors of HCV infection showing that more than one third of subjects (39.6%) who had jobs related to blood exposure, 47.5% of drug abusers, were positive (**Awadalla, 2011**).

Ozone Therapy Patients: Forty percent (n=20) of our study patients received ozone therapy, thirty four percent (n=17) had Intravenous ozone (AHT) and, (n=17) thirty four percent had ozone insufflations. Twelve patients from our study sample (24%) had ozone after having received conventional drug therapies and eighteen percent only had ozone as treatment. All the interviewed patients had positive attitudes towards ozone for HCV. Half of them claimed ozone therapy was burden on their budget. Physicians attitudes towards ozone and the limitation of its use in governmental organization, ministry of health and, university hospitals for the treatment of HCV, 35.7% (N=15) assumed that ozone therapy conflicts pharmaceutical industry and corporate interests, while 33.3% (N=14) disapproved this argument. The remaining 31% (N=13) failed to respond. Sixteen physicians (38.1%) claimed ozone is not scientific evidence medicine and seventeen (40.5%) failed to respond. Nine (21.4%) claimed scientific evidence is not the true cause of limitation of ozone use.

Investigating the actual research, internet information, and verbal inquiries about ozone clinics and organizations showed that ozone therapy is only provided in private and army clinics. The cold plasma ozone generation method (or dielectric barrier discharge method) is to produce ozone (**Čech et al., 2017**). In Russia, Ukraine and China and Ozone therapy is commonly used and most of the patients are treated with ozone therapy (**Sagai et al., 2011**): The American National Institute of Health's Office of Alternative Medicine developed a classification of CAM that differentiates seven categories and, includes intravenous ozone as one of the pharmacological and biologic treatments (**Gordon, 1996**). Others advocate ozone as a medical act and, the World Federation of Ozone Therapy in 2015 Reviewed the Evidence Based Ozone Therapy with over 1300 references (**Noci et al. 2015**).

Relevance of the Study: Our study was carried on patients receiving and delivering treatments for HCV. Thus, the real figures of the population behavior towards CAM therapies may be exceed the current figures of data, since self medicated patients will generally not be met at treatment sites. A study in Alexandria, Egypt, aimed to describe the prevalence, pattern and reasons for self-medication among adults, found the majority practiced self-medication (86.4%), mostly using both drugs and CAM (77.5%).

The most frequently used CAM, were herbs (91.6%), spiritual healing (9.4%) and, cupping and acupuncture (6.4%). CAM improved the condition according to 95.2% of users (**El-Nimr et al., 2015**). These findings are in accordance with alternative and complementary medicine for liver diseases provides benefits by regulating immunity, controlling disease progression, improving quality of life, and prolonging survival (**Guan et al., 2013**).

Ozone is not expensive and not patentable. It is regretful that local health authorities, concerned by the increased medical costs, do not take advantage of this inexpensive act. Unlike all other complementary approaches, the biochemical, physiological and pharmacological actions drawn out by ozone are in the realm of orthodox medicine (**Bocci, 2011**). This study highlights the need for educational interventions and the importance of providing physicians ready access to evidence-based information regarding ozone therapies as well as complementary and alternative medical acts.

Recommendations:

More research is needed to elucidate the debate concerning ozone therapy.

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