OZONE THERAPY IN PATIENTS WITH VIRAL HEPATITIS "C" A CLINICAL STUDY

By
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Abstract:

Hepatitis "C" is a medical problem in Egypt. The usual line of treatment is very expensive with major side effects and low efficacy especially in type 4, which is common in Egypt. The aim of this study is to evaluate the role of ozone as a safe line of treatment. This study included 50 type 4 hepatitis "C" patients, 44 males and 6 females. Their age ranged between 23 and 58 years. Investigations including C.B.C., liver function tests, A.F.P., serological tests for Bilharziasis, P.C.R. quantitative for H.C.V., prothrombin time and concentration and abdominal ultrasonography were done before and 8 weeks, 24 weeks after treatment with ozone. Patients received combined treatment of Major AutoHaemotherapy in a dose range from 2.8 mg to 8.4 mg and rectal insufflation in a dose range from 6mg to 12 mg per visit. The numbers of visits were three times per week for 12 weeks followed by twice per week for 12 weeks. The general condition in 94 % of cases improved. There was a decrease in the quantitative P.C.R. (viral load) in 71.8 % of cases that reached –ve P.C.R. in 24 % of cases after 8 weeks treatment. The number of -ve P.C.R. cases for HCV virus increased to reach 36 % of cases after 24 weeks treatment. There was a statistically significant improvement as regards the parameters of SGOT, SGPT, albumin, bilirubin and prothrombin after 8 weeks from the start of the study. Ozone therapy was found to be an effective, safe and less expensive method in Hepatitis "C" patients.

Key Wards

Hepatitis, Ozone, HCV

Aim of the Study

This study was made to evaluate the effectiveness of ozone therapy in hepatitis C genotype 4 infections and to evaluate a proposed ozone therapy protocol in HCV genotype 4 treatment.

Introduction

Hepatitis C (HCV) is a worldwide medical problem. It is estimated that more than 300 millions on earth are suffering from HCV. Hepatitis C is a major medical problem in Egypt. It is postulated that more than 15% i.e. more than 10 millions of the population in Egypt are suffering from HCV. This disease is slowly progressing, detected mainly accidentally, devitalizing and difficult to treat. The usual line of treatment is very expensive with major side effects and low efficacy [1, 2].

HCV in most cases leads to complications e.g. liver cirrhosis, ascitis, liver carcinoma and ultimately liver cell failure. Liver Cirrhosis is estimated to develop in 20 -25 % of patients with HCV within 20 years. Hepato-cellular carcinoma in 5% of patients.

It is not only a medical problem, but also an economic problem (less work, less production and very high costs of usual treatment).

So far there are six genotypes of HCV with worldwide prevalence of genotypes 1, 2 &3. In Africa genotype 4 and 5 are more dominant. In Asia genotype 6 is more dominant. Genotype differences have shown varying susceptibility to antiviral therapy. In Egypt genotype 4 is prevalent and it is known that is relatively resistant to antiviral treatment [3].

The main line of treatment nowadays for hepatitis C includes interferon and ribavirin. Ribavirin and interferon have significant medical and psychiatric side effects [1].

Antiviral effect of ozone

Ozone is a powerful oxidizing agent. It disrupts viral envelope proteins, lipoproteins, lipids, and glycoproteins. The presence of numerous double bonds in these unsaturated molecules makes them vulnerable to the oxidizing effects of ozone. Molecular architecture is disrupted and widespread breakage of the envelope ensues. Deprived of an envelope, virions cannot sustain nor replicate themselves. Ozone proper, and the peroxide compounds it creates, may directly alter structures on the viral envelope, which are necessary for attachment to host cells. Peplomers, the viral glycoproteins protuberances that connect to host cell receptors are likely sites of ozone action. Alteration in peplomer integrity impairs attachment to host cellular membranes foiling viral attachment and penetration [4 -12].

Ozone stimulate leucocytes function and cytokine production

Ozone is a powerful oxidant by itself and leads to production of peroxides with an oxidative power. H2O2 crosses the cell membrane and activates the cytoplasmic gene-regulatory nuclear factor kappa B, ultimately causing the transcription of mRNAs of several cytokines, namely interleukin (IL-1,2,4,6,8,10), tumor necrosis factor (TNF-$\propto$) and interferon (IFN β and γ) [13, 22].

In HCV, viral load appears to be a major factor in the invasiveness and virulence of the disease process. Ozone induces the release of cytokines by leucocytes. Stimulation of the immune mechanisms will lead to significant reduction of circulating virions [14 – 22].

Patients and methods

This study included 50 type 4 hepatitis "C" patients, 44 males and 6 females. Their age ranged between 23 and 58 years. Investigations including C.B.C., liver function tests, A.F.P., serological tests for Bilharziasis, P.C.R. quantitative for H.C.V., prothrombin time and concentration and abdominal ultrasonography were done before and 8 weeks, 24 weeks after starting treatment with ozone. Patients received combined treatment of Major AutoHaemotherapy in a dose range from 2.8 mg to 8.4 mg and rectal insufflation in a dose range from 6 mg to 12 mg per visit. The numbers of visits were three times per week for twelve weeks followed by twice per week for another twelve weeks. Investigations were repeated after 8 and 24 weeks of treatment. General health and daily activity were observed.

Ozone Treatment Protocol

First session of major AutoHaemotherapy was given in a concentration of 20 µ/ml ozone in oxygen for two successive times, then increased to 25 µ/ml ozone in oxygen for another two successive times and so on, increasing the concentration by 5µ/ml every two sessions till reaching a maximum of 60µ/ml were this concentration was fixed till the end of treatment course. The rationale of start low and go slow was respected. The ozone in oxygen volume was fixed in all sessions at 140 ml. The blood weight was constant in each session at 140 gm.

First session of rectal insufflation was given in a concentration of 15 µ/ml ozone in oxygen with a volume of 250 ml for two successive times, then increased to 20 µ/ml ozone in oxygen with the same volume for another two successive times, then 25 µ/ml x 250 ml twice, then 30 µ/ml x 250 ml twice followed by 30 µ/ml x 300 ml, then 35µ/ml x 300 ml twice till we reach a maximum of 40µ/ml x 300 ml were this concentration and volume was fixed till the end of treatment.

Results

It was found that following eight weeks of ozone therapy, the viral load decreased in 63.85% of cases (P value < 0.004) that reached zero reading in 24 % 0f cases (P value <0.001). Following 24 weeks of ozone therapy, there was further decrease of the viral load that reached 71.84% of cases (P value < 0.005) with a zero reading in 36 % 0f cases (P value <0.001). After eight weeks of ozone therapy, the abnormal enzyme levels were back to normal in 58 % of cases (P value <0.001) for the SGPT enzyme, and were back to normal in 52 % of cases (P value <0.001) for the SGOT enzyme (normal levels are ≤ 40 U/L) table 1 figure 1– 4.

After eight weeks of ozone therapy, the abnormal bilirubin levels (normal value ≤ 1 mg%) were back to normal in 28% of cases (P value < 0.001). Following also the same period of therapy, the abnormal albumin parameters (normal value ≥ 3.5 mg %) were back to normal in 18% of cases (P value < 0.032). The prothrombin concentration improved towards the normal level (P value < 0.001) table 2 figure 5-7.

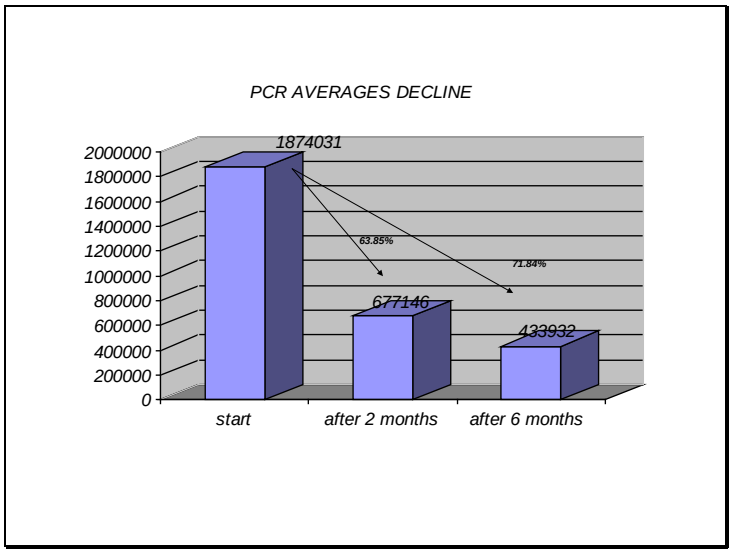
Table 1

Number	Sex	PCR	PCR 2mnth	PCR 6 mnth	SGOT	SGOT2mnth	SGPT	SGPT2mnth
1	Male	5540000	3035000	5750000	39	37	75	12
2	Male	200000	0	0	70	35	65	33
3	Male	91000	31000	12000	80	21	76	22
4	Male	10000000	7003000	3400000	46	33	50	32
5	Male	199010	11000	3500	90	46	50	46
6	Male	2030000	700000	27000	78	33	65	22
7	Male	100000	0	0	69	24	75	17
8	Male	164000	54000	0	38	22	30	25
9	Male	89000	43000	15000	62	40	61	23
10	Male	12000000	5000000	3400000	123	88	232	85
11	Male	1200000	0	0	138	27	112	33
12	Male	1300000	22000	2800	80	36	60	39
13	Male	650000	4500	0	138	71	314	31
14	Female	1115000	3000	1200	24	14	24	17
15	Male	3400000	810000	53000	38	35	23	21
16	Female	954618	1500	0	156	44	163	45
17	Male	1500	0	0	60	33	59	31
18	Male	550000	240000	84000	34	40	50	32
19	Female	500000	1300	0	76	50	85	44
20	Male	103000	36000	5100	80	15	60	13
21	Female	1300000	58000	36000	95	30	85	24
22	Male	1200000	720000	53000	54	40	61	29
23	Male	320000	61000	24000	96	40	80	33
24	Male	586000	119000	82000	44	38	30	39
25	Female	260000	117000	29000	67	36	40	20
26	Male	29223496	10920000	7680000	84	44	120	43
27	Female	10000	0	0	22	21	28	31
28	Male	980000	95000	35000	52	21	17	24
29	Male	240000	180000	0	33	30	42	28
30	Male	1500000	350000	150000	78	65	42	41
31	Male	120000	90000	50000	31	29	34	22
32	Male	300000	100000	5000	78	46	61	29
33	Male	1352000	0	0	65	33	59	39
34	Male	389000	140000	39000	68	49	107	57
35	Male	29605	0	0	50	37	107	43
36	Male	92000	0	0	43	28	53	22
37	Male	120000	65000	11000	147	30	89	30
38	Male	822000	0	0	92	42	92	30
39	Male	157000	68000	40000	70	35	73	28
40	Male	1000000	500000	320000	55	33	59	32
41	Male	470000	210000	36000	63	45	83	33
42	Male	690000	45000	75000	62	31	59	30
43	Male	550000	0	0	143	43	105	45
44	Male	210000	120000	49000	56	26	41	37
45	Male	2250000	5000	0	98	37	75	34
46	Male	112000	0	0	30	31	45	22
47	Male	8756307	2742000	168000	72	29	32	26
48	Male	27000	0	0	28	24	18	20
49	Male	288000	90000	36000	60	110	54	99
50	Male	160000	67000	25000	65	45	60	46

Table 2

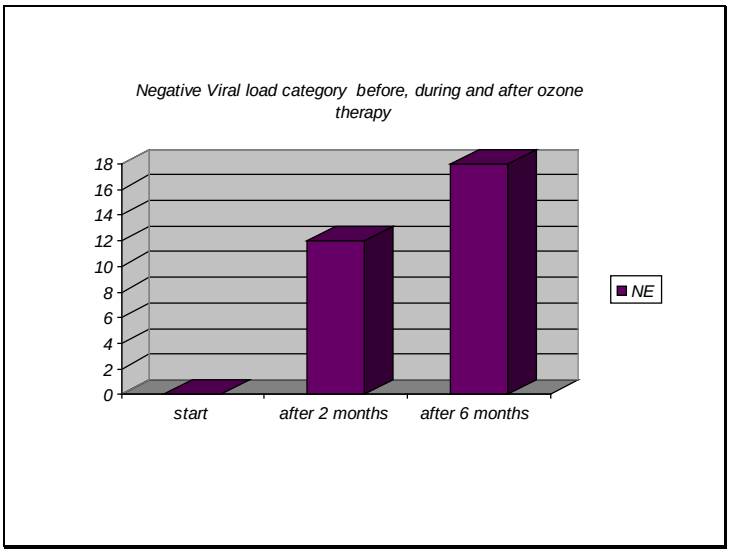
Number	Bil.	Bil. 2 mnth	Alb.	Alb. 2 mnth	Prothro.%	Prothro.% 2 mnth	HB %	HB 2 mnth
1	0.9	0.9	3.9	4.0	90	91	13.5	13.8
2	0.8	0.8	3.2	3.9	77	86	12.2	14.1
3	2.3	1.3	4.3	4.3	96	96	15.2	15.6
4	1.0	0.9	4.1	4.2	80	82	15.1	15.2
5	0.8	0.8	3.9	4.1	85	99	13.9	14.0
6	1.1	1.2	3.3	3.5	80	86	14.2	14.3
7	0.8	0.7	4.6	4.7	70	76	15.5	16.7
8	0.7	0.8	3.9	4.2	72	84	13.5	14.3
9	0.6	0.7	4.2	4.3	86	92	15.8	16.1
10	1.1	0.7	4.1	4.5	82	100	12.0	13.1
11	2.0	1.1	4.2	4.4	89	90	13.0	13.2
12	1.2	1.1	3.9	3.6	90	91	15.1	15.1
13	2.1	0.8	2.8	4.7	85	100	12.7	12.9
14	0.7	0.8	3.9	0.4	75	80	11.9	12.1
15	0.8	0.8	4.8	4.9	100	100	14.8	15.0
16	1.1	1.0	3.4	3.8	80	90	13.6	14.0
17	1.2	0.8	4.1	4.3	92	100	14.0	14.2
18	0.9	0.8	3.8	3.9	40	76	14.2	14.4
19	1.4	1.2	2.8	3.1	60	68	11.6	12.0
20	0.7	0.7	4.1	4.3	88	89	13.9	14.0
21	3.3	2.0	2.8	3.0	64	70	10.0	11.0
22	1.0	0.9	3.7	3.8	77	87	13.1	14.5
23	0.6	0.6	4.0	4.4	79	80	13.2	13.9
24	1.0	0.6	4.7	4.6	82	96	13.6	13.1
25	1.2	0.8	3.2	4.3	65	87	11.2	13.5
26	0.5	0.6	3.9	4.0	80	86	15.0	16.3
27	0.8	0.7	3.8	3.9	100	100	12.9	12.8
28	1.2	0.9	3.2	4.0	68	98	14.0	14.1
29	1.2	0.8	3.5	3.5	83	89	12.7	12.9
30	1.7	1.1	3.9	4.2	71	80	13.6	14.2
31	0.6	0.7	3.8	4.2	100	100	13.9	14.5
32	1.6	1.1	2.7	3.3	56	82	14.2	14.7
33	0.5	0.6	3.9	4.1	75	86	13.6	14.9
34	1.7	0.8	3.6	3.5	82	87	13.9	15.2
35	1.8	1.2	3.9	3.9	88	90	13.1	13.3
36	0.9	0.9	3.2	3.2	92	96	13.5	14.1
37	1.2	0.8	3.3	3.8	56	86	13.2	14.1
38	1.1	0.7	3.3	3.9	68	85	12.3	13.8
39	1.2	0.7	3.7	3.8	92	100	12.8	13.6
40	1.2	1.1	4.1	4.3	86	85	14.2	14.3
41	1.0	0.8	4.1	4.3	94	100	13.4	14.8
42	0.7	0.8	3.9	3.4	79	84	14.4	11.9
43	1.2	1.0	3.9	4.2	85	90	12.8	13.9
44	1.6	1.2	2.1	2.7	52	72	12.3	13.0
45	1.9	0.8	3.2	3.8	75	89	12.5	13.0
46	0.9	0.8	4.2	4.5	97	100	14.2	14.3
47	0.7	0.4	3.4	3.5	90	90	13.9	14.1
48	0.7	0.7	3.7	4.1	93	100	13.5	14.2
49	1.3	0.9	2.8	3.6	67	75	13.4	15.2
50	0.8	0.9	4.2	4.2	90	91	14.1	14.4

Fig. 1



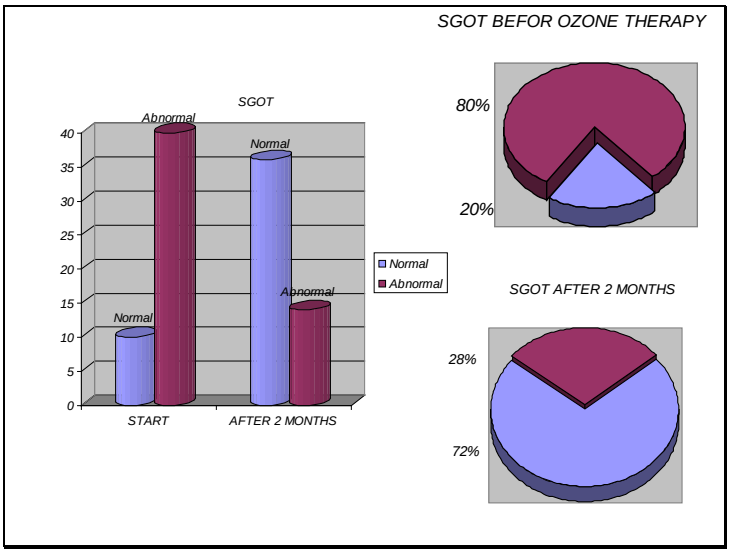
PCR average number before, during and after ozone therapy

Fig. 2



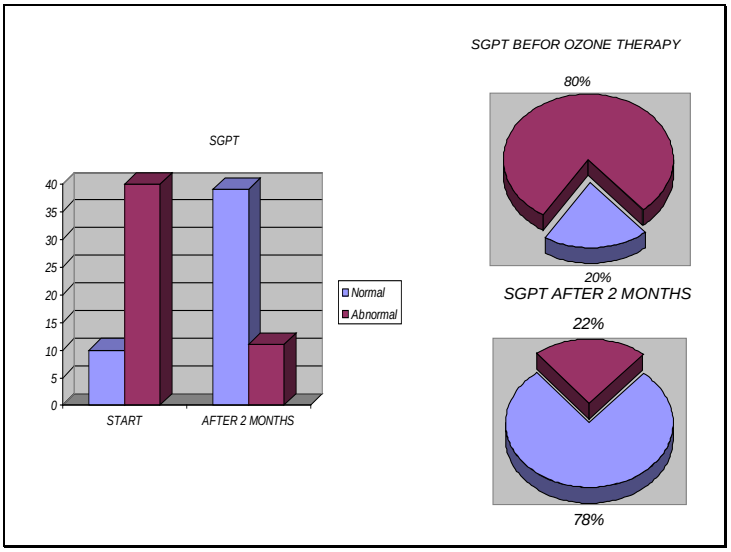
Number of PCR negative cases during and after ozone therapy

Fig. 3



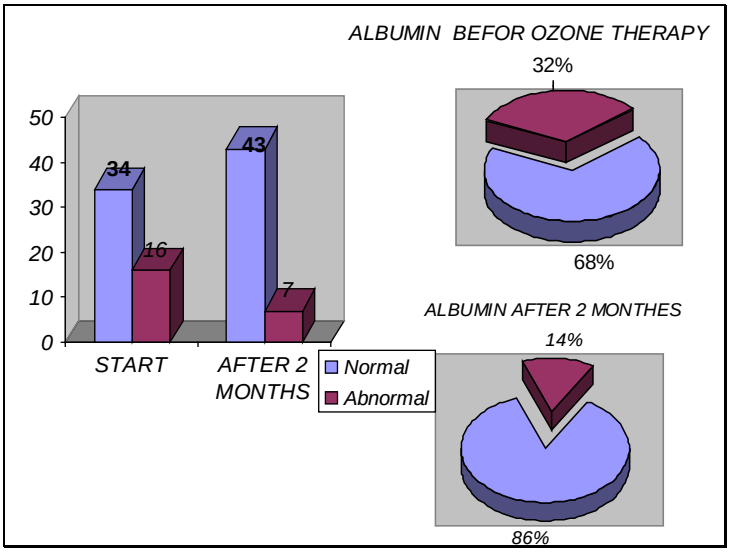
Normal and abnormal SGOT enzyme levels before and after ozone therapy

Fig. 4



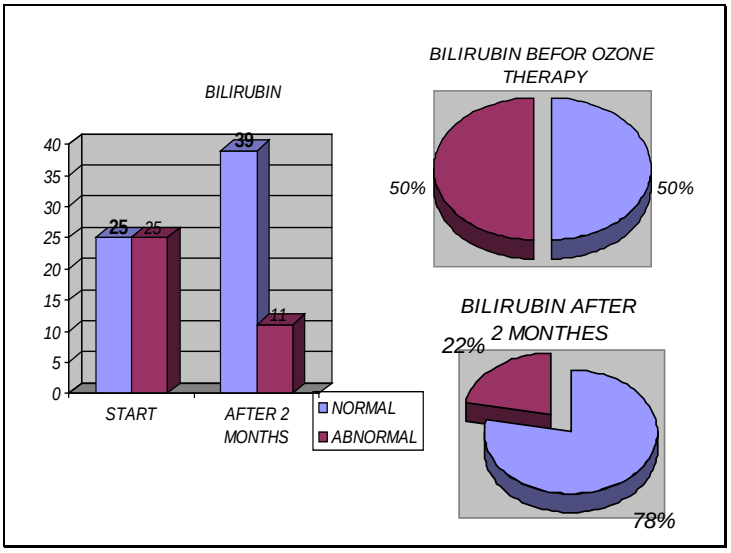
Normal and abnormal SGPT enzyme levels before and after ozone therapy

Fig. 5



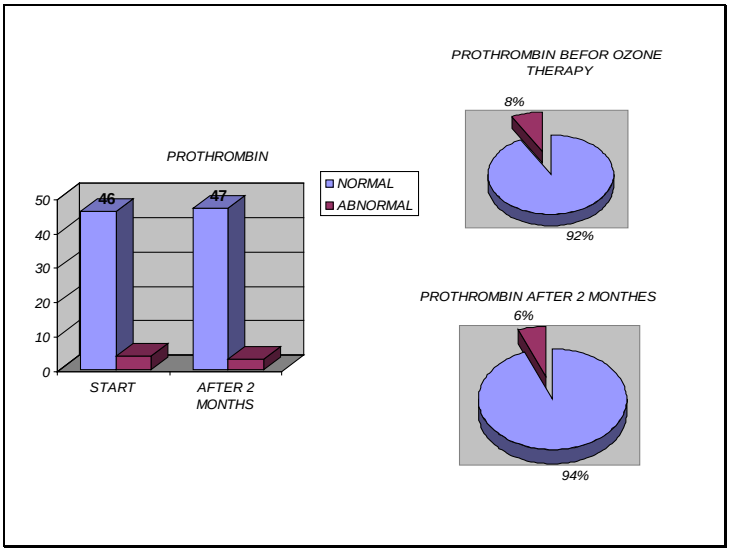
Normal and abnormal albumin levels before and after ozone therapy

Fig. 6



Normal and abnormal bilirubin levels before and after ozone therapy

Fig. 7



Normal and abnormal prothrombin levels before and after ozone therapy

Discussion

The significant decrease in viral load is an important factor – among other factors – for judging the improvement of a case of hepatitis C virus. In this study, it was found that following ozone therapy; there was a significant reduction of viral load. This decrease was evident after 8 weeks and further decline following another 16 weeks of ozone therapy.

Normal enzyme levels are a very important indicator denoting the sound integrity of liver cells. In this study, it was found that following ozone therapy; there was a significant change of abnormal enzyme levels towards normal values. Some patients received DDB pills that are a Chinese herbal medicine capable of lowering the enzyme level, but without any anti-viral action. Stoppage of DDB will be followed by increase in enzyme level to the previous level. This can explain why some of the patients had a normal enzyme level before starting ozone therapy.

One of the major important parameters that signify liver function are the bilirubin and albumin levels. In this study it was found that both parameters were improved and back to normal with a statistically significant readings denoting liver function improvement.

Clinical observations and questioning of the patients revealed that in 94 % of cases the general condition improved and some of patients returned to work after they were staying at home. Moreover in most cases there were improvement of the quality of life and they had the sense of well-being. All these data points to the important role of ozone a safe, effective method of therapy.

It is understandable that the response to treatment will be less in complicated cases with e.g. liver cirrhosis and ascitis or cases associated with chronic diseases e.g. diabetes and bilharziasis, but however, these were not considered as factors in ineffectiveness.

In this study there was no control group and the patient was considered a control to himself and the main issue, as a clinical study was to compare the clinical and laboratory findings before and after ozone therapy for each patient. In order to reach a proper protocol for ozone therapy, several pilot studies had to be accomplished. Trial MAH twice/week for 2 months, MAH three times/week for 2 months, RI twice/week for 2 months, RI three times /week for 2 months following rationale of start low and go slow. Good results were obtained but not as good as the protocol of this study. Combination of MAH and RI was important the deliver ozone therapy to both systemic and portal circulation. Ozone therapy was found to induce hyper-oxygenation of portal circulation.

Conclusion

As a preliminary study Ozone therapy was found to be an effective, safe and less expensive method in Hepatitis "C" patients but further studies are important.
The protocol of ozone therapy in this study was found to be the best of many other protocols dealing with hepatitis C type 4.

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