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EFFICIENCY OF VIBRO-ACOUSTICAL METHOD OF THERAPY FOR CHRONIC VIRUS HEPATITIS TREATMENT

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Treatment of chronic virus hepatitis is a huge medical problem all over the world. In our research were involved 16 patients (9 women and 7 men, 18-34 years old), 8 of them - with a chronic virus hepatitis B in a stage of replication and 8 - with a chronic hepatitis C in a phase of a reactivation. The duration of disease vary from 1 till 5 years. The patients before inspection were not treated by antiviral preparations. Concentration of serum interferons determined by an immunoenzyme method and a degree of manifestation of a cytolytic syndrome by definition of activity of serum alanin-amino-transferase were assessed. The blood interferons concentration was significantly higher and the levels alanin-amino-transferase were much less after the vibroacoustic treatment. Thus the application of a physiotherapeutic method of treatment with the use of the device "Vitafon IR" in complex therapy of chronic virus hepatitis raises its efficacy. The effect from influence by the device is connected to its stimulating of the interferonogenesis in a liver.

INTRODUCTION

Treatment of chronic virus hepatitis is a huge medical problem all over the world [3]. At the current stage of medicine development this problem is far from its salvation. The efficacy of hepatitis treatment (achievement of a proof remission) by modern antiviral agents is insufficient and makes on the average 40-60 % [4]. This problem is especially urgent for Russia, that is linked to a high case rate by parenteral hepatitis in the country among the young population, and inaccessibility of treatment to the majority of the patients because of its high cost. This service is not included in the programs of obligatory medical insurance. In the absence of treatment of chronic

hepatitis the risk of their transformation into cirrhosis or hepatocarcinoma is very high. And despite of this process prorogates for decades, if infected in young age the chronic hepatitis can essentially affect lifetime of the patient.

Insufficient efficacy and high cost of the treatment of chronic virus hepatitis force to search for alternative methods of therapy, including physiotherapeutic. In various time with this purpose were offered microwave and magnet-laser therapy [1, 5], ultrasonic sound [2], electrophoresis [6]. However their influence was focused, basically, on the achievement of anti-inflammatory effect and did not influence on infestant.

The device "Vitaфон IR" produced by Vitaфон Ltd. (St.-Petersburg) renders combined vibroacustical and infra-red influence on an organism. Active vibrating part of the device, which called vibrophone provokes microvibration of tissues. The infra-red head influences a tissue by infra-red radiance. Frequency of microvibration and average vigor of infra-red radiance automatically continuously vary in accordance with the program.

The medical effect of the device is based on mutual intensifying combined influence of microvibrations and impulsive infra-red radiance.

In an operative range of vibrophone under influence of microvibration the downstroke of a hydrodynamical vascular resistance is observed. Thereafter there is an increasing of osmotic fluid flow, that results in local augmentation of capillary blood and lymph flow in the radius of 7-10 cm from the center of vibrophone.

In an operative range of an infra-red ultrasonic head the heating of superficial layers of tissues and vasodilatation are observed, which also activite the microcirculation.

The intensifying of capillary blood and lymph flow in the struck tissues is a necessary and important direction of the treatment of chronic inflammatory diseases, including chronic virus hepatitis, both promotes to achieve the resorption of an inflammatory edema, revascularization of tissues, and also improves the delivery of drug agents in the locus of an inflammation. Besides the influence of this effect on the interferon production is possible because of the increased output of immunocompetent cells in interstitium and augmentation of the frequency of their contacts with each other and with hepatocytes.

MATERIALS AND METHODS

1. Research of influence of the device "Vitaфон IR" on serum concentrations of interferons α and γ .

In our research were involved 16 patients (9 women and 7 men, 18-34 years old), 8 of them - with a chronic virus hepatitis B in a stage of replication and 8 - with a chronic hepatitis C in a phase of a reactivation. The duration of disease vary from 1 till 5 years. The patients before inspection were not treated by antiviral preparations.

The ultrasonic heads were established in range of a liver: in the beginning on dextral range F, then on its projection to a forward surface of a thoracal cell - range M4. A high intensive regimen (№ 4) was applied. The duration of influence was progressively enlarged from 5 up to 20 minutes by each body surface (in the absence of unpleasant sensations in range of a liver). The procedures carried out 1 time a day

in four days on fifth within 4 weeks. A blood was taken in 1 hour and 3 day after procedure. Concentration of serum interferons determined by an immunoenzyme method with the help of test-systems SPU «Protein contour» (St.-Petersburg). Simultaneously estimated a degree of manifestation of a cytolytic syndrome by definition of activity of serum alanin-amino-transferase (ALT) in patients on the biochemical analyzer "Spectrum".

2. Application of the device "Vitaфон IR" in treatment of the patients with chronic virus hepatitis C.

Under our observation there were 18 patients with the diagnosis of chronic virus hepatitis C at the phase of reactivation, RNA HCV positive (genotyping and biopsy were not carried out)-- 15 women and 3 men in the age from 28 till 57 years, duration of disease from 1 till 14 years. All patients had attributes of biochemical activity of a hepatitis - rising ALT in 2-5 times, in two cases the expressed disproteinemia was marked. 7 patients had inspissation of a liver, perivascular fibrosis, narrowing of the hepatic veins, and in two cases - dilating v.portae and attributes of an ascites by the data of ultrasound scanning.

All patient were undergone the procedures of combined physiotherapeutic treatment with the help of the device "Vitaфон IR" with the our special program during 6-12 months. The antiviral therapy was not carried out. The control inspections (serum ALT, RNA HCV, ultrasound scanning of the liver) were carried out 1 time in 3 months.

RESULTS AND DISCUSSION

Results of our study (concentration of serum interferons α and γ in patients with chronic virus hepatitis B and C treated with the device "Vitaфон IR") are submitted in Table 1 and Table 2.

The contents of interferons- α and γ , activity of serum ALT in the patients with chronic virus hepatitis B who was undergone the treatment by the device "Vitaфон IR"

Table 1

Sub- stra- te	Nom	Day of the therapy										
		0	1	6	9	11	14	16	19	21	24	26*
IF- α Fg/ ml	0- 50	32,2 ± 7,2	75,2 ± 8,8*	112, 5± 17,3 *	50,4± 9,5	126,1± 17,9*	69,4 ± 11,7 *	179, 6± 24,2 *	87,9 ± 11,2 *	206,0± 23,5*	78,3± 10,2*	261,2± 28,3*
IF- γ Fg/ ml	0- 50	26,4 ± 5,7	25,3 ± 5,9	32,1 7,5	27,5± 6,6	47,2± 7,4*	32,3 ± 5,0	55,8 ± 7,3*	42,7 ± 7,7*	59,3± 8,2*	50,4± 8,5*	58,5± 8,8*
ALT U/l	to 54	187 ± 24	192 ± 20	220 ± 28	147± 18	232± 26	112 ± 17*	240 ± 31	98± 13*	248± 27*	84± 14*	279± 33*

* - the differences are authentic with the conforming parameters of zero day (p < 0,05)

The contents of interferons- α and γ , activity of serum ALT
in the patients with chronic virus hepatitis C who was undergone the
treatment by the device "Vitaфон IR"

Table 2

Substrate	Norm	Day of the therapy										
		0	1	6	9	11	14	16	19	21	24	26*
IF- α Fg/ml	0-50	26,8 ± 4,5	49,7 ± 6,3*	86,5± 13,2*	42,2 ± 8,4	112, 8± 10,9*	67,5 ± 9,8*	155,6± 20,7*	70,8± 12,6*	183,2± 20,4*	72,1 ± 11,3*	210,5± 25,4*
IF- γ Fg/ml	0-50	20,2 ± 3,4	24,1 ± 4,2	30,1 4,9*	22,7 ± 6,6	38,9 ± 5,6*	30,1 ± 4,3	44,9± 6,2*	33,8± 6,2*	50,3± 7,1*	39,2 ± 7,4*	55,3± 7,8*
ALT U/l	up to 54	123 ± 15	149 ± 17	205± 21*	158 ± 18	218 ± 23*	127 ± 15*	228± 25*	84± 11*	214± 19*	80± 12*	202± 29*

* - the differences are authentic with the conforming parameters of zero day (p < 0,05)

The note: days of realization of the procedures discharged by the bold font

As shown in the tables that contagious process in patients with chronic hepatitis B and C was not accompanied with rising of serum concentrations of interferons α и γ (data of the zero day). So the immune system of the patients with chronic virus hepatitis B and C does not react adequately to virus introduction, is tolerant to it.

The influence on the range of a liver with the help of the device "Vitaфон IR" resulted in essential increase of concentration of the serum interferon- α in the patients right after the first procedure. The longer influence, the more essential rising of concentration of an interferon, especially at the day of procedure. Between procedures the fall of cytokines concentrations, in the beginning up to an initial level was observed. Subsequently the degree of this drop was decreased, and the concentrations of serum interferon constantly remained at the authentically increased level. Serum concentrations of interferon- γ during therapy by the device tended to ascending. At the end of a course they authentically exceeded those at the patients in the beginning of treatment. The initial level of ALT exceeded the limit of norm more than in 2 times. During treatment there was ascending activity of this enzyme proportional to the duration of procedure. When duration of influence consists of 15-20 minutes on each body surface the activity of ALT grew in 2-2,5 times. Between the procedures activity of this enzyme was reduced, and in the beginning down to the initial levels, and at the end of a course - even below initial levels. It is necessary to note, that the rise of ALT activity was accompanied by clinical exhibitings of an exacerbation of a hepatitis in all patients. The patients marked the appearance of the light tenderness by the liver area arising soon after the end of procedure or immediately at the moment of its realization (when duration of the influence more than 15 minutes). Within the day after procedure moderate weakness (4), drop of appetite (3), nausea (1), urine colour changings (2), mild icterus (1) were marked. If

clinical symptomatology appeared we decreased the duration of procedures by 3-5 minutes and continued the treatment in this regimen, achieving mild intensifying of cytotoxicity (ALT rising no more than in 2 times) in the absence of expressed clinical evidences of disease. Thus, the complex physiotherapeutic influence by the device "Vitaфон IR" on the range of a liver promotes augmentation of serum concentrations of interferons α and γ and ALT activity in patients with chronic virus hepatitis B and C. This study result in the development of the treatment scheme of chronic virus hepatitis B and C with the help of the device "Vitaфон IR", submitted in tab. 3.

In the circuit of the treatment in addition to the influence right on the liver (points M4 and right F) was entered the acting on the ranges K and M. Points K are the projection of the kidneys on the back body surface. The influence on range of kidneys promotes activation of their perfusion and leads to augmentation of the diuresis. The vibratory influence on a liver is accompanied by intensifying of metabolic processes and increased formation and accumulation of toxic metabolites. Therefore vibratory influence on the ranges K it is necessary for the desintoxication. Besides the influence on range K involve exposure on the adrenal glands. It is known, their hormones have anti-inflammatory action and enlarge the adaptation capacity of the organism. The range M is a projection of gallbladder and bile ducts on a forward body surface. It is known, the chronic virus hepatitis is characterized by the infringement of the process of bile evacuation with frequent clinical and laboratory exhibitings of a bile stasis, dyskinesia or infection contamination of bile ducts. Vibratory influence on this range promotes normalization of function of bile evacuation. During treatment of 18 patients with chronic hepatitis C under the given circuit the cases of a biochemical and complete remission were recorded. After 3 months of treatment in 4 patients was registered the complete (biochemical + virologic) remission and in 2 cases - biochemical remission. After 6 months of treatment in 4 additional patients the biochemical remission was marked, and in 1 - complete remission. Thus, the primary answer to a semi-annual course of treatment by the device "Vitaфон IR" with achievement of a complete remission was received in 8 cases (44,4 %), biochemical - in 1 case. The patients who achieved the complete remission were transferred on a maintaining course of therapy. The circuit of a maintaining course is shown in tab. 4. As you can see in the table, the influence was pruned for the range F и M4 to 5/5 minutes and was carried out 1 time per week, and the procedures on range K and M were carried out 2 times per week. Duration of a course was not less than 12 months.

The inspection which has been carried out after 9 months has revealed, that despite of realization of a maintaining course of therapy, in two patients with the complete remission which has come in 3 months from beginning of the treatment, the reactivation of contagious process was marked. In one patient who has not answered the usual circuit of treatment during 6 months, the complete remission with application of the special circuit of therapy was achieved.

After 12 months in two patients the reactivation of contagious process (one after 3 and one after 6-month's courses of treatment by the device) was developed. A complete remission in 2 patients received therapy on the special circuit was registered.

Treatment scheme of the patients with chronic virus hepatitis B and C
by the device "Vita fon IR" (scheme 1)

Table 3

Day #	Number of procedures per day	SEQUENCE of the PROCEDURES		
		Duration of influence on a range of « K » in «4» regimen.	Duration of influence on a range of « M » in «1» regimen.	Duration of influence on a range of «right F + M4» in «4» regimen.
1	1	-	-	5/5
2	2	10	5	-
3	2	10	5	-
4	1	-	-	7/7
5	2	15	10	-
6	2	15	10	-
7	2	15	10	-
8	2	15	10	-
9	1	-	-	10/10
10	2	20	10	-
11	2	20	10	-
12	2	20	10	-
13	2	20	10	-
14	1	-	-	13/13

After that we provide the augmentation of influence on range "right-F" and "M4" on 3/3 min each five days before appearance of attributes of a clinical and biochemical exacerbation (but no more than 25/25 minutes), then returned at one - two step back and continued the treatment for 6 months.

Total 12-month's observations over 18 patients with chronic virus hepatitis C received only physiotherapeutic treatment with the help of the device "Vita fon IR" under the our circuits was shown, that to the terminal of the observation period it was possible to reach a proof complete remission at 7 (38,9 %) patients.

The causes of insufficient efficacy of six-month treatment by the device were analyzed. Was discovered that bunch not answered on treatment included the patients with duration of disease more than 8 years who have ultrasound attributes of widespread fibrosis in the hepatic tissue or portal hypertension, i.e. patients in cirrhotic stage of a chronic hepatitis. For such patients the special circuit of therapy was developed. Enlarged the number of the procedures per day on the range of a liver (after two days on the third), as more intensive influence on a liver was achieved, and the method of "shaking", i.e. alternating of duration of each procedure was applied. The sense of this circuit consists in attempt of achievement of an exacerbation of a chronic hepatitis that is much more difficult for achieving at appreciable replacement of a parenchyma of a liver by a connective tissue.

Scheme of a maintaining of the course of therapy by the device "Vitaфон IR"
in patients with chronic virus hepatitis after the complete remission was reached
(scheme 2)

Table 4

Day #	Number of procedures per day	SEQUENCE of the PROCEDURES		
		Duration of influence on a range of « K » in «4» regimen.	Duration of influence on a range of « M » in «1» regimen.	Duration of influence on a range of «right F .+ M4» in «4» regimen.
1	1	-	-	5/5
2	1	20	10	-
3	-	-	-	-
4	-	-	-	-
5	1	20	10	-
6	-	-	-	-
7	-	-	-	-
8	1	-	-	5/5
9	1	20	10	-
10	-	-	-	-
11	-	-	-	-
12	1	20	10	-
13	-	-	-	-
14	-	-	-	-
15	1	-	-	5/5
16	1	20	10	-
And than so on till the 12 months period.				

In our opinion intensive vibroacustical influence extending on 7-10 cm deep into a liver, considerably activate immune responses in the tissues due to increased output of immunocompetent cells in the interstitium and augmentation of frequency of their contacts with each other and cells of a liver. As a result of intercellular interaction there is the releasing of the cytokines, including interferons, which can stimulate the development of the immune inflammation.

The intensifying of inflammatory reaction is accompanied by augmentation of activity of serum ALT - the marker of cytolysis of the hepatocytes.

As known, basic producents of an interferon- α are the macrophages and B-lymphocytes. Inducers of the cytokine producing are the viruses and cells transformed by the virus, bacteria and other antigens. The process of the induction is very short-term. In result in a tissue, where the induced cells concentrate, there is a fast accumulation of the interferon. This cytokine is well soaked up from the locus of an inflammation, accordingly in short time from a beginning of an inflammation its concentrations in a blood grow.

Interferon- γ is basically produced in the sensitized T-lymphocytes. The term of an operating time of a clone of sensitized lymphocytes is necessary for its accumulation. Therefore serum concentrations of this cytokine begin to raise only at a stage of an immune inflammation.

The dosed influence of microvibration with gradual augmentation of its duration and intervals between procedures allows to achieve the effect of a moderate exacerbation of chronic inflammatory process, activation of mechanisms of the immune defense and nonspecific resistance, what proves to be true by the augmentation of serum concentrations of interferons- α and γ under the influence of treatment by the device.

CONCLUSION

1. The application of a physiotherapeutic method of treatment with the use of the device "Vitaфон IR" in complex therapy of chronic virus hepatitis raises its efficacy.

2. The effect from influence by the device is connected to its stimulating influence on the interferonogenesis in a liver.

3. The patient without the expressed attributes of a fibrosis of a liver (on the data of ultrasound scanning or morphological inspection) is recommended to begin therapy under the scheme № 1. In case of achievement of a complete remission after 3 months we recommend to continue the treatment using this scheme still during 3 months and then pass to a maintaining therapy.

4. Patient with the expressed attributes of a fibrosis of a liver the treatment should be carried out under the scheme № 3 during 6 months. When the remission is achieved after 3 months the transfer to the scheme № 1 is possible.

5. In case of an inefficiency of six-month treatment it is necessary to refuse vibroacoustic monotherapy. The device can be recommended as an additional agent to antiviral therapy of chronic hepatitises under the same schemes.

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