

The Combined Treatment of Chronic Viral Hepatitis B, C and Mixed B and C with Cytomix + Guna liver + Interferon Gamma

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Abstract

The combined treatment with Cytomix + Guna liver + Interferon gamma was favored the improvement of clinical symptoms in patients with HVBC, HVC and HVBC+HVCC, the decrease and normalization of liver and spleen sizes, moderate decrease of cytolysis indices values (ALAT, ASAT), seroconversion in the AgHBs and anti-HBs system with the formation of anti-HBs (protective antibodies) in 2 patients with the diagnosis HVBC and in one patient with the mixed hepatitis HVBC+HVCC. The improvement of immune status indices, which was more marked in patients with HVCC there were not noted clinical, biochemical and immunological improvement in patients of the control group.

Key words: hepatitis B, chronic hepatitis C, chronic, Cytomix, Guna liver, Interferon gamma.

Комбинированное лечение Цитомиксом, Гуна ливером, Интерфероном гамма больных хроническим вирусным гепатитом В и С и микст гепатитом В+С

Комбинированное лечение Цитомиксом, Гуна ливером, Интерфероном гамма привело к исчезновению клинической симптоматики у больных хроническим вирусным гепатитом В и С и микст гепатитом В+С, с нормализацией размеров печени и селезенки и умеренным снижением активности АЛАТ и АСАТ. Произошла сероконверсия в системе HBsAg и анти-HBs с образованием анти-HBs у двух больных с хроническим вирусным гепатитом В и у одного с микст гепатитом В+С. Наблюдалось улучшение иммунологического статуса более выраженное у больных с хроническим вирусным гепатитом С. У пациентов контрольной группы клинические, биохимические, и иммунологические улучшения не выявлены.

Ключевые слова: гепатит В, хронический, гепатит С, хронический, Цитомикс, Гуна ливер, Интерферон гамма.

Introduction

The viral hepatitis problem remains to be one of worldwide significance, their consequences affecting the health of hundreds of million of people. Both viral acute and chronic hepatitis make a touchstone. New therapeutically methods appeared recently in medical practice/first of ale antiviral which has counter indications and side effects. Only 30–40% of patients usually benefit of antiviral treatment, but what about the rest?

The purpose of the study was to determine the efficiency of Cytomix therapy + Guna liver + Interferon gamma in viral chronic hepatitis B, C and B and C

Material and methods

2 patients groups were been included in the study: - I (first) group of patients, who were administered three therapy with Cytomix+Interferon gamma+Guna liver – 17 patients;

- II (second) control group – 16 patients.

17 patients have been included in the experimental group, who were administered three therapy: 9 men and 8 women aged between 18 and 80 years, among them 8 had the diagnosis HVBC, the disease stage was between 1 and 13 years. 7 patients had the diagnosis HVCC, the disease stage was between 1 and 9 years and 2 patients with mixed chronic viral hepatitis B+C, in one patient the disease stage was equal with 1 year and in the second HVBC was detected 28 years ago, and HVCC was revealed 2 years ago.

There were included 16 patients in the control group: 10 men and 6 women aged between 27 and 72 years. Among, them 6 patients with the diagnosis of HVBC and 8 patients

with the diagnosis HVCC, and 2 patients with the mixed chronic viral hepatitis B+C. The disease length was between 5 to 17 years in patients with HVBC. The disease length was between 1 to 12 years in patients with HVCC. The disease length in patients with mixed chronic viral hepatitis B+C was: in one patient both hepatitis forms were traced out 8 years before and in the second patient HVCC was diagnosed 12 years ago, and HVBC – 10 years ago.

The clinical exam

Patients with HVCC, HVBC and mixed HVCC+HVBC were clinically examined: anamnesis, liver and spleen palpation and percussion, chest auscultation and percussion and heart auscultation if needed.

The dynamics of paraclinical and clinical investigations

Laboratory exams: serologic investigations: the reveal of AgHBe, anti-HBe, anti-HBs, anti-HVC IgM; biochemistry investigations: the values determination of ALAT, ASAT, bilirubin, thymol test, prothrombin; clinical exam – hemogram and immunological status were made at the start and at the end of treatment.

The treatment lasted for 3 months.

The modality of medicines administration in the first group was

The first month of treatment:

1. Interferon gamma – 26 days, 20 drops twice a day sublingual (in the morning and evening) one hour before meals or one hour after meals. On Sundays the medicine was not administered.

- Guna Liver – 26 days, 3 granules twice a day sublingual in the morning and evening one hour before the meals or one hour after the meals. The medicine was indicated the next 15 minutes after the administration of Interferon gamma.
- Cytomix 10 granules twice a day sublingual, in the morning and evening the first 5 days, the next 21 days 3 granules twice a day sublingual, in the morning and evening 15 minutes after administration of Guna Liver. On Sundays the medicine was not administered.

The second and the third month of treatment

- Cytomix - 26 days 3 granules twice a day sublingual in the morning and the evening one hour before the meals or one hour after the meals.
- Guna Liver - 26 days 3 granules twice a day sublingual in the morning and evening 15 minutes after Cytomix administration.
- Interferon gamma - 26 days 20 drops twice a day sublingual in the morning and evening 15 minutes after Guna Liver administration.

Results and discussion

Tab. 1 demonstrating the symptomatology poverty, but more frequent were revealed next symptoms: pains in the right hypochondrium, asthenia, hepatomegalia, spleenome-

galy. The clinical symptomatology was richer at the treatment start in patients with HVBC. They demonstrated one larger gamma of symptoms comparatively with patients with HVCC and HVBC+HVCC.

The clinical symptomatology had ameliorated after 3 months of treatment and at the end of it were persisting only 2 clinical symptoms: asthenia and pains in right the hypochondrium in patients with HVBC. The liver and spleen dimensions had decreased in all three groups with over 50% at the treatment' end comparatively with the liver and spleen dimensions at the treatment's start.

The clinical symptomatology in patients of the control group (tab. 2), demonstrating the poverty of clinical manifestations, they being quite the same both in patients with HVBC and HVCC. But the evolution analysis of these symptoms in dynamics had revealed its insignificant amelioration. Hepatomegalia and spleenomegalia were the revealed with the same frequency – 83% and 87.5% respectively at the start and the end of the study.

The analysis of biochemistry indices in patients of the experimental group (tab. 3) conducts us to some conclusions: ALAT had normalized in a small number of patients - 2 with HVBC and 4 with HVCC, and the increased ASAT values had normalized in 4 patients, and had increased discreetly in 4 patients with normal values.

Table 1

Clinical symptomatology and its evolution dynamics in patients of the experimental group and of the control group

Symptom	At the treatment's start			At the treatment's end		
	HVBC n = 8	HVCC n = 7	HVBB+ HVCC n = 2	HVBC n = 8	HVCC n = 7	HVBB+ HVCC n = 2
Asthenia	3 (37.5%)	-	1	1 (12.5%)	-	-
Pains in the right hypochondrium	5 (62.5%)	2 (28.5%)	-	1 (12.5%)	-	-
Vertigo	2 (25%)	-	-	-	-	-
Myalgia	1 (12.5%)	2 (28.5%)	1	-	-	-
Arthralgia	1 (12.5%)	2 (28.5%)	-	-	-	-
Nausea	2 (25%)	-	1	-	-	-
General weakness	2 (25%)	-	-	-	-	-
Pruritus	1 (12.5%)	-	-	-	-	-
Hepatomegalia	6 (75%)	5 (71.7%)	2	2 (25%)	3 (43%)	1
Spleenomegalia	5 (62.5)	3 (43%)	1	1 (12.5%)	1 (14.3%)	1

Table 2

Clinical symptomatology and its evolution dynamics patients of the control group

Symptoms	At the treatment's start			At the treatment's end		
	HVBC n = 6	HVCC n = 8	HVBB+ HVCC n = 2	HVBC n = 6	HVCC n = 8	HVBB+ HVCC n = 2
Asthenia	5 (83%)	2 (25%)	-	4 (66.6%)	1 (12.5%)	-
Pains in the right hypochondrium	3 (50%)	5 (62%)	1	3 (50%)	2 (25%)	-
Vertigo	-	1 (12.5%)	-	-	1 (12.5)	-
Myalgia	1 (16.6%)	-	-	-	-	-
Arthralgia	1 (16.6%)	2 (25%)	-	-	2 (25%)	-
Nausea	1 (16.6%)	1 (12.5%)	-	1 (16.6%)	1 (12.5)	-
General weakness	3 (50%)	2 (25%)	-	3 (50%)	1 (12.5)	-
Prurigo	-	-	-	-	-	-
Hepatomegalia	5 (83%)	7 (87.5)	1	5 (83%)	7 (87.5%)	1
Splenomegalia	5 (83%)q	4 (50%)	2	5 (83%)	4 (50%)	2

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Bilirubin increased values had been revealed in patients with the Gilbert's Syndrome - 30 mcmol/l and 24 mcmol/l.

Thymol test values did not modify.

The prothrombin index was normal in the majority of patients included in the study and only in one patient with the diagnosis HVBC and 2 with HVCC had decreased with 80 – 70%.

The analysis of biochemistry indices in patients of the control group (tab. 4) to find one absence of modifications in biochemistry indices during three months of observation. The increased bilirubin level was revealed in patients with Gilbert's Syndrome. The prothrombinic index was decreased - in 2 patients with HVBC, 3 – with HVCC and 2 – with

HVBC+HVCC, its values being between 80 and 70%.

The tab. 5 shows the AgHBe reveal at the start and the end of treatment in the same patients, seroconversion of HBe-anti-HBe had not happened.

AntiHBs had formed in 2 patients with the diagnosis of chronic viral hepatitis B and in one patient with mixed chronic viral hepatitis B+C. This fact demonstrated a benefic action of the three therapy with Interferon gamma+Guna liver+Cytomix. These medicines, probably, possess antiviral actions.

Anti-HVC IgM was revealed with the same frequency at the start and the end of treatment. This fact demonstrates the antiviral properties absence of the hepatitis C virus.

Table 3

The dynamics of biochemistry indices in patients with three therapies at the treatment's start and finish and of the control group

Biochemistry indices	At the treatment's start			At the treatment's finish		
	HVBC n = 8	HVCC n = 7	HVBB+ HVCC n = 2	HVBC n = 7	HVCC n = 5	HVBB+ HVCC n = 2
ALAT (increased)	7	6	2	5	2	1
ASAT (increased)	5	4	1	5	4	1
Bilirubin (increased)	1 (Syndrome Gilbert)	2 (Syndrome Gilbert)	-	2 (Syndrome Gilbert)	1 (Syndrome Gilbert)	-
Thymol test (increased)	4	5	1	4	5	1
Prothrombinic Index (decreased till 70%)	1	2	1	1	1	1

Table 4

The dynamics of biochemistry indices in patients of the control group

Biochemistry indices	At the observation's start			At the observation's finish		
	HVBC n = 6	HVCC n = 8	HVBB+ HVCC n = 2	HVBC n = 6	HVCC n = 8	HVBB+ HVCC n = 2
ALAT (increased)	4	5	1	4	4	1
ASAT (increased)	4	4	-	4	5	1
Bilirubina (increased)	3	1	-	3	-	-
Thymol test (increased)	3	1	2	1	2	-
Prothrombinic Index (decreased)	2	3	2	2	2	-

Table 5

The dynamics of markers (serologic indices) in patients of the experimental group and of the control group

Markers	at the start of treatment			at the end of treatment		
	HVBC n = 8	HVCC n = 7	HVBC+ HVCC n = 2	HVBC n = 8	HVCC n = 7	HVBC+ HVCC n = 2
AgHBe	1	-	-	1	-	-
Anti-HBe	7	-	2	7	-	2
Anti-HBs	-	-	-	2	-	1
Anti-HVC IgM	-	7	2	-	7	2

Table 6

The dynamics of viral markers in patients of the control group

Markers	at the start of observations			at the end of observations		
	HVBC n = 6	HVCC n = 8	HVBB+ HVCC n = 2	HVBC n = 6	HVCC n = 8	HVBB+ HVCC n = 2
AgHBe	-	-	-	-	-	-
Anti-HBe	6	-	1	6	-	1
Anti-HBs	0	-	-	0	-	0
Anti-HVC IgM	-	6	1	-	6	1

Table 7

The dynamics of immunological indices in patients treated with Cytomix+Guna liver+Interferon gamma at the treatment's start and at the end of it

Indices	Normal values	At the treatment's start			At the treatment's end		
		HVBC n=8	HVCC n=7	HVBC+HVCC n=2	HVBC n=8	HVCC n=7	HVBC+HVCC n=2
Leucocytes (10 ⁹ /l)	4.5-8.0	7.625 ± 0.851	5.828 ± 0.459	5.05 ± 0.45	7.162 ± 1.08	6.614 ± 0.914	5.0 ± 0.6
Lymphocytes (%)	22-38	31.625 ± 2.499	32.142 ± 3.261	40 ± 4	35.125 ± 3.286	33.428 ± 3.379	35.5 ± 0.5
Lymphocytes (10 ⁹ /l)	1.2-2.4	2.395 ± 0.309	1.775 ± 0.182	2.06 ± 0.36	2.393 ± 0.277	2.085 ± 0.219	1.8 ± 0.3
Lymphocytes Ta (%)	20-34	21.5 ± 2.352	19 ± 3.199	19.5 ± 8.5	19.375 ± 2.583	18.428 ± 1.95	20.5 ± 3.5
Lymphocytes Ta (10 ⁹ /l)	0.3-0.7	0.517 ± 0.103	0.364 ± 0.072	0.45 ± 0.25	0.505 ± 0.108	0.402 ± 0.062	0.4 ± 0.1
Lymphocytes Ttot (%)	55-75	45.625 ± 3.035	40.857 ± 2.364	40.5 ± 1.5	45 ± 4.246	45.285 ± 4.892	53.5 ± 19.5
Lymphocytes Ttot (10 ⁹ /l)	0.9-1.5	1.072 ± 0.197	0.755 ± 0.112	0.86 ± 0.16	1.178 ± 0.222	0.985 ± 0.166	0.91 ± 0.19
Lymphocytes Tterm (%)	0-5	4.75 ± 2.335	4.571 ± 1.862	6 ± 4	0	0	0
Lymphocytes Tterm (10 ⁹ /l)	0-0.09	0.126 ± 0.072	0,085	0.135 ± 0.105	0	0	0
Lymphocytes TFR-E-RFC (%)	38-58	28.875 ± 2.286	26.428 ± 2.457	25 ± 2	28.625 ± 2.764	31.428 ± 3.329	37.5 ± 11.5
Lymphocytes TFR-E-RFC (10 ⁹ /l)	0.7-1.1	0.71 ± 0.128	0.491 ± 0.096	0.52 ± 0.13	0.756 ± 0.114	0.677 ± 0.122	0.67 ± 0.07
Lymphocytes TFS (%)	12-28	16.75 ± 1.997	14.428 ± 1.659	15.5 ± 0.5	16.875 ± 2.191	13.428 ± 2.021	16 ± 8
Lymphocytes TFS (10 ⁹ /l)	0.23-0.43	0.406 ± 0.077	0.252 ± 0.032	0.315 ± 0.045	0.448 ± 0.103	0.275 ± 0.041	0.265 ± 0.095
Lymphocytes EAC-RFC (%)	9-18	31 ± 3.835	26.428 ± 2.715	25.5 ± 1.5	33.75 ± 4.934	25.285 ± 3.727	35.5 ± 4.5
Lymphocytes EAC-RFC (10 ⁹ /l)	0.18-0.32	0.753 ± 0.156	0.481 ± 0.085	0.525 ± 0.125	0.873 ± 0.178	0.482 ± 0.053	0.655 ± 0.185
CIC (U.E.)	≤ 60	42.625 ± 8.635	72 ± 29.125	67 ± 22	41 ± 9.924	51.166 ± 34.82	133.5 ± 26.5
LTL	4-7	7.78 ± 0.718	8.422 ± 1.080	5.95 ± 0.55	6.756 ± 0.753	7.171 ± 0.722	5.85 ± 1.85
T/B	2.0-5.0	1.632 ± 0.204	1.628 ± 0.124	1.6	1.512 ± 0.182	2.028 ± 0.395	1.625 ± 0.775
TFR/TFS	2.0-4.0	1.992 ± 0.370	2.0 ± 0.303	1.6 ± 0.2	1.862 ± 0.265	2.442 ± 0.218	2.675 ± 0.575

Table 8

The dynamics of immunological indices in control group of patients at the start and end of treatment

Indices	Normal values	At the observation's start			At the observation's end		
		HVBC n=6	HVCC n=8	HVBC+HVCC n=2	HVBC n=6	HVCC n=8	HVBC+HVCC n=2
Leucocytes (10 ⁹ /l)	4.5-8.0	5.6 ± 0.700	5.775 ± 0.480	5.55 ± 1.15	5.5 ± 0.705	4.937 ± 0.546	5.15 ± 0.85
Lymphocytes (%)	22-38	34.333 ± 2.333	35.625 ± 2.87	40 ± 7	39.333 ± 4.247	36.125 ± 2.247	34.5 ± 4.5
Lymphocytes (10 ⁹ /l)	1.2-2.4	1.961 ± 0.230	2.081 ± 0.254	2.13 ± 0.07	2.205 ± 0.405	1.812 ± 0.245	1.75 ± 0.05
Lymphocytes Ta (%)	20-34	15.333 ± 2.788	17.25 ± 1.655	15.5 ± 3.5	13.166 ± 2.056	14.75 ± 1.760	18.5 ± 8.5
Lymphocytes Ta (10 ⁹ /l)	0.3-0.7	0.288 ± 0.036	0.366 ± 0.060	0.345 ± 0.045	0.338 ± 0.089	0.272 ± 0.042	0.35 ± 0.15
Lymphocytes Ttot (%)	55-75	42.666 ± 4.038	37.125 ± 1.949	41 ± 2	34.666 ± 3.938	34.875 ± 3.943	39.5 ± 9.5
Lymphocytes Ttot (10 ⁹ /l)	0.9-1.5	0.873 ± 0.147	0.781 ± 0.101	0.85 ± 0.05	0.823 ± 0.197	0.687 ± 0.125	0.7 ± 0.2
Lymphocytes Tterm (%)	0-5	0.666 ± 0.494	0.5 ± 0.5	1 ± 1	0.166 ± 0.372	0	0
Lymphocytes Tterm (10 ⁹ /l)	0-0.09	0.013 ± 0.011	0.015 ± 0.015	0.02 ± 0.02	0.001 ± 0.001	0	0
Lymphocytes TFR-E-RFC (%)	38-58	30.166 ± 2.676	26.125 ± 2.614	26.5 ± 0.5	24.833 ± 2.903	22.25 ± 2.403	30 ± 9
Lymphocytes TFR-E-RFC (10 ⁹ /l)	0.7-1.1	0.595 ± 0.092	0.551 ± 0.088	0.575 ± 0.025	0.586 ± 0.132	0.433 ± 0.085	0.55 ± 0.15
Lymphocytes TFS (%)	12-28	12.5 ± 1.979	11.25 ± 1.221	14.5 ± 2.5	9.833 ± 1.777	12.625 ± 2.419	9.5 ± 0.5
Lymphocytes TFS (10 ⁹ /l)	0.23-0.43	0.255 ± 0.052	0.226 ± 0.041	0.305 ± 0.065	0.231 ± 0.062	0.238 ± 0.059	0.165 ± 0.015
Lymphocytes EAC-RFC (%)	9-18	21.666 ± 2.333	22.25 ± 2.160	24.5 ± 4.5	16.166 ± 3.070	18.375 ± 4.597	24.5 ± 0.5
Lymphocytes EAC-RFC (10 ⁹ /l)	0.18-0.32	0.43 ± 0.074	0.456 ± 0.060	0.525 ± 0.115	0.356 ± 0.076	0.361 ± 0.107	0.43 ± 0.02
CIC (U.E.)	≤ 60	46.333 ± 2.564	54.125 ± 12.99	80 ± 15	55.666 ± 14.061	90.375 ± 27.56	38.5 ± 31.5
LTL	4-7	7.066 ± 0.828	8.168 ± 0.99	6,5 ± 1	7.8 ± 0.977	8.125 ± 0.909	7.65 ± 0.95
T/B	2.0-5.0	2.191 ± 0.442	1.768 ± 0.171	1.725 ± 0.225	2.483 ± 0.406	2.731 ± 0.539	1.605 ± 0.355
TFR/TFS	2.0-4.0	2.988 ± 1.336	2.668 ± 0.538	1.875 ± 0.375	3.058 ± 0.858	2.017 ± 0.302	3.1 ± 0.8

In of the control group (tab. 6) demonstrates the absence of AgHBe in patients being in the study with chronic viral hepatitis B, but there were revealed antibodies anti-HBe. There were not revealed cithers AgHBe or anti-HBe in one patient with the diagnosis of mixed chronic viral hepatitis B+C. This fact represents one mutation on the level of AgHBe in chronic viral hepatitis with the virus B. Anti-HBs had not formed in

10 patients with hepatic virus B. Anti-HBs had formed in 3 patients from 10 in control group (30%) and in 1 patient treated with Cytomix.

Data from the tab. 7 show a T cell immunosuppression at the treatment's start in patients with the diagnosis HVBC: in III degree – 37.5%, II degree – 50% with a concomitant lymphocytosis B increase in 75% patients. There was determined

a T cell immunosuppression amelioration till normal values at the end of treatment - in 37.5% patients, but with the B lymphocytosis maintenance of various degrees- in 87.5% patients.

There was determined an immunosuppression: III degree - in 14.3%, II degree - in 71.4% and a B lymphocytosis II degree - in 57.1%, an increased level of CIC - in 28.5% patients with HVCC.

An amelioration of the immunosuppression till normal values was determined in 42.8%, with the normalization of B lymphocytosis - in 57.1% patients at the end of treatment, but in 42.8% it had revealed a tendency to a B lymphocytosis increase in I degree as a result of the humoral reactivity. CIC returned to normal limits in 85.7% and only in one single patient it persisted at increased values, but there were considerably decreased - approximately twice (14.3%).

There were not found positive modifications in patients with the diagnosis mixed chronic hepatitis B+C after treatment. Probably this fact was conditioned by patients a small number.

Tab. 8 shows a T cell immunosuppression persistence in all patients from control group in II and III degree, that constitutes 81.3% and a B lymphocytosis in II degree in 68.7%, CIC with a high level - in 18.75% at the treatment start and with a tendency for increase in 43.7% during the study. These data confirm the need in an immunomodulator treatment.

Conclusions

The combined treatment with Cytomix+Guna liver+Interferon gamma had contributed to:

- the amelioration of clinical symptomatology in patients with HVBC, HVCC and HVBC+HVCC;

- the liver and spleen dimensions had normalized in all patients from the study, but more frequently in patients with HVBC (above 50% of cases) comparatively with patients from control group.

There were found hepatomegaly and splenomegaly in patients of control group with the same frequency before and after treatment:

- there was a moderate decrease of the cytolysis index value (ALAT, ASAT);

- there was established a seroconversion in the AgHBs system in 2 from 8 patients with the diagnosis of HVBC and in 1 from 2 with the diagnosis of HVBC+HVCC;

- the formation of anti-HBs (protective antibodies) comparatively with AgHBs in 3 patients suggests us that these medicines possess probably antiviral capacities.

Anti HVC IgM had been revealed with the same frequency in patients with HVCC both at the start and the end of treatment, that means a possible antiviral capacity in C hepatic virus had not confirmed:

- it was found an amelioration of immune status, which was more marked in patients with HVCC.

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Клиническая эффективность цитиколина в комплексном лечении постреанимационного синдрома

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Отделение реанимации и интенсивной терапии

Муниципальная Клиническая Больница «Святая Троица», Кишинёв

K. Zubarev, I. Baidauz, C. Zota, K. Maxim, V. Sterpu, K. Gutsu-Bahov, B. Scurtu Citicoline Clinical Efficiency in Intensive Therapy of Postresuscitation Syndrome

The problem of global cerebral dysfunction occupies the important place in the postresuscitation syndrome (PRS) clinic. The problems of effective treatment of this dysfunction are still valid today. Recently, for the CNS dysfunctions correction Piracetam has been used. The results of clinical research of two patient's groups (group A and B) with PRS after a successful resuscitation that during standard therapy were included in treatment Citicoline and Piracetam, respectively, have been presented. The citicoline positive influence in PRS clinic on the level of broken consciousness, duration of its violation and on the progressive renewal of mental dysfunctions has been shown. Also, the clinical results of the Citicoline use for patients with PRS have been argued.

Key words: postresuscitation syndrome, global cerebral dysfunction, Citicoline, Piracetam.