

As a manuscript

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**APPLICATION OF HIRODOTHERAPY IN COMPLEX TREATMENT OF PATIENTS WITH TRUE POLICETHEMIA**

Specialty-14 00 51 - restorative medicine, therapeutic

physical culture and sports medicine, balneology and physiotherapy

Abstract of dissertation for the degree of candidate of medical sciences

Moscow, 2007

003060827

The work was performed on the course of restorative medicine of the medical faculty of the Peoples' Friendship University of Russia

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The defense of the thesis will take place 2007 in "/ L hours on

meeting of the dissertation council D 208.060 01 at FGU Russian Scientific Center for Restorative Medicine and Balneology of Roszdrav at: 121069, Moscow, trans. Borisoglebsky, house 9.

The dissertation can be found in the library of the Federal State Institution Russian Scientific Center for Restorative Medicine and Balneology at Roszdrav at. 121069, Moscow, trans. Borisoglebsky, house 9.

The abstract is distributed "

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**GENERAL DESCRIPTION OF WORK.**

The urgency of the problem. One of the areas of restorative medicine is the medical rehabilitation of sick people and people with disabilities with somatic diseases and irreversible and morphological changes in organs and tissues. The goal of restorative medicine is to increase functional reserves, compensate for impaired functions, secondary prevention of diseases and complications, restore reduced labor functions or return limited capacity against the background of partial health deficiency (AL Razumov, IL Bobrovnitsky, 2005) technologies for regenerative medicine amount to natural and other non-drug factors (physical, plant and animal origin), which unlike drugs have milder Train impact on various functional systems, increase their reserve capacity and have virtually no side effects (Anrazumov et al., 1997-

2006). Among such methods, occupational therapy is of particular interest (VA Zhernov, LB Lazebnik, 2001; KG Seleznev, 2003, NL Sulim, 2003).

The medicinal leech *Hirudo medicinalis* provides the effect of bloodletting and is the source of a number of biologically active substances that affect the hemostasis system (Sp. Baskova, 2004, F. Markwardt, 1994, SR. Stone, 1991 IP Baskova, GL Nikonov, AV Mazurov, 1987) These effects inherent in occupational therapy can be very promising in the rehabilitation treatment of one of the problematic diseases of the hematopoietic system, such as polycythemia vera (erythremia, Vaisez disease, polycythemia red), which is a chronic myeloproliferative disease with expressions stem cells, proliferation of germs three hematopoiesis, increased formation of red blood cells and to a lesser extent, platelets and leukocytes, and which are the major manifestations of syndrome plethorichesky erythrocytosis, increase in hemoglobin, hematocrit,

The purpose of the use of restorative medicine technologies for patients suffering from polycythemia is the correction of plethoric syndrome, which allows to level the macro- and microcirculatory organ disorders associated with it, compensate functional disorders and carry out prevention of possible and often fatal complications, and ultimately improve the quality of life of this category of patients

An important role in the correction of the plethoric syndrome is played by mechanical methods of blood exudation, which include venous bleeding by venipuncture and erythrocytapheresis. Often there is a need for their frequent repetition and patients develop poor tolerance for bleeding (RI Komarov, 2003). Both venous bloodletting and erythrocytapheresis sharply reduce the excessive amount of the cellular component of blood, which can cause iron deficiency, as well as the development of "rebound" syndrome

In addition, by mechanically executing blood, these methods dramatically increase the thrombogenic potential, which requires the mandatory medical provision of these procedures with anticoagulants and disaggregates

All this testifies to the need to find new ways of more physiological and affordable for the practical physician to correct the plethoric syndrome in patients with true polycythemia

Purpose of the study. Justification and determination of the effectiveness, feasibility and safety of occupational therapy in the rehabilitation correction of the functional state in the treatment of patients suffering from polycythemia in the complex therapy

Objectives of the study.

1 To study the effect of occupational therapy, venous bleeding, erythrocytapheresis as part of complex treatment on the correction of the plethoric syndrome: the number of erythrocytes, hemoglobin, hematocrit, leukocytes, platelets in patients suffering from true polycythemia based on a comparative analysis of clinical and laboratory indicators

2. To study the dynamics of platelet-vascular and plasma hemostasis on the background of occupational therapy, venous bleeding, erythrocytosis in patients in this category

3. To prove the clinical significance of occupational therapy in the correction of psycho-

emotional disorders and cognitive impairment

4 To study the long-term results of the use of occupational therapy in the rehabilitation treatment of patients suffering from polycythemia.

Scientific novelty.

For the first time, it was shown that the effectiveness of the correction of the plethoric syndrome in patients with true polycythemia is comparable to venous bleeding and erythrocytapheresis and can serve as a method for choosing blood exudation anticoagulants and antiagregaty It was revealed that during occupational therapy clinically significant (over 10% of the original figures) fluctuations art Blood pressure is noted 8.4 times less often than with venous bleeding and 3.7 times less than with erythrocytapheresis. The anxiolytic, thymoleptic and cognitotropic efficacy of occupational therapy was first established in patients with true polycythemia in the form of anxiety disorders reduced by 1.7 times, the level of depression by 2,

Practical significance.

Hirudotherapy comparable in terms of the effectiveness of the correction of hemogram indicators with venous bleeding and erythrocytapheresis has the advantage of excluding drug anticoagulants and antiplatelet agents.

The combined effect of occupational therapy, providing the best tolerability of treatment, allows its use in patients of older age groups with a burdened somatic status.

The revealed changes in psychometric parameters and a lower, compared with venous bleeding and red blood cell fever, the risk of developing secondary hematological complications are essential for the prolongation of the active period of life.

The simplicity of the occupational therapy method, which does not require special equipment and proven safety, makes this method available for use in hospitals of various levels of equipment, both in inpatient and outpatient settings.

Introduction to health care practice. The research materials are introduced into the practice of the work of the City Clinical Hospital No. 60 of the Moscow Department of Health

Level of implementation - local, republican

Provisions for protection.

1 Hirudotherapy provides effective correction of the plethoric syndrome, comparable to venous bleeding and erythrocytapheresis, having a more physiological effect, as evidenced by the absence of abrupt dynamics of hemogram parameters and a significantly less pronounced reactive response from the hematopoietic system.

2 The hematotropic complex of biologically active substances in the composition of the salivary gland secretion of the medicinal leech allows, through occupational therapy, to effectively level thrombophilic changes in the hemostasis system without the use of medicinal anticoagulants and antiplatelet agents

3. Hirudotherapy has a complex mechanism of action, improves the quality of life by correcting psycho-emotional disorders and cognitive impairment, provides secondary prevention of complications and is advisable in the rehabilitation treatment of patients with true polycythemia

Approbation of work. The main provisions were presented and discussed at 9 international and Russian conferences, a joint meeting of the Department of Hospital Therapy and the Course of Restorative Medicine of the Medical Faculty of the Peoples' Friendship University of Russia.

Publications. According to the materials of the dissertation, 12 published works were published, of which 1 were methodical recommendations (co-authored) with the stamp of the Ministry of Health of the Russian Federation, 5 articles, of which 3 - in journals recommended by HAC.

The scope and structure of the work. The thesis has a generally accepted structure, consists of introduction, review of literature, chapters "Materials and methods" and "Results of own research", discussion, conclusions and practical recommendations. The work is presented on pages, illustrated with tables and figures. References are presented by sources (domestic and foreign authors)

CONTENTS OF WORK Material and methods of research.

A total of 96 patients were examined, including 42 men (43.75%) and 54 women (56.25%). The average age was  $67.3 \pm 2.7$  years. 8 (8.3%) patients suffered from the first stage of true polycythemia, 88 patients (91.7%) suffered from the stage of true polycythemia, 52 of them (54.2%) were patients with PA, stage II - 36 (37.5%) patients. The study did not include patients who had , state of hypocoagulation, peptic ulcer and 12 duodenal ulcer in the acute stage, III stage of true polycythemia, allergic reaction to the medicinal leech

Physical methods. Evaluation of the clinical manifestations of true polycythemia was carried out according to the developed protocol of patient management before and after the session, evaluation of the clinical efficacy of treatment, traditional clinical studies

Laboratory methods. The indicators of a comprehensive clinical analysis of blood, plasma and thrombocyte-vascular hemostasis were studied. Blood sampling was carried out in the morning on an empty stomach from a finger, the determination of hemoglobin, hematocrit, blood cells, erythrocyte sedimentation rate was carried out on an automated apparatus "Sysmax" (Japan). The study of plasma hemostasis was performed on the Start Diagnostica Stago coagulograph (France), platelet vascular hemostasis using the Biola Ltd aggregometer (Russia). Blood was collected in the morning on an empty stomach from the ulnar vein.

Instrumental methods. Daily blood pressure monitoring using the monitor MDP-NS-01 (Russia), which is used to monitor blood pressure for 24 hours

Daily Holter ECG monitoring using a MEDITEK monitor (Hungary) with the calculation of the total daily ischemia, the number of episodes of myocardial ischemia per day and the maximum ST segment depression, the total depth (in mm) of all episodes of ST reduction; control of heart rate.

Dopplerography of the intracranial arteries of the head was carried out using the Angiodin ultrasonic Doppler diagnostic system with the Doppler Diagnostics software (Russia) with a frequency sensor

2 MHz, operating in pulsed mode, recorded average blood flow velocity ( $V_m$ ), pulsating index PI (Gosling index), peripheral vascular resistance index RI (Pourcelot index) in the middle cerebral arteries (SMA, Ml) and main artery (OA) paired arteries (SMA) was determined hemispheric linear velocity asymmetry (CA). The study was conducted twice before treatment and the 24th day of treatment

Neuropsychological testing. Questionnaire "Hospital Anxiety and Depression Scale" - as a tool for identifying and assessing the dynamics of anxiety and depression in general medical practice in somatic patients

Brief scale of mental status - MINI-MENTAL STATE EXAMINATION (MMSE) (MF Folstein, SE. Folstein, PR Hugh, 1975) - a brief 11-point scale assessing cognitive impairment in six aspects orientation, registration, attention, ability to account, memory, language, praxis. Methods of rehabilitation treatment.

Patients were divided into three treatment groups, taking into account the method of blood exhalation, comparable to the main clinical indicators of one main and two comparison groups (Table 1).

Table 1

Patient groups

Indicator 1st group n = 32 2nd group n = 32 3rd group n = 32

The method of blood exfusion Hirudotherapy (GT) Venous bloodletting (VC) Erythrocytapheresis (EF)

According to the format of the study, in the 1st group, blood exhalation was carried out by an occupational therapy (GT) method using standard medical leeches (NTS) in a volume of  $118.0 \pm 3.7$  ml of blood every other day, zones productions were determined by concomitant symptomatology, in the 2nd group - venous bleeding (VC) by venipuncture 1 every 4 days in 350.0 ml of blood, in the 3rd group - red blood cell (EF) 1 every 4 days in 350.0 ml blood. Sessions of exfusion therapy were carried out before normalization of laboratory parameters.

Allocated the following criteria for the effectiveness of treatment "improvement" - a combination of positive dynamics of both subjective and objective characteristics, "minor improvement" - positive changes only subjective indicators, "no effect", "deterioration".

Studies were conducted in dynamics, with computer-statistical data processing by the Student's criterion and the alternative Fisher criterion, which allows to evaluate the reliability of differences in the frequency of occurrence of a particular trait.

## RESULTS OF OWN OBSERVATIONS AND THEIR DISCUSSION

According to the research format, in the 1st group, an average of  $9.3 \pm 0.21$  was carried out, in the 2nd -  $4.6 \pm 0.12$ , in the 3rd group -  $4.7 \pm 0.12$  sessions of blood exsation

On the background of the treatment, a significant decrease in the number of erythrocytes, hemoglobin, hematocrit in all three groups was revealed, is presented in table 2.

table 2

Dynamics of erythrocytes, hemoglobin, hematocrit on the background of various \_\_\_ exfusion methods\_

Groups Indicators

BSh, ( $\times 10^{12}$  / l) NOV, (g / l) BST, (%)

Group I (GT) n = 32 TO treatment  $7.18 \pm 0.43$   $173 \pm 9.49$   $52.9 \pm 1.50$

24th day  $4.37 \pm 0.32$   $142 \pm 5.15$  \*  $43.2 \pm 0.95$

P group (VK) p = 32 TO treatment  $7D6 \pm 0.41$   $176 \pm 8.72$   $53.1 \pm 1.37$

24th day  $4.24 \pm 0.53$   $133 \pm 5.81$   $42.1 \pm 1.03$

W group (EF) p = 32 before treatment  $7,16 \pm 0,34$   $173 \pm 6,35$   $52,9 \pm 1,45$

24th day  $4.20 \pm 0.29$   $128 \pm 4.87$   $42.9 \pm 1.12$

Note within groups, differences are statistically significant ( $p < 0.001$ ),

\* - statistically significant difference of the studied group with control groups

( $P < 0.001$ )

Analysis of the obtained data suggests that by the 24th day of treatment, erythrocytes and hematocrit in the 1st group (GT) significantly ( $p < 0.001$ ) decreased by 35.1% and 17%, respectively red blood cells by 36.3%

36.9% in erythrocytapheresis ( $p \ll \text{SCHN}$ ), hematocrit - in 20.6% in venous bleeding and 18.9% in erythrocytapheresis ( $p < 0.001$ ). There were no statistically significant differences in these parameters in the studied and control groups, which indicates the equivalence of methods in the final correction of these hemogram indicators. In the control groups, hemoglobin decreased by 24.3% in the 2nd group (VC) and by 26% in the 3rd group (EF), which is significantly higher ( $p < 0.01$ ) of this indicator in the 1st group (GT), where its decrease was 17.9%, as shown in Table 2.

This confirms the possibility of anemization of patients with this pathology in mechanical methods of exfusion of blood.

The nature of the decrease in hemogram values in the studied groups had its own characteristics (Fig. 1). In the 1st group (GT), the decrease in red blood cells, hemoglobin, hematocrit was milder, maintaining a tendency to decrease throughout the treatment.

8 7 6 5 4 3 2 1 About

Fig. 1, Dynamics of changes in the level of erythrocytes ( $\times 10^3$  / l) in the blood with different methods of treatment. In each troupe, all values are presented in the following order - before treatment and after 4, 8, 12, 16, 20 and 24 days of treatment.

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So, in the 1st group (GT) by the 12th day there was a slight increase in red blood cells (2%) compared with the previous blood test. In the control groups, an abrupt growth of erythrocytes was observed by the 8th day by 11.6%. by the 16th day by 20.8% ( $p < 0D > 1$ ) in the 2nd group (VC); to 8-wise by 15.5%, to the 16th day by 21.7% ( $p < 0.01$ ) in the B-group

(EF). Thus, in the control groups, the instability of the dynamics of the number of erythrocytes was revealed, mostly in the 3rd group (EF). Dynamics of

1st group <GT> 2nd group (VK) 3rd group {EF}

matokokrita in all groups maintained a tendency, similar to the dynamics of erythrocytes, to an abrupt type of change, which Figure 2

Figure 2 Dynamics of hematocrit in the treatment process when using various methods of blood exfusion

These data confirm the need for venous bleeding and erythrocytapheresis to include disaggregants and anticoagulants in treatment regimens in order to avoid thrombotic complications, the risk of which increases at the height of this indicator

The dynamics of hemoglobin parameters was of a different nature (Fig. 3)

treatment

Figure 3 Dynamics of hemoglobin parameters in the treatment process when using various exfusion techniques

There was a corresponding rise in red blood cells, an increase in hemoglobin by the 8th day by 12.1% in the 2nd group (VC) and 13.2% in the 3rd group (EF), no further fluctuations in the level of this indicator were noted in spite of the spasmodic dynamics of red blood cells, which may indicate a pronounced

different degree of hypochromia of new pools of abnormal erythrocytes.

Changes in the number of reticulocytes observed in all three groups. In the 1st group (HT), reticulocytosis was observed in 6 (18.7%) patients and did not exceed  $14.7 \pm 2.3$  ( $\times 10^9 / l$ ). Reactive reticulocytosis was most pronounced in the 3rd group (EF) and was observed in 18 (56.2%), reaching a level of  $32.7 \pm 3.1$  ( $\times 10^9 / l$ ) In the 2nd group (VC), these figures were respectively 15 (32.2%) patients and  $28.8 \pm 2.7$  ( $\times 10^9 / l$ ), while the differences in indicators in the main and control groups were statistically significant ( $p < 0.01$ ). The obtained data indicate a high sensitivity of bone marrow hematopoiesis patients with true polycythemia to hemorrhagic manipulations and indicate a more physiological nature of hirudotherapy

During treatment, a change in the number of leukocytes and platelets in all 3 groups was also noted. In group 1 (GT), leukocytosis with blast cells was observed in 4 (12.5%) patients and averaged  $10.3 \pm 0.43$  ( $\times 10^9 / l$ ), while in the 2nd (VK) and 3rd (EF) groups, leukocytosis with the presence of blast forms was observed in 10 (31.2%) and 13 (40.6%) patients and amounted to  $12.6 \pm 0.75$  and  $13.8 \pm 0.71$  ( $\times 10^9 / l$ ), respectively, which is significantly higher ( $p < 0.01$ ) than in the 1st group (GT) (Fig. 4)

Figure 4 Dynamics of the concentration of leukocytes in the blood in the treatment process with the use of various exfusion techniques

Leukopenia was not observed in the main group; in the control groups, leukopenia was noted in isolated cases (in 1 patient of the 2nd group (VC), in 2 patients of the 3rd group (EF))

These data reflect the reactive response of the granulocyte germ and should certainly be alarming in the conditions of the neoplastic nature of blood

The dynamics of the number of platelets, taking place against the background of the use of various methods of blood exudation, is presented in Figure 5

■  $< 180 \times 10^9 / l$  □  $(180-320) \times 10^9 / l$  □  $> 320$  [1 (G / c

1st group (PG) 2nd group (VK) 3rd group (EF)

Figure 5 Dynamics of the number of platelets in the peripheral blood in the treatment process with the use of various exfusion techniques

Analysis of the data showed that when using occupational therapy in 28 (87.5%) patients, changes in platelet count did not go beyond the laboratory norm, thrombocytosis was observed in 4 (12.5%) patients within  $396.8 \pm 23.5$  ( $\times 10^9 / l$ ), which is significantly lower ( $p < 0.01$ ) than in the comparison groups, where thrombocytosis was observed in 11 (34.3%) patients of the 2nd group (VC) and was  $512.4 \pm 63.3$  and in 14 (43.7%) patients of the 3rd group (EF)  $533.6 \pm 72.4$  ( $\times 10^9 / l$ ) At the same time there was no thrombocytopenia in the 1st group (GT), in the 2nd (VC) and 3 th (EF) groups thrombocytopenia was observed respectively in 5 (15.6%) patients per level not  $128.3 \pm 20.6$  ( $\times 10^9 / l$ ) and in 6 (18.7%) patients of the 3rd group at the level of  $123.6 \pm 22.1$  ( $\times 10^9 / l$ ), which to some extent can be associated with adverse the action of geyarinoterapii conducted by patients in the control groups.

An important property of the salivary gland secretion of the medicinal leech is its ability to reduce platelet aggregation, both spontaneous (due to the presence of viburnum in the secret) and induced by ADP, collagen, adrenaline (due to the presence of alirase, collagenase in the secret). A decrease in spontaneous platelet aggregation was observed in all 3 groups In the VC group, it was 43.7%, in the EF group - 46.6%, in the GT group - 38.2%. The results of the analysis of the obtained values of 5tkM ADP induced platelet aggregation are presented in table 3

5shkM ADP induced platelet aggregation, (%)

Groups before treatment 4th day 8th day 12th day 16th day 20th day 24th day

Group 1 (GT)  $79.2 \pm 1.8$   $65.6 \pm 2.5$  17.2%  $58.5 \pm 2.2$  26.1%  $53.4 \pm 1.7$  32.5%  $53.8 \pm 1.6$  32%  $53.3 \pm 1.4$  32.7%  $52.1 \pm 3.2$  \* # 34.2%

Group 2 (VK)  $76.9 \pm 3.4$   $64.5 \pm 2.6$  16.1% 55, III, 9 28.3%  $45.4 \pm 2.1$  40.9%  $40.3 \pm 2.6$  47, 5%  $37.7 \pm 2.4$  50.9%  $36.7 \pm 2.3$  \* 52.2%

Group 3 (EF)  $78.5 \pm 3.1$   $65.2 \pm 3$ , b 16.9%  $53.4 \pm 2.1$  31.9%  $44.7 \pm 1.9$  43%  $41.8 \pm 2$ , 7 43.1%  $38.5 \pm 3.2$  50.9%  $38.3 \pm 3.4$  \* 51.2%

Note \* significant differences within groups ( $p < 0.001$ ), # reliable differences

the study group with control groups ( $p < 0.001$ )

As can be seen from the data presented on the background of the treatment, the thrombotic potential decreases in all groups, but in the control groups it is more pronounced and by the 16th day a shift towards antiaggregation is observed. The decrease in 5t ADT induced aggregation in the 2nd group (IC) was 52, 7%, in the 3rd (EF) group -51.2%, which is significantly higher ( $p < 0.001$ ) than in the 1st group (GT), where 5t ADT induced platelet aggregation decreased by 34.2% and amounted to  $52, 1 \pm 3.2$  (%) ( $p < 0.001$ ), which is within the physiological values of this indicator and indicates sufficient these antiplatelet potential of GT in the dose used without the use of drug antiplatelet agents

Considering that the influence of the medicinal leech on plasma hemostasis is carried out at the level of the internal coagulation mechanism, without activating the external, to study the effect of MP on plasma hemostasis, we investigated the indicators of activated partial thromboplastin time (APTT) increase in plasma fibrinolytic activity (FA) of varying severity in all 3 groups (Table 7)

Dynamics of APTT and fibrinolytic activity (FA)

Indicator I group (GT) n = 32 II group (VC) n = 32 III group (EF) n = 32

before treatment 24th day before treatment 24th day before treatment 24th day

APTT (s)  $23.1 \pm 0.6$   $32.4 \pm 0.8$  \*  $23.7 \pm 1.8$  41, SD  $22.9 \pm 1.7$   $9.9 \pm 2.1$

FA (min)  $26.8 \pm 1.4$   $8.1 \pm 0.8$  \*  $28D \pm 1.7$   $3.8 \pm 0.5$   $27D \pm 1.4$   $4.1 \pm 0.7$

Note \* - statistically significant differences with control groups

$p < 0,001$

By the 24th day of treatment, effective correction of these disorders was observed both in patients of the control groups receiving anticoagulant therapy and in the main group not receiving anticoagulants. In the 1st group (HT), the APTT increased by 40.4% and amounted to  $32 \pm 4 \pm 0.8$  (sec), which indicates the normalization of this indicator, while in the 2nd (VK) and 3rd (EF) groups of APTT increased by 73.4% and 74.2% and amounted to  $41.1 \pm 1.2$  and  $39.9 \pm 2.1$  (s), respectively, which was significantly higher ( $p < 0.001$ ) than in the 1st group and indicates a significant hypocoagulation shift, creating a certain risk of hemorrhagic complications. The mean value of FA by the 24th day of treatment in the 1st group (GT) was  $8.1 \pm 0.8$  (min), in the control groups of FA it decreased to  $3.8 \pm 0.5$  (min) with VK and  $4.1 \pm 0.7$  (min) with ESP, which is significantly lower than in the main group ( $p < 0$ ),

In a psychometric study using the Hospital Anxiety and Depression Scale, anxiety disorders were detected in 10 (31.2%) patients of the 1st group, 8 (25%) patients of the 2nd group and 12 (37.5%) patients of the 3- Depression of varying severity was detected in the 1st group in 17 (53.12%) patients, in the control groups it was detected in 14 (43.73%) and 13 (40.62%) patients. By the 24th day treatment analysis of psychometric indicators revealed a decrease in the level of relevant disorders in varying severity

Anxiety disorders decreased in all groups, but in the control groups it was not statistically significant ( $p > 0.05$ ). In group 1 (GT), the level of anxiety

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decreased by 39.8% from baseline and amounted to  $5.5 \pm 0.36$  points ( $p < 0.001$ ). The decrease in the level of anxiety in the control groups was 7.4% for venous bleeding and 4.9% for erythrocytapheresis, reaching  $8.17 \pm 0.83$  and  $8.76 \pm 0.69$  points, respectively.

The dynamics of depressive disorders in the form of an increase in the thymoleptic effect clearly emerged in the 1st group of (HT), where the baseline indicators  $11.23 \pm 0.35$  points decreased to  $4.9 \pm 0.28$  points ( $p < 0.001$ ), which amounted to 56.36%. In the control groups, the dynamics of depressive disorders were also characterized by their decrease, but to a much lesser extent and without statistical significance ( $p > 0.05$ ). Comparison of the dynamics of psychometric parameters in the studied groups revealed a reliable ( $p < 0.001$ ) anxiolytic and thymoleptic efficacy of occupational therapy, which does not contradict the literature data (Z.V. Yasnopolskaya, 1983, LV Voloshina, OA Bukhanovskaya 2001)

The study of the state of cognitive functions revealed disorders, the severity of which correlated with the degree of cerebrovascular disorders. In patients of the 2nd (VC) and 3rd (EF) improvement groups in the cognitive sphere had no statistical significance ( $p > 0.05$ ). Significant positive dynamics of these indicators were detected in the 1st group (GT). The maximum cognitotropic effect was observed in patients younger than 65 years and amounted to 9.31%, reaching a level of  $27.1 \pm 0.22$  points ( $p < 0.01$ ). groups of positive dynamics amounted to 6.16%, reaching a level of  $24.1 \pm 0.22$  ( $p < 0.001$ ) points. A comparative analysis of the obtained results revealed a reliable ( $p < 0$ ),

Improvement of cerebral hemodynamics, which undoubtedly occurred during correction of the plethoric syndrome, contributed to the improvement of cognitive functions to a certain extent.

A comparative assessment of blood flow in the SMA and OA revealed in patients of the 1st group (GT) an increase in the average blood flow rate in the MCA by 11.2%, in OA by 9.93% ( $p < 0.001$ ), while the decline and amounted to 8.04% and 6.10% ( $p < 0.01$ ), decrease in M -7.54% and 7.27% ( $p < 0.05$ ), inter-hemispheric asymmetry decreased by 8.57% ( $p < 0.01$ ). In control groups, the dynamics of the studied parameters was less pronounced \* an increase in the mean blood flow velocity along the SMA and OA was 6.1% and 5.06% at VK

( $p < 0.01$ ), with EF - 6.26% and 4.88% ( $p < 0.01$ ), decrease in P1 was at VK 4.21% and 3.10%, with EF - 4.11% and 2.97% ( $p < 0.05$ ) M decreased by 3.92% and 3.92% with VC and by 3.70% and 3.57% with EF. The decrease in inter-hemispheric asymmetry was 4.71% with VC and 5.1% ( $p < 0.05$ ) with ESP. The increase in blood flow velocity in the intracranial vessels with a decrease in the pulsation index, the circular resistance index and the degree of interhemispheric asymmetry of the blood flow, was most pronounced during occupational therapy ( $p < 0.01$ ), which is undoubtedly due to its ability not only to level the plethoric syndrome, to improve rheological properties of blood, but also with its inherent reflex-humoral ability to regulate (in this case reduce) peripheral resistance in the cerebral arteries of the middle and Christmas caliber

The tolerability of various methods of blood exudation is presented in Table 5, which demonstrates a clear advantage in the degree of tolerability of the procedure in patients of the 1st group (HT).

Table 5



Tolerability of various methods of blood exudation (1st day)

Signs 1st group (GT) 2nd group (WY \* 3rd group (EF) #

n% n% n%

Weakness 3 "# 9.37 13 40.6 11 34.3

Headache 1 \* 3.12 7 21.8 5 15.6

o E Vertigo 0 \* # 0 7 21.8 4 12.5

Cooling limbs 0 0 2 6.25 0 0

and >0 Nausea 0 0 4 12,5 3 9,37

Heart pain 0 0 3 9.37 1 3.12

Sinus tachycardia (TACHY) 0 \* 0 5 # 15.6 2 6.25

Sinus bradycardia (BRADY) 0 0 2 6.25 3 9.37

U Paired ventricular extrasystoles (COUPLET) 2 6.25 5 15.6 4 12.5

Single supraventricular extrasystoles (SINGLE SVE s) 1 \* # 3.12 5 15.6 4 12.5

about depression ST 0 0 3 9.37 2 6.25

Note superscripts show significance of differences between groups on the Fisher alternative criterion.

17

Increased systolic blood pressure was more common in the 3rd group (EF) (in 24 patients) by  $7.6 \pm 2.8$  (%) from baseline, less often in the 2nd group (VC) (in 10 patients) on 7,  $1 \pm 2.4$  (%) and significantly less and to a lesser extent in the 1st group (GT) (in 6 patients) by  $3.75 \pm 1.2$  (%) ( $p < 0.001$ ) Decrease in systolic blood pressure it was more often noted in the 1st (GT) (in 24 patients) and 2nd (VC) (in 22 patients) groups, but in the 1st group it was  $5.2 \pm 0.8$  (%) from the initial level, which is significantly lower ( $p < 0.001$ ) than in the control groups, where the indicator was

$8.3 \pm 2.7$  and  $8.5 \pm 2.4$  (%) in the 2nd (VC) and 3rd (EF) groups, respectively. Raising of the diastolic blood pressure in the 1st group (GT) was detected in 4 patients and was clinically insignificant, making up  $1.6 \pm 0.4$  (%) of the initial level In the comparison groups, the rise of diastolic blood pressure was observed in 10 patients of the 2nd group (VC) and in 18 patients of the 3rd group (EF) at 3,  $4 \pm 1.3$  and  $4.1 \pm 1.7$  (%), respectively. A decrease in diastolic blood pressure was detected in 28 patients of the 1st group (GT), 22 patients of the 2nd group (VC) and 14 patients of the 3rd group (EF) and did not reach the clinically significant level, respectively  $9.1 \pm 0.4$ ,  $8.4 \pm 1.7$  and  $8.2 \pm 2.0$  (%).

Adverse events revealed during the study of tolerability of occupational therapy, due to their clinical insignificance did not cause premature termination of treatment with this method

Further monitoring of patients with monthly laboratory control did not reveal any reliable dependence of the timing of the appearance of hematological changes from the previous method of blood exudation. Patients of the 1st group repeated courses were conducted with an increase in the level of erythrocytes and hematocrit by 710%. In the 1st group (GT), 21 patients were treated 2 times a year, 7 patients 1 time a year, 4 patients had year there was no evidence for exfusion treatment. In the control groups, the exfusion treatment was administered based on traditional criteria. The majority of patients 19 (%) in the 2nd (VC) and 16 (%) in the 3rd (EF) groups received exfusion treatment 1 time per year, 10 (%) and 12 (%), respectively, twice a year.

The frequency of ischemic events requiring hospitalization for 12 months of follow-up is shown in Table 6.

Table 6

Frequency Ischemic events throughout the year

Complication 1st group (GT) 2nd group (VK) 3rd group (EF)

n% n% n%

Myocardial infarction 0 0 2 "6.25 1" 3.12

Cerebral infarction 0 3,12 0 1 3,12

TELA 0 0 0 0 1 "3.12

Unstable angina 1 3.12 1 3.12 2 6.25

TIA 0 0 2 6.25 1 3.12

Retinal thrombosis 0 0 1 3,12 0 0

Acute thrombosis of the popliteal artery 1 3.12 0 0 0 0

Thrombophlebitis of the lower extremities 0 0 1 3.12 0 0

Total 2 9.37 7 21.8 6 18.7

Note: • - case of death

Thus, regular laboratory monitoring (at least 1 time per month) and conducting occupational therapy with an increase in the level of red blood cells and hematocrit already within 7-10% impede the development of pronounced plethoric syndrome and complications, including fatal ones.

#### FINDINGS

1 Comparative analysis of clinical, functional and hematological parameters in hirudotherapy, venous bleeding, erythrocytapheresis revealed the effectiveness of correction of the plethoric syndrome in occupational therapy, no less than in venous bleeding and erythrocytapheresis. Reduction of erythrocytes has a systematic character without spasmodic rises characteristic of venous bloodletting and erythrocytapheresis by the 8th and 16th days 95.8% lower than in erythrocytapheresis.

nineteen

Reactive leukocytosis in occupational therapy is 1.8 times less than in venous bleeding and 4.4 times less than in erythrocytapheresis. Reactive thrombocytosis in occupational therapy is less pronounced, it is noted in 10.5% of cases, which is 2.8 times less often than in venous bloodletting, and 3.7 times less often than in erythrocytapheresis systems for occupational therapy, which is very important in conditions of the neoplastic nature of blood formation in true polycythemia

2 Dynamics of platelet-vascular hemostasis and plasma demonstrated that occupational therapy effectively corrects thrombophilic disorders in patients with polycythemia vera, reducing spontaneous platelet aggregation at 38,2%, 5mkm ADP-induced platelet aggregation 34.2%, the fibrinolytic activity of plasma of 3.3 times, increasing the level of APTT by 1.7 times, leads to the normalization of these indicators without the use of medicinal anticoagulants and antiplatelet agents

3 Hirudotherapy effectively corrects psycho-emotional disorders, reducing anxiety levels by 38.8%, and depression by 56.3%, increasing cognitive potential in patients younger than 65 years old by 9.31%, in patients older than 65 years old

by 6.16% , which is significantly higher than these indicators in venous bleeding, erythrocytapheresis and is a factor that improves the quality of life of these patients

4. According to the daily blood pressure monitoring during occupational therapy, clinically significant (over 10% of baseline numbers) fluctuations in blood pressure values are detected in only 9.4% of patients in the occupational therapy group, while in venous bleeding - in 37.5%, and with erythrocytapheresis in 34.3%. Negative ECG dynamics according to the daily ECG Holter monitoring were not observed during occupational therapy, while in venous bleeding it was observed in 25%, and in erythrocytapheresis in 12.5% of patients. This indicates a better tolerability of occupational therapy in comparison with venous bleeding and erythrocytapheresis. 5. According to the results of remote studies, it was established that the persistent positive effect of the use of occupational therapy as part of complex treatment lasts for  $5.4 \pm 0.8$  months in 69,

a group of patients who received venous bleeding, 3 times with a group of patients who received erythrocytapheresis.

#### PRACTICAL RECOMMENDATIONS

Hirudotherapy as a corrective technology of restorative medicine, it is advisable to use in complex treatment of patients with true polycythemia. Exclude patients with laboratory signs of hypocoagulation, gastric ulcer and 12 duodenal ulcer in the acute stage, W stage of true polycythemia, allergic reaction to medical leech. Use certified standard medical leech. Hirudotherapy should be aspirated, in the position of the patient lying, under control of hemodynamic parameters and applying a sterile dressing on the skin wound area. Efficiency of treatment should be monitored by laboratory and instrumental methods. At least 2 times at initial laboratory manifestations of plethoric syndrome. year

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before

Order number 462. Volume 1 square. Circulation 100 copies.

Printed by Petrush LLC. Moscow, st. Paliha-2a, tel. 250-92-06 www.postator.ru

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