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Research Article

Effect of Efferent Therapy on Clinical and Laboratory Parameters in Complex Treatment of Patients with Thromboangiitis Obliterans at the Critical Ischemic Stage

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Abstract

The Aim of the Study: To improve the results of conservative and surgical treatment of Buerger's disease (BD) using plasmapheresis (PF) and ultraviolet irradiation of blood (UVİB).

Materials and Methods: the studies were carried out in 170 patients (study group-89, control group-81) with grade III-IV critical limb ischaemia and in patients with stage II-III chronic ischaemia (216 pain in total). Contrast angiography and duplex scanning of peripheral arteries, computed rheography and plethysmography were performed, oxygen partial pressure (tcpO2) was measured, and general clinical, biochemical and immunological studies were performed. In addition to surgical operations, complex drug therapy was carried out in both groups. PF procedures were carried out - in case of unbearable pain and intoxication, 3-6 operations every 1-2 days, in other cases 2-3 with a break of 3-5 days with an exfusion of 700-1500 ml of plasma, and 4 (8) mg of dexamethasone was administered (in 3 patients-pulse therapy: 1000 mg of metipred for 3 days). The number of UVIB determined the severity of BB and was performed every 1-2 days, from 5 to 10 sessions. Patients from both groups underwent catheterization epidural analgesia (CEA) at the LII-LIII level and administered 10 ml of 2% lidocaine solution every 3-6 hours for 7-14 days to prevent acute pain. In the study group, all patients underwent PF in parallel.

Outcomes: In comparison with the parameters in the patients of the control group in the study group, there was a significant improvement in many instrumental and laboratory studies (RI, ABI, TcpO2, CIC, DE, F, IgG, LA (respectively $t = 2.12$, $p < 0.05$; $t = 2.00$, $p < 0.05$; $t = 21.20$, $p < 0.001$; $t = 3.64$, $p < 0.001$; $t = 5.57$, $p < 0.001$; $t = 3.77$, $p < 0.001$; $t = 4.89$, $p < 0.001$; $t = 14.14$, $p < 0.001$) except for PA, CRP, İgM and ESR. Immediate satisfactory results significantly depend on the tactics of complex treatment ($\chi 2 = 8.907$; $p = 0.003$). The reduction in the frequency of "large + small" amputation in patients of the study group also significantly depends on the tactics of complex treatment ($\chi 2 = 6.815$; $p = 0.010$).

Conclusion: The use of ET methods in the presented treatment regimen (CEA + PF + UV + glucocorticosteroid + drug therapy) made it possible to correct the multilateral disorders caused by Buerger's disease and improve the results of complex treatment.

Keywords: Buerger's Disease; Critical Ischemia; Plasmapheresis; Ultraviolet Irradiation of Blood; Epidural Analgesia

Introduction

Thromboangiitis obliterans (TO) (Buerger's disease) is a polyetiological and polypathogenetic disease, characterized mainly by distal lesions of the arteries of the lower and upper extremities. The disease is especially common in the countries of Southeast Asia, and is relatively rare in European countries [1,2].

Among the etiological factors, tobacco smoking, impaired immune system of the body [3,4], imbalance in the cytokine status of the body [5], increased homocysteine in the blood, and other disorders in homeostasis play a particularly important role [6,7].

Due to damage to the distal segment of the arteries, TO is treated conservatively using various methods of conservative therapy [8-11], but the short- and long-term results obtained do not always satisfy patients and clinicians [12].

In recent years, indirect methods of revascularization alone and in combination with gene therapy have been successfully used to treat patients with thromboangiitis obliterans in critical ischemia [13-16].

Thanks to the development of high technology, endovascular methods of direct revascularization began to be widely introduced in clinical practice with encouraging results [17-19].

Material and Methods of Research

The study was carried out in 170 patients with Buerger's disease in the stage of III-IV degree of chronic ischemia, who are on inpatient treatment in the Department of Vascular Surgery, and in 46 patients with the same pathology in the stage of II-III degree of chronic ischemia, who are in the day hospital of the Department of Extracorporeal Detoxification of the Scientific Center of Surgery named after academician M.A. Topchubashov. To establish the diagnosis of thromboangiitis obliterans, the criteria of Shionoya S. (1998) [20] Out of 170 patients, 89 patients underwent efferent therapy (study group), in 81 cases complex treatment was carried out without the use of efferent therapy (control group). The age of the patients ranged from 18 to 65 years. There are 200 men and 16 women. Anamnestically, tobacco smoking was detected in 97.9% of patients. Terms of development of critical limb ischemia: in the acute stage of the disease - 2-4 weeks; in the chronic form of pathology - from 6 months to several years. The level of arterial occlusion in patients on inpatient treatment: occlusion of the crural arteries in 101 (59.4%) patients; stenoocclusion of the arteries of the femoropopliteal segment in 57 (33.5%) patients; steno-occlusion of the iliacofemoral segment in 12 (7.1%) patients. Plasmapheresis was carried out by filtration and gravitational methods on the apparatus "Gambro" (Sweden) and "Rotixa 50RS" (Germany). Since 2015, the device for plasmapheresis "Haemonetics MCS+ (USA") has also been used.

Filtration plasmapheresis was carried out in the acute and subacute phases of the disease 3-6 sessions every 1-2 days. The volume of exfusion plasma was 700-1500 ml. Gravitational plasmapheresis was carried out at the chronic stage of the disease 2-3 sessions every 2-3 days. The volume of exfusion plasma at each session was 400-500 ml. Exfusion plasma was compensated by intravenous injection of an adequate volume of 0.9% sodium chloride solution and protein preparations. Taking into account changes in the humoral system in 89 patients, after exfusion of 700-1500 ml of plasma, 4 (8) mg of dexamethasone was administered intravenously, only 3 patients underwent pulse therapy with methipred (1000 mg) for 3 days.

The patients were comparable in terms of the duration of the disease, the period of exacerbation, the level of arterial damage, the degree of chronic ischemia, the nature and volume of drug therapy.

Ultraviolet irradiation (UVI) of autoblood with the apparatus "Isolda" (Russia) and "Julia" (Russia). In the acute phase of the disease, 10 sessions were carried out daily, in the chronic stage - 5-6 sessions in 1-2 days.

To relieve acute pain at the level of Lii-Liii, caterization epidural analgesia was performed with the introduction of 2%-10 ml of trimecaine solution or 0.5%-3-5 ml of bupivacaine solution after 3-4 hours for 7-14 days, depending on pain relief. In the study group, stage III of chronic ischaemia was observed in 8 (9.0%) patients, stage IV of chronic ischaemia was observed in 81 (91%) patients, and catheterization epidural analgesia was used in 45 (50.6%) of them.

To establish a diagnosis and assess the effectiveness of the complex treatment in dynamics, instrumental [multispiral computer-tomographic peripheral angiography, Doppler

ultrasound with ankle-brachial index (ABI), rheovasography with rheographic index (RI), thermovisiometry, determination of the partial pressure of oxygen in the skin (tcpO2)] and laboratory studies [erythrocyte deformability (ED), circulating immune complex (CIC), C-reactive protein (CRP), Ig G, Ig M, fibrinogen (F), fibrinolytic activity (FA), lactate (L), erythrocyte sedimentation rate (ESR)].

The obtained clinical, instrumental and laboratory data were processed by the method of parametric and nonparametric statistics with the calculation of M ± m, Student's t-tests at the level of confidence P = 0.95 ($p < 0.05$), Pearson criteria of agreement ($\chi 2$) at the level of confidence P = 0.95 ($p < 0.05$).

Results Obtained and their Discussion

In patients with stage I and II chronic ischaemia treated in the day hospital, 12 (26.1%) patients underwent plasmapheresis (PF) (25 procedures), 10 (21.7%) patients underwent ultraviolet irradiation of blood (UVIB) (28 procedures), and 24 (52.2%) patients underwent PF+UVIB (53 procedures), and all patients underwent complex drug therapy (CDT). This group of patients did not undergo catheterization epidural block (CEB), lumbar sympathectomy and vascular reconstructive surgery (Table 1).

Treatments	Main group, n = 135		Control group n = 81
	Outpatient treatment (grade I-II ischemia) n = 46	Inpatient treatment (grade III-IV ischemia) n = 89	
Plasmapheresis (PF)	12 (26,1%) -25 (procedures)	27 (36,3%) -108 (Procedures)	-
Ultraviolet irradiation of blood (UVIB)	10 (21,7%) -28 (procedures).	15 (16,9%) - 82 (procedures)	-
PF +UVIB	24 (52,2%) -53 (procedures)	47 (52,8%) - 221 (procedures)	-
Long-term epidural block (LEB)	-	45 (50,1%)	72 (88,9%)
Lumbar sympathectomy (LSE)	-	28 (31,5%)	65 (80,3%)
Vascular plastic surgery		8. (9,9%)	24. (29,6%)
Drug treatment	100%	100%	100%

Table 1: Methods of efferent therapy and surgical treatment in patients with Buerger's disease.

In 46 patients treated in the day hospital, only efferent therapy and drug treatment were performed. In 89 patients treated in an inpatient setting, efferent therapy and drug treatment were carried out simultaneously with surgical placements and prolonged epidural block. And in 81 patients of the control group, drug treatment was carried out simultaneously with surgical receptacles and long-term epidural block.

The results of instrumental and laboratory studies were analyzed. It was revealed that the parameters of instrumental studies (RI, ABI, TcpO2) significantly improved in both groups. Laboratory parameters (CIC, ED, F, FA, SRP, IgG, Ig M, ESR, LA) are also significantly improved, except for PSA and IgM in the control group (Table 2). In comparison with the parameters in the patients of the control group, there was a significant improvement in many instrumental and laboratory studies in the study group (RI, ABI, TcpO2, CIC, ED, F, IgG, AD respectively $t = 2.12$, $p < 0.05$; $t = 2.00$, $p < 0.05$; $t = 21.20$, $p < 0.001$; $t = 3.64$, $p < 0.001$; $t = 5.57$, $p < 0.001$; $t = 3.77$, $p < 0.001$; $t = 4.89$, $p < 0.001$; $t = 14.14$, $p < 0.001$) except for FA, CRP, IGM and ESR (respectively $t = 1.73$, $p > 0.05$; $t = 1.07$, $p > 0.05$; $t = 0.04$, $p > 0.05$; $t = 1.22$, $p > 0.05$).

Indicators	Before treatment	After treatment	
		Main group	Control groups
Rheographic indx (RI) (unit)	0,12 ± 0,07	0,9 ± 0,08 (t = 7,34; p < 0,001)	0,66 ± 0,05 (t = 6,28; p < 0,001)
Ankle-brachial index (ABI) (unit)	0,33 ± 0,04	0,8 ± 0,09 (t = 4,77; p < 0,001)	0,61 ± 0,03 (t = 5,60; p < 0,001)
$TcpO_{2,}$ mmHg	27,3 ± 0,75	49,5 ± 0,4 (t = 26,2; p < 0,001)	38,9 ± 0,3 (t = 14,36; p < 0,001)
Circulating immune complex (CIC), (unit)	165,4 ± 11,3	68,2 ± 4,7 (t = 7,94; p < 0,001)	99,8 ± 7,3 (t = 4,88; p < 0,001)
Red blood cell deformability (ED)(unit)	1,35 ± 0,12	1,9 ± 0,65 (t = 4,23; p < 0,001)	1,6 ± 0,02 (t = 2,05; p < 0,05)
Fibrinogen (F)(mq)	16,9 ± 0,8	12,6 ± 0,3 (t = 5,03; p < 0,001)	14,8 ± 0,5 (t = 2,23; p < 0,05)
Fibrinolytic activity (FA) (%)	8,2 ± 0,4	13,5 ± 0,9 (t = 5,38; p < 0,001)	11,8 ± 0,4 (t = 6,30; p < 0,001)
C-reactive protein (CRP) (mq/l)	29,5 ± 9,8	10,1 ± 4,7 (t = 1,78; p < 0,05)	15,3 ± 1,3 (t = 1,44; p > 0,05)
IgG (q/l)	39,2 ± 1,35	11,2 ± 0,23 (t = 20,45; p < 0,001)	17,9 ± 1,25 (t = 11,1; p < 0,0001)
IgM (q/l)	2,27 ± 0,58	1,05 ± 0,12 (t = 2,06; p < 0,05)	1,45 ± 0,31 (t = 1,25; p > 0,05)
ESR (mm/h)	26,5 ± 1,7	10,2 ± 3,5 (t = 4,19; p < 0,001)	14,9 ± 1,6 (t = 4,97; p < 0,001)
Lactic acid (LA), mmol/l	2,43 ± 0,1	1,42 ± 0,03 (t = 9,67; p < 0,001)	1,93 ± 0,02 (t = 4,90; p < 0,001)

Table 2

We have analyzed the immediate results of complex treatment of patients with Buerger's disease and are presented in Table 3.

Group of patients	Satisfactory	Not satisfactory	
		Major amputation	Minor amputation
The main group (n = 89).	79 (88,8%)	2 (2,2%) at the level of the lower leg	8 (9%) necrectomy (6) and metatarsal amputation (2)
Control group (n = 81)	57 (70,4%)	9 (11,1%) at the level of the lower leg (6) and thigh (3)	15 (18.5%) necroectomy (8) and metatarsal amputation (7)

Table 3: Results of complex inpatient treatment in patients with Buerger's disease with efferent therapy.

At the end of inpatient treatment in patients of the main group, satisfactory results were obtained in 88.8% of patients, unsatisfactory (major and minor amputations) in 11.2% of patients. And in the control group, satisfactory results were observed in 70.4% of patients, unsatisfactory (major and minor amputations) in 29.6% of patients.

In our opinion, an increase in RI, ABI, TcpO2 mm Hg, DE, fibrinolytic activity, and a decrease in fibrinogen contribute to the stimulation of peripheral blood circulation, and a decrease in lactic acid indicates an improvement in metabolism in the soft tissues of the ischemic limb. These factors create good prerequisites for improving satisfactory results in patients with Buerger's disease in the stage of critical ischemia.

By nonparametric method of statistics, it was established that immediate satisfactory results significantly depend on the tactics of complex treatment ($\chi 2 = 8.907$; $p = 0.003$). The reduction in the frequency of "large + small" amputation in patients of the study group also significantly depends on the tactics of complex treatment ($\chi 2 = 6.815$; $p = 0.010$).

Conclusion

The use of efferent therapy (plasmapheresis, ultraviolet irradiation of blood) in the complex surgical treatment of patients with Buerger's disease stimulates regional blood flow, improves the indicators of hemostasis, blood hemorheology, metabolism in the soft tissues of the ischemic limb, as a result of which the immediate results of treatment improve.

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