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Parameters of the oxidative-reduction system of the homeostasis in female transplant patients with tumors of the reproductive system treated with hyperbaric oxygen therapy

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Introduction. *Studies on the effects of hyperbaric oxygenation have often been represented as animal model experiments. Currently, the number of studies on the use of hyperbaric oxygen therapy in the post-transplant period in humans is growing. The need in investigating the efficacy of hyperbaric oxygen therapy in the postoperative period in female transplant patient with tumors of the reproductive system is dictated by time.* ***The aim of the study*** *was to evaluate the efficacy of hyperbaric oxygen therapy in the complex treatment of transplant patients at an early stage of the postoperative period.*

Material and methods. *We have studied the course of an early postoperative period in 8 female transplant patients with reproductive system tumors treated in N.V. Sklifosovsky Research Institute for Emergency Medicine,*

using hyperbaric oxygenation. The hyperbaric oxygen therapy sessions were provided in a single-patient hyperbaric chamber at 1.2–1.6 ATA for 40 minutes. The status of the redox homeostasis system was assessed based on the data of the platinum electrode open circuit potential measured in blood plasma by using the potentiometric method; and the blood plasma antioxidant activity was assessed by cyclic voltammetry.

Results. *The analysis of the results showed that there was a direct relationship indicating the positive effect of hyperbaric oxygen therapy on the balance status of the pro- and antioxidant systems of the body, and on the improvement of blood counts.*

Conclusion. *The early inclusion of hyperbaric oxygen therapy in the complex treatment of transplant patients with tumors of the reproductive system contributes to a more rapid recovery of pro- and antioxidant systems of the body, blood counts.*

Keywords: kidney transplantation, female transplant patient women with tumors of the reproductive system, hyperbaric oxygen therapy, open circuit potential, cyclic voltammetry

Conflict of interests Authors declare no conflict of interest

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AO, antioxidants

AOA, antioxidant activity

ATA, technical atmosphere absolute

ATP, adenosine triphosphate

$CD45^{+}$, cluster of differentiation 45 antigen

CI, color index

HBO, hyperbaric oxygenation

HG, hemoglobin

HIF-1α, hypoxia-inducible factor 1-alpha

IL-1β, Interleukin 1-beta (Interleukin-1β)

IL-6, Interleukin 6 (Interleukin-6)

LPO, lipid peroxidation

MCHC, mean corpuscular hemoglobin concentration (in a red blood cell)

OCP, open circuit potential

Q, a quantity of electricity or charge

ROS, reactive oxygen species

TNF-α, tumor necrosis factor alpha

Introduction

Currently hyperbaric oxygenation (HBO) is the therapeutic method recognized as one of the most important components of interdisciplinary intensive care, providing a wide range of therapeutic effects. One of the trends in HBO development and application is its using it after organ transplantation, specifically, of such organs as liver, kidneys, and pancreas [1–5]. Only few studies on the effect of HBO therapy in the post-transplant period have been reported in literature. Animal experiments have shown its positive effect in transplantation of bone fragments in rabbits [6], spinal cord tissue in rats [7], islet transplantation of pancreatic cells in mice [8], and in ischemic-reperfusion damage to the kidney in rats [9–11]. Meanwhile, the

study conducted at the Kidney and Pancreas Transplantation Department of N.V. Sklifosovsky Research Institute for Emergency Medicine, demonstrated that ischemic transplant disorders during kidney transplantation develop in 40-50% of recipients [12].

The efficacy of HBO has been shown at the stage of both ischemia and reperfusion (Fig. 1), which is characterized by a decrease in mitochondrial damage [13], a restored activity of oxidative enzymes [14], an increased activity of the nitric oxide synthase and increased nitric oxide synthesis [15], the activation and proliferation of peripheral blood mononuclear cells [16], decreased lipid peroxidation intensity [17], leukocyte adhesion to endothelial cells [18], the sequestration of neutrophils [19], cytokine levels (TNF-α, IL-1β, IL-6), and the affinities of the major histocompatibility complex class I molecules [1], the expression of HIF-1α [20], the inhibition of the $CD45^+$ leukocyte differentiation antigens [16].

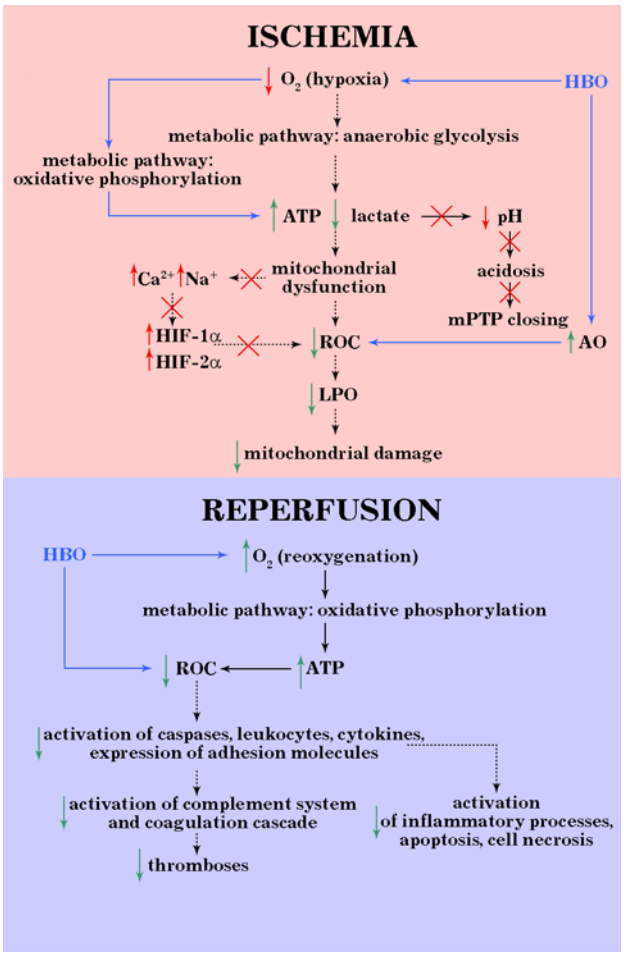

Fig. 1. The scheme of pathophysiological processes in ischemia and reperfusion under conditions of hyperbaric oxygenation

Moreover, the use of HBO has been shown to reduce the degree of the ischemic damage to the transplanted organ [2], reduce edema [21], improve capillary proliferation and vascular area, and to stimulate the collagen matrix formation [5, 22]. HBO poses a bactericidal and bacteriostatic effect on a number of microorganisms [20, 23]. It should be noted that all of the indicated effects of HBO were obtained in experimental studies. No studies have been repoted on the clinical HBO use in women with reproductive system tumors and transplanted organs.

The purpose of the study was to investigate the HBO efficacy in the complex treatment of transplant patients in the early postoperative period.

Material and methods

In the period from December 2016 to June 2019, 30 transplant female patients (cadaveric kidney, liver, and transplantation of a cadaveric kidney and pancreas complex) with tumors of the reproductive system at the Urgent Gynecology Department of N.V. Sklifosovsky Research Institute for Emergency. Surgical interventions of various extents were performed by applying either laparotomy, or laparoscopy, or vaginal access. HBO was used postoperatively in 8 patients. After the first HBO session, 2 women were excluded from the group due to developed claustrophobia. A group of 6 patients included women aged from 34 to 63 years old, the mean age being 44 years; one patient was older 60 years. Four women were recipients of cadaveric kidney allotransplantation, one patient had received combined retroperitoneal kidney and pancreas transplantation, and one more patient had the previous history of liver transplantation. Histological examination revealed hysteromyoma in 4 patients in combination with the uterus endometriosis secondary to cervical dysplasia of the II–III degree in one case and malnutrition of the node in another one; an endometrial polyp was revelaed in 1 more case, and serous cystadenoma of the right ovary was diagnosed in another one.

All patients underwent the surgical inrevention of uterine extirpation with or without uterine appendages through laparotomic and video laparoscopic access with the biopsy of the peritoneum and omentum, as well as hysteroresectoscopy followed by a diagnostic curettage of the uterine mucosa and endocervical curettage in separate procedures. In one case, the

uterine extirpation with appendages was performed through vaginal access, followed by colpoperineorrhaphy and levatoroplasty.

All patients suffered from secondary arterial hypertension. All patients who received HBO sessions showed secondary iron deficiency anemia with hemoglobin (HG) of 80 g/L to 101 g/L (normal range 120–140 g/L), and a decreased mean corpuscular GH concentration in a red blood cell to 260–280 g/L (normal range 310–360 g/L), the decreased color index to 0.4–0.7 (normal range 0.85–1.05). HBO sessions were initiated on day 1 (from several hours to 24 hours) after the surgical stage of treatment. HBO was performed in a Sechrist 2800 resuscitation hyperbaric chamber or in the BLKS-303M and BLKS-307 hyperbaric chambers at 1.2–1.6 ATA for 40 minutes. Patients received from 1 to 7 sessions. The main reasons for a premature cessation of HBO therapy course were claustrophobia and uncontrollable hypertension.

In 4 patients receiving HBO sessions, the redox homeostasis system status was assessed based on the platinum electrode open-circuit potential (RPC) data measured by the potentiometric method in blood plasma [24] and by measuring the antioxidant activity (AOA) of blood plasma by means of cyclic voltammetry [25]. The data were statistically processed with the calculation of the Wilcoxon test using Statistica 10.0 software (StatSoft).

Results and discussion

A comparative assessment of blood parameters in patients before and after HBO sessions showed the decreases in hemoglobin, the mean corpuscular HG concentration in an erythrocyte, and color index (CI) to the lower limit of normal range in 4 of 6 patients (Table 1) .

Table 1. The data on a hemoglobin level, the mean corpuscular hemoglobin concentration in an erythrocyte, color index before and after hyperbaric oxygenation

N	Full Name	Age	Before HBO	After HBO
1	Patient M.	50	HG: 80 g/L	HG: 2 g/L
			CI: 0.4	CI: 0.6
			MCHC: 260 g/L	MCHC: 283 g/L
2	Patient C.	41	HG: 101 g/L	HG: 111 g/L
			CI: 0.8	CI: 1.2
			MCHC: 290 g/L	MCHC: 305 g/L
3	Patient K.	34	HG: 87 g/L	HG: 93 g/L
			CI: 0.5	CI: 0.72
			MCHC: 279 g/L	MCHC: 298 g/L
4	Patient P.	63	HG: 93 g/L	HG: 98 g/L
			CI: 0.62	CI: 0.68
			MCHC: 279 g/L	MCHC: 291 g/L
5	Patient C.	62	HG: 96 g/L	HG: 97 g/L
			CI: 0.67	CI: 0.67
			MCHC: 312 g/L	MCHC: 312 g/L
6	Patient R.	45	HG: 103 g/L	HG: 102 g/L
			CI: 0.7	CI: 0.7
			MCHC: 310 g/L	MCHC: 312 g/L

Note: MCHC, the mean corpuscular hemoglobin concentration in a red blood cell

Based on our previously obtained data on the effect of HBO therapy on the redox homeostasis system status in the body [26–29], one could have

expected a positive effect of the therapy in the studied group of patients. In addition, the used diagnostic technique of measuring the platinum electrode OCP had already shown its efficacy in patients after organ transplantation [30–35].

Indeed, during a HBO session, a decrease in the value of the platinum electrode OCP in the blood plasma (in 10 of 11 HBO sessions) and an increase in the quantity of electricity (Q) (in 8 of 11 HBO sessions) were recorded in most cases, reflecting the AOA of blood plasma (Fig. 2-5). After a HBO session, the mean shift of the OCP value in blood plasma was –16.20 ± 10.99 mV (Fig. 6), and Q in blood plasma was 0.76 ± 0.80 μC (Fig. 7). Summarized data on the changes in the pro- and antioxidant balance over time are presented in Table 2. The differences in the platinum electrode OCP and Q between their values in blood plasma before and after the HBO sessions calculated using the Wilcoxon test were statistically significant: $p = 0.004$, and $p = 0.021$, respectively.

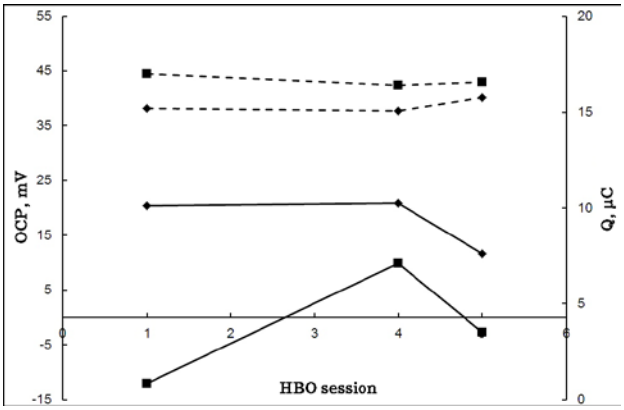

Fig. 2. The values of a platinum electrode open circuit potential in blood plasma (-) and the blood plasma antioxidant activity (---) of Patient M. before (♦) and after (■) a hyperbaric oxygenation session

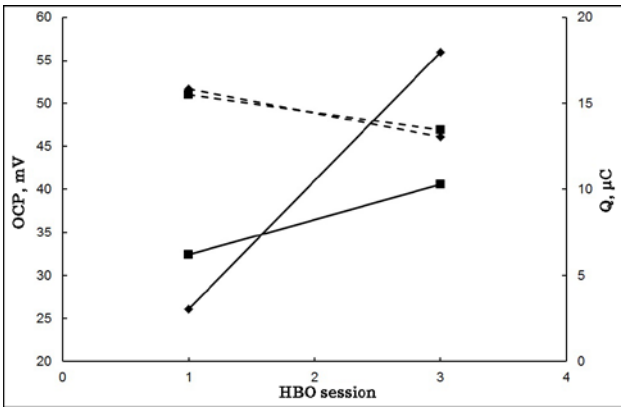

Fig. 3. The values of a platinum electrode open circuit potential in blood plasma (-) and the blood plasma antioxidant activity (---) of Patient S. before (♦) and after (■) a hyperbaric oxygenation session

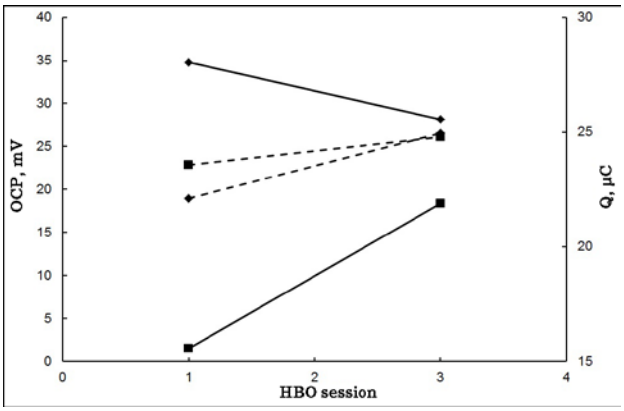

Fig. 4. The values of a platinum electrode open circuit potential in blood plasma (-) and the blood plasma antioxidant activity (---) of Patient K. before (♦) and after (■) a hyperbaric oxygenation session

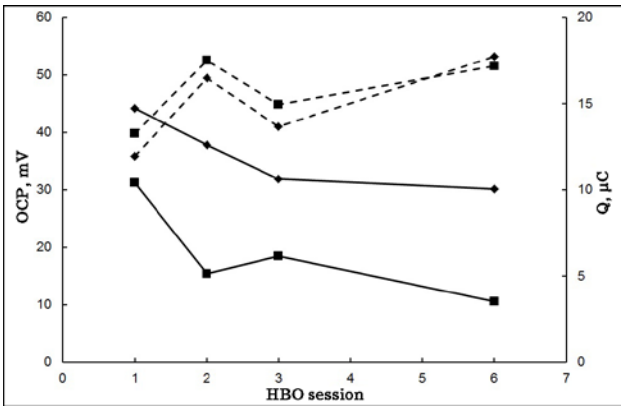

Fig. 5. The values of a platinum electrode open circuit potential in blood plasma (-) and the blood plasma antioxidant activity (---) of Patient P. before (♦) and after (■) a hyperbaric oxygenation session

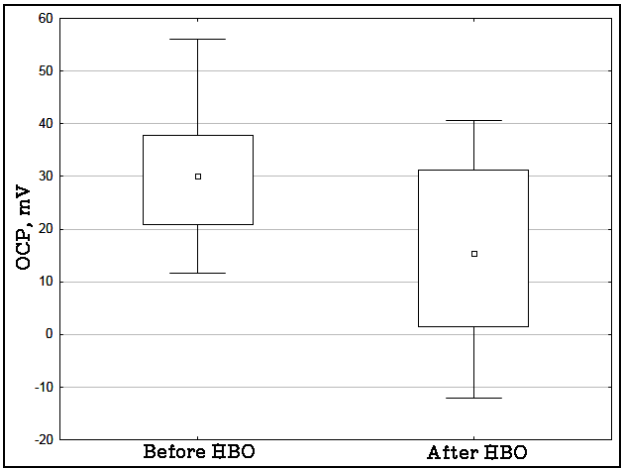

Fig. 6. The diagram showing the range of values for a platinum electrode open circuit potential in blood plasma before and after a hyperbaric oxygenation session

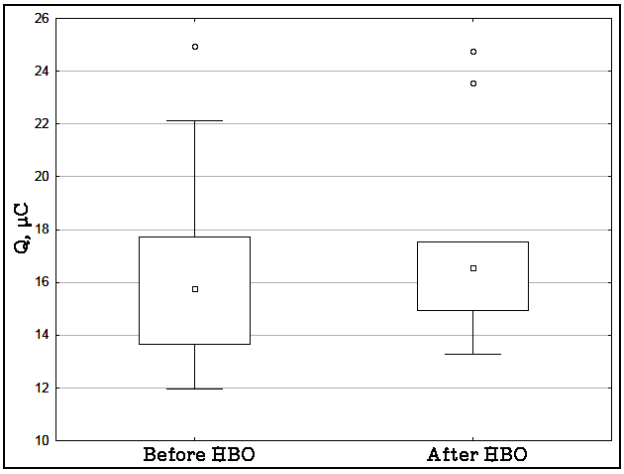

Fig. 7. The diagram showing the range of Q values in blood plasma before and after a hyperbaric oxygenation session

We noted that the OCP values in blood plasma of the studied patients (Table 2) generally corresponded to the range typical of our examined kidney transplant patients (-17 ÷+ 32 mV) [30]. In addition, within the course of HBO therapy, a shift in OCP values was observed in patients M. and P.: from 20.46 mV to 11.58 mV in the first case and from 44.20 mV to 30.11 mV in the second case, which corresponded to the increase in the antioxidant activity from 15.21 µC to 15.78 µC in the first case and from 11.95 µC to 17.73 µC in the second case. This observation might indicate a positive effect of HBO on the balance status in the pro- and antioxidant systems of the body.

Table 2. Summarized data on measuring the platinum electrode open circuit potential and Q in blood plasma of patients before and after a hyperbaric oxygenation session

Full name	Age	HBO session No.	OCP, mV	Δ OCP, mV	Q, μC	Δ Q, μC
Patient M.	50	1, before	20.46	-32.62	15.21	1.78
		1, after	-12.16		16.9	
		4, before	20.85	-11.01	15.07	1.33
		4, after	9.84		16.4	
		5, before	11.58	-14.28	15.78	0.77
		5, after	-2.70		16.55	
Patient C.	41	1, before	26.06	6.37	15.83	-0.33
		1, after	32.43		15.5	
		3, before	55.98	-15.44	13.05	0.42
		3, after	40.54		13.47	
Patient K.	34	1, before	34.75	-33.21	22.12	1.45
		1, after	1.54		23.57	
		3, before	28.18	-9.84	24.95	-0.17
		3, after	18.34		24.78	
Patient P.	63	1, before	44.20	-12.93	11.95	1.33
		1, after	31.27		13.28	
		2, before	37.84	-22.40	16.5	1.02
		2, after	15.44		17.52	
		3, before	31.85	-13.32	13.67	1.27
		3, after	18.53		14.94	
		6, before	30.11	-19.49	17.73	-0.55
		6, after	10.62		17.18	

Conclusion

The analysis of the obtained results has shown that the early inclusion of hyperbaric oxygenation in a complex postoperative therapy in transplant

patients with tumors of the reproductive system contributes to a more rapid recovery of pro- and antioxidant systems of the body, the normalization of blood counts, as a result of the restored tissue respiration and acid-base balance in blood.

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