

TREATING PATIENTS WITH UROLITHIASIS AFTER PERFORMING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY COMBINED WITH OZONE THERAPY

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СИЙДИК ТОШ КАСАЛЛИГИ БИЛАН ОҒРИГАН БЕМОРЛАРНИ ОЗОНОТЕРАПИЯ БИЛАН ЭКСТРАКОРПОРАЛ ЗАРБА-ТУЛҚИНЛИ ЛИТОТРИПСИЯДАН СЎНГ ДАВОЛАШ

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ЛЕЧЕНИЕ БОЛЬНЫХ С МОЧЕКАМЕННОЙ БОЛЕЗНЬЮ ПОСЛЕ ЭКСТРАКОРПОРАЛЬНОЙ УДАРНО-ВОЛНОВОЙ ЛИТОТРИПСИИ В СОЧЕТАНИИ С ОЗОНОТЕРАПИЕЙ

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35 нафар уролитиаз билан хасталанганларга экстракорпорал тулқинли литотрипсия утказилгандан кейин 10 кун давомиди ички озонотерапия утказилиб, калькулез пиелонефрит касаллигининг кечишига таъсири курилди. Унинг кулланишидан ижобий таъсир конда липидларнинг перекисли оксидланиш махсулотларнинг камайиши, антиоксидант фаоллигининг купайиши оркали исботланди.

Калит сўзлар: *калькулез пиелонефрит, экстракорпорал зарба-тулқинли литотрипсия, перекисли оксидланиш липидлари, антиоксидант химоя ферментлари, озонотерапия.*

35 человек с уролитиазом были вовлечены в исследования для того, чтобы узнать, как в течение 10 дней внутривенная озонотерапия влияет на ход течения с калькулезным пиелонефритом после проведенного экстракорпоральной ударно-волновой литотрипсии. Было установлено, положительный лечебный эффект вызванный его применением, которая была доказана путем уменьшения продуктов перекисного окисления липидов в крови, и по увеличению антиоксидантной активности.

Ключевые слова: *калькулезный пиелонефрит, экстракорпоральная ударно-волновая литотрипсия, липиды перекисного окисления, ферменты антиоксидантной защиты, озонотерапия.*

Introduction. Urolithiasis is one of the most common urologic diseases and, according to many researchers, is one of the urgent problems of modern urology [1]. This is caused both by its prevalence and features of its etiology, pathogenesis, diagnosing and of therapeutic approach to this disease. The development of urolithiasis caused by excretory renal dysfunction at the stage of tubular reabsorption and secretion [1,3].

Invention of extracorporeal shock wave lithotripsy (ESWL) and its introduction into clinical practice allowed us to increase the quality and effectiveness of the treatment of various clinical forms of urolithiasis [2, 9].

Special attention is paid to finding effective and reasonably priced methods of the treatment. The ozone therapy has been widely used recently for the same reason [5, 8]. Methods of combined local and intravenous ozone therapy, together with active surgical tactics, contributed to the improvement of the general condition of patients, to reducing indices of endotoxemia, early elimination of microorganisms, acceleration of regenerative processes as well as to the reduction in the duration of hospital treatment [4,6,9].

Material and methods. The effect of ozonated solutions on biochemical indices of blood, system of lipidperoxidation (LPO) and antioxidant defence (AOD) were investigated in 35 patients, suffering from urolithiasis with chronic calculous pyelonephritis while treating them by means of ESWL method.

Ozone was obtained, using an automated ozone plant "Bozon" produced by NPP "Econica" in Odessa. The technological process of production of ozone containing saline was conducted by following a standard technique of preparing ozone containing saline for parenteral injection according to methodical recommendations of Health Ministry of Ukraine in 2004. A standard set for ulnar artery catheterization was used for intravenous infusion.

For the procedure, sterile saline in an amount of 200-400 ml was poured into a quartz vessel of the plant "Bozon", set in the mode of desired concentration of ozone in saline (1-5 mg / l), waited for the procedure of the preparation of ozone in required concentration in saline to be over, then it was injected intravenously to patients at a speed of 80-100 drops per minute [2, 5, 10] for 10 days.

Investigation of biochemical blood parameters, system activity of lipid peroxidation and antioxidant defense were conducted in 30 patients suffering from urolithiasis with calculous pyelonephritis in the preoperative period, on the 3rd-4th day and 9th-10th day after the session of extracorporeal shock-wave lithotripsy. ESWL was performed by means of the apparatus Magna Duet of Direx firm, after fluoroscopic directing the working part on the concrement. Beginning with the minimum amplitude and force of impact, lithotripsy session started. Gradually the strength and frequency of shocks were increased to 6 HV and 120 beats / min, respectively. Lithotripsy session lasted up to 3000 bpm.

The condition of blood biochemical parameters, lipid peroxidation, antioxidant defense in 30 patients with urolithiasis against the background of calculous pyelonephritis treated in the urological department of «Emergency Hospital» Chernivtsi were studied. Comparison group consisted of 20 relatively healthy blood donors and those who were on the examination in urological department.

Oxidation of lipids was evaluated in terms of: content of primary products in blood- conjugated dienes (CD) in units of optical density of lipids (considering methodical recommendations of V.B. Havrylova and M.I. Myshkorudna, 1983), as well as in terms of contents of secondary reactive compounds in the plasma, such as malonic aldehyde (MA) in mcm/l of blood (Staleva, 1977), of cholesterol, triglycerides and lipids (V.V. Menshikov, 1965).

As to the antioxidant enzymes, they were tested for vitamin E (α -tocopherol) in mm / l in the serum (R.S. Kysylevych, 1972); ceruloplasmin activity in the serum (E.V. Ten, 1981); catalase activity in the blood ME -103 (M.A. Koroliuk and co-authors, 1988); peroxidase activity in the blood, s.u / liter. (for 1 s.u. of the activity is accepted the change of the optical density of the reaction medium at 520 nm over 0.001 per h at 37 ° C); glutathione peroxidase activity in blood glutathione mm / min l (B.P.

Pleshkov, 1976); glutathione reductase activity in blood oxidized glutathione m / l min (M.I. Ridkyi, 1997), as well as general antioxidant activity using M.P. Grigorieva's technique (1984).

Statistical analysis of the data was performed on modern PC IBM by analysis of variations, determining Student's criteria using the standard application package STATISTICA "Statgraficsplus 7.0" and "BioStat" [7].

Results and discussion.

Effect of ozonated solutions on biochemical indices of blood lipid peroxidation system and AOD in patients with urolithiasis with chronic calculous pyelonephritis while using ESWL method showed that dynamic of changes of urea content in the blood is markedly different from that of the comparison group patients. Thus, in the group ESWL + O₃ the level of urea increased from $6,34 \pm 0,048$ mg / l to $6,82 \pm 0,05$ mmol / l, which was 7.5% compared with a group of healthy individuals), and in the comparison group, the figure was 20.6%. Thus the difference in the increase was 13.1%. The big difference between the rates was noted in the analysis of creatinine in the blood (44%). Obviously, for this reason, in patients treated with ozone therapy, there were no significant deviations of creatinine clearance. Thus, the filtration capacity of the kidneys is not impaired (Table. 1).

It should be noted that creatinine content in the blood nine days after ESWL + O₃ was lower than before the operation, closer to that of the group of healthy individuals.

Content of lipids in plasma in patients of this group increased slightly in the postoperative period on the background of ozone therapy. Without a use of ozonated solutions on the 3rd-4th day after ESWL the content of total lipids in plasma as well as cholesterol and triglyceride rates increased by 12.6%, 19.2%, and 38.8%, respectively, while after application of ozone therapy these figures only increased by 1.4%, 8.6% and 5% respectively. Atherogenic index did not increase so sharply.

Table 1

Indices of LPO products and renal function after ESWL + ozone therapy performing

Indices	Units	Raw data (n=35)	3 rd -4 th day after ESWL	P	9 th -10 th day after ESWL	P
Clearance.	ml/min.	102,3±0,87	99,5±1,2	>0,05	98,1±0,75	>0,05
Lipids gen..	g/l	5,64±0,12	5,72±0,14	>0,05	5,2±0,11	<0,05
triglycerides	mmol/l	1,19±0,07	1,25±0,05	<0,05	1,15±0,08	<0,05
Plasma DC	Un.opt.Дещ.	0,308±0,03	0,349±0,021	<0,05	0,305±0,03	<0,05
MA	Mcmol/l	0.785±0,0128	0.960±0,015	<0,05	0.891±0.013	<0,05
Urea	mmol/l	6,34±0,048	6,82±0,05	<0,05	6,7±0,04	<0,05
creatinine	mmol/l	0,085±0,004	0,198±0,004	<0,05	0,10210,005	<0,05
Atherogenic index		2,34±0,12	2,59±0,04	<0,05	2,18±0,09	<0,05

Note: The validity of the results at P <0.05

Table 2

Values of carbohydrate metabolism after ESWL+ ozone therapy

Values	Units	Raw data (n=35)	3rd and 4th days after ESWL	P	9 th and 10 th days after ESWL	P
Blood glucose	mM/l	4,81 ± 0,15	4,02 ± 0,2	<0,05	4,7 ± 0,16	<0,05
Lactate	mM/l	1,02 ± 0,017	0,85 ± 0,01	<0,05	0,89 ± 0,012	<0,05
Pyruvate	mM/l	0,08 ± 0,004	0,06 ± 0,003	<0,05	0,074 ± 0,005	<0,05
L/Pyruvate	mM/l	12,75 ± 1,02	14,16 ± 0,8	>0,05	12,02 ± 10,65	<0,05

Note: The validity of the results at P < 0,05

In the application of ozone therapy it increased $2,59 \pm 0,04$, whereas patients in the comparison group, it increased to $3,8 \pm 0,1$, i.e the difference was 46%. These data support the view that the high content of oxygen in the blood due to introduced ozone improves lipid oxidation, prevents the transformation of suboxide products of fats into cholesterol. The favorable tendency of increased utilization of blood lipids in patients suffering from urolithiasis with chronic calculous pyelonephritis in parenteral injections of ozone solutions is also observed in more distant periods of observation.

Pronounced effect of ozonized solutions in the course of urolithiasis with chronic calculous pyelonephritis after ESWL is observed at the level of carbohydrate metabolism: lactate and pyruvate. Thus, the concentration of lactate decreased from $1,02 \pm 0,017$ mmole / l to $0,85 \pm 0,001$ mmole / l on the 3rd-4th day after a session of ESWL, representing 32.8% of the indicators of healthy individuals. At the same time, in patients in the comparison group, the figure was 17.0%. During the next days after the ESWL there was an increase in lactate (Table. 2).

On the 3rd-4th day after ESWL pyruvate rate decreased by 25% from the baseline (from $0,08 \pm 0,004$ mg / l to $0,06 \pm 0,006$ mmol / l). On the 3rd, 4th, and 9th, 10th postoperative day the pyruvate rate remained below the original one. Ratio lactate / pyruvate for the entire observation period remained at the level of the control parameters. The concentration of glucose oxidation products decreased and remained lower than in the preoperative period. This tendency showed a significant effect of ozone on the body's energy processes in examined patients, suffering from urolithiasis with chronic pyelonephritis. It can be assumed that increasing the amount of oxygen in the blood normalizes the ratio both of aerobic and anaerobic ways of glucose oxidation, thereby stimulating more efficient process of energy production. Activation of oxygen dependent ways was accompanied by increased glucose utilization. On the 3rd -4th day after ESWL glucose rate decreased from $4,81 \pm 0,15$ mmol / l to $4,02 \pm 0,2$ mmol / l and was 16% from the basal value.

The level of serum ceruloplasmin in patients with urolithiasis with chronic pyelonephritis after

ESWL and ozone therapy dramatically increased from $0,31 \pm 0,05$ units of opt. dens. to $0,61 \pm 0,031$ un. of opt. dens., representing 49% of the basal value, while the concentration of uric acid remained mostly the same.

The level of concentration of α -tocopherol in patients with urolithiasis with the treatment using ESWL and ozone therapy on the 3rd -4th day was 9.9% from the baseline. On the 9th day after ESWL the level of α -tocopherol concentration increased by 22% from the basal value. However, in the comparison group there was a reduction of α -tocopherol by 11% on the 3rd -4th days and 13% - on the 9th day of post-operative course.

It is obviously that less intense process of α -tocopherol formation and reduction in its concentration in patients of the comparison group was a result of its more intensive use in the reaction of "catching" free radicals, while the use of ozonated solutions stimulates the synthesis of α -tocopherol.

It can be assumed that the activation of aerobic ways of energy production contributed to the biosynthetic functions, such as accelerated biosynthesis of proteins and enzymes, including ceruloplasmin enzyme.

An important effect of ozone therapy in patients with urolithiasis on the processes of free radical oxidation of lipids and on enzymatic activity of antioxidant protection system occurs with excessive ozone, which significantly weakens the formation of conjugated dienes and malonic aldehyde. Thus, if we compare, without using ozone in the control group, on the 3rd -4th day after ESWL, the concentration of CD and MA increased by 51,2% and 68%, respectively.

In the group of patients who used ozone therapy at the same time the concentration of both primary (CD) and secondary products (MA) of lipid peroxidation in the blood increased only by 13.3% and 22.2% respectively.

9-10 days later after ESWL and ozone therapy the level of lipid peroxidation products decreased in patients with urolithiasis, approaching to that of the preoperative period.

Table 3

Indices of antioxidant enzymes after extracorporeal shock wave lithotripsy combined with ozone therapy

Indices	Units	Raw data (n=35)	3 rd -4 th day after ESWL	P	9 th -10 th day after ESWL	P
Catalase	MEx10 ³	19,44±1,35	22,06±1,19	<0,05	24,61±1,1	<0,05
Peroxidase	s.u./l	127,3±4,36	152,4±5,48	<0,05	149,5±4,91	<0,05
Gl.peroxidase	MEx10 ³	19,44±1,32	24,71 ±2,3	<0,05	23,14±2,1	<0,05
Gl.reductase	ME	585,1±46,3	671,9±34,21	<0,05	708,3±24,9	<0,05
α-tocopherol	mg/%	1,92±0,02	2,11±0,015	<0,05	2,34±0,01	<0,05
uric acid	mm/l	232,6±26,4	285,9±29,6	<0,05	315±34,7	<0,05
Ceruloplasmin	Un.ofopt.dens.	0,31±0,05	0,61 ±0,031	<0,05	0,49±0,04	<0,05

Note: The validity of the results at P < 0,05

Table 4.

Indices of blood and urine lactate dehydrogenase isozyme spectrum after ESWL +ozone therapy

Indices	Units	Raw data(n=35)	3 rd -4 th day after ESWL	P	9 th -10 th day after ESWL	P
Gen.bl.LDG	mcM(ls)	1,6±0,013	1,7±0,03	<0,05	1,56±0,012	>0,05
LDG1	mcM(ls)	0,509±0,0062	0,598±0,0054	<0,05	0,515±0,006	<0,05
LDG2	mcM(ls)	0,69 1 ±0,003	0,698±0,0029	<0,05	0,675±0,0025	0,05
LDG3	mcM(ls)	0,259±0,002	0,269±0,0012	<0,05	0,246±0,0018	>0,05
LDG4	mcM(ls)	0,093±0,008	0,088±0,006	<0,05	0,087±0,006	<0,05
LDG5	mcM(ls)	0,048±0,001	0,042±0,0012	>0,05	0,055±0,0015	>0,05
Gen.ur.LDG	mcM(ls)	0,196±0,067	0,294±0,05	<0,05	0,275±0,041	<0,05
LDG1	mcM(ls)	0,07 1 ±0,015	0,121 ±0,004	<0,05	0,117±0,035	<0,05
LDG2	mcM(ls)	0,058±0,015	0,076±0,01	<0,05	0,081 ±0,02	<0,05
LDG3	mcM(ls)	0,036±0,0014	0,044±0,001	<0,05	0,034±0,001	<0,05
LDG4	mcM(ls)	0,015±0,001	0,021 ±0,002	<0,05	0,018±0,001	<0,05
LDG5	mcM(ls)	0,017±0,003	0,032±0,007	<0,05	0,025±0,005	<0,05

Note: The validity of the results at P < 0,05

A significant weakening of free radical oxidation of lipids was the result of the activation of enzymatic antioxidant defense system. Activation of defense mechanisms under the influence of ozone therapy occurred with less intensity compared with the processes of lipid peroxidation, and it is seen well judging by the catalase activity rate. On the 3rd - 4th day its activity was 22,06 ± 1,19 Meh103 from the baseline. Only nine days after ESWL its activity does not differ at all from that of the comparison group of individuals (24,61 ± 1,1 Meh103).

The activity of the enzyme glutathione peroxidase and glutathione reductase in the early postoperative period, i.e. on the 3rd -4th day, in patients of the comparison group tended to a sharp decline and remained at a lower level than at the preoperative stage. At the same time, the activity of glutathione reductase and glutathione peroxidase after ozone therapy tended to increase by 15% and 27% on the 3rd -4th day, and further the activity indices remained at a consistently high level.

The enzyme activity of peroxidase increased. After 3-4 days and on the 9th-10th days its activity

was higher in patients who had undergone ozone therapy and accounted for 19.6% of the initial level. The atomic oxygen (ozone decay product) may be a specific inducer, under whose influence the synthesis of this enzyme in tissues takes place (Table. 3).

Changes in the activity of the blood LDG, in general, resembled the development of changes in the comparison group of people, who hadn't used the ozone therapy. Indices of LDH activity 10 days after ESWL did not differ from that of the activity of healthy individuals. In LDG isozyme spectrum of blood LDG 1,2,4 fractions prevailed in 3-4 days after ESWL. However, after 10 days of postoperative course there was a slight increase in activity of fractions LDG4 and LDH5 which indirectly points to an increasing permeability of parenchymatous organs cellular membranes.

More significant differences in the activity of LDG isozyme spectrum were noted in the urine. This is due to the fact that extracorporeal lithotripsy dramatically increases the activity of fractions LDGD and LDG5. Parenteral application of ozonized solutions in the preoperative and postoperative

period significantly alters the intensity of the activity and the distribution of LDG isoenzymes of urine.

3-4 days after ESWL there was a higher activity of LDG fractions in the urine :from $0,071 \pm 0,015$ mmol/ s to $0,121 \pm 0,004$ mmol / s (70%), LDG3 from $0,036 \pm 0,001$ mmol / s to $0,044 \pm 0,001$ mmol / s (22%) and LDG5 from $0,017 \pm 0,003$ mmol / s to $0,032 \pm 0,007$ mmol / s (88.2%).

These results suggest that extracorporeal lithotripsy affects the renal parenchyma and, in particular, the nephrocytebiomembranes. Using ozonated solutions in pre- and postoperative periods reduces the destructive processes significantly.

Thus, our studies of the impact of ozone on post-operative condition of parenchymal organs – the kidneys, the liver and the most important blood parameters exhibit significant prospects of the treatment in urology we had chosen.

Unlike the previous series of studies (comparison group), LDG activity of the urine on the 3rd - 4th days grew slightly under the influence of ESWL + ozone therapy (1.5 times). Subsequently, the activity of the urine LDG reduced to the preoperative level faster (Table. 4).

Thus, the use of ozonized solutions promotes energy supply, reduces primary pathogenetic link in cell membranes damage - lipid peroxidation and improves the use of lipids in energy processes, reduces cholesterol atherogenity, stabilizes processes of aerobic and anaerobic ways of glucose oxidation, stimulates enzyme activity and non-enzymatic components of the antioxidant defense of the body.

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TREATING PATIENTS WITH UROLITHIASIS AFTER PERFORMING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY COMBINED WITH OZONE THERAPY

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35 people with urolithiasis were involved in the study in order to find out how the intravenous ozone therapy, performed during 10 days, influenced the course of the disease with calculous pyelonephritis after conducted extracorporeal shock wave lithotripsy. It was established a positive curative effect caused by its application which was proved by a reduction of lipid peroxidation products in the blood, by an increase of antioxidant activity.

Key words: *calculous pyelonephritis, extracorporeal shock wave lithotripsy, lipid peroxidation, enzymes of antioxidant defense, lactate, ozone therapy.*