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The influence of plasmapheresis and hemosorbition through “Ovosorb” hemosorbent on albumin binding capacity in patients with sepsis

Wpływ plazmaferezy i hemosorbpcji przez hemosorbent „Ovosorb” na wiążącą funkcję albuminy u chorych na sepsę

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None

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S u m m a r y

Introduction. Sepsis continues to be one of the most serious diseases in modern medicine. It is associated with changes in serum albumin qualities.

Aim. The aim of the study is the evaluation of functional properties of albumins in sepsis treatment.

Material and methods. Study included 60 patients, among which 34 had pancreatitis, 12- peritonitis, 10 – urinary tract inflammation, 2 – pneumonia, 2 – caries. In every case, the disease has been complicated with sepsis. All patients underwent preservative treatment: antibiotic therapy, intravenous infusions of crystalloids or colloids, immunotherapy, respiratory therapy, alignment of electrolyte and acid – base disturbances, glycemia and hemoglobin levels as well as hemostasis disorders. For evaluation of patients condition during hospitalization, APACHE II scale has been used.

Patients were divided into 3 groups. In case when the number of points was 30 and more, patients underwent plasmapheresis, as it was stated above the therapy of “despair”. When the condition of patients has been estimated for 30 points or less according to APACHE II scale, they were randomly divided by a computer software into two groups: examined and control.

Results. We’ve determined that albumin coupling capacity is decreased drastically with sepsis. Hemosorption with “Ovosorb” hemosorbent restores albumin functioning, improves condition status according to APACHE II and reduces general treatment time. Plasmapheresis also improves coupling capacity, but not so much as “Ovosorb” hemosorbent.

Conclusions. Plasmapheresis improved albumin binding function, however, in comparison to hemosorbition the effect is less visible. It brings a conclusion that application of hemosorbition is reasonable and allows to preserve proteins and other – less important – compounds especially in patients in severe condition when the body accumulates auto antibodies and toxins irreversibly changing albumin transport function.

Streszczenie

Wstęp. Sepsa jest poważnym problemem współczesnej medycyny. Zauważono, że podczas rozwoju choroby funkcja albuminy surowicy krwi się zmienia.

Cel pracy. Celem pracy jest badanie właściwości funkcjonalnych albuminy w leczeniu sepsy.

Materiał i Metody. Badaniom poddano 60 osób, z których 34 miały zapalenie trzustki, 12 – zapalenie otrzewnej, 10 – zapalenie układu moczowego, 2 – zapalenie płuc, 2 – próchnicę. W każdym przypadku choroba była powikłana sepsą. Wszyscy chorzy byli leczeni zachowawczo: antybiotykoterapia, wlewy dożylnie krystaloidów lub koloidów, immunoterapia, terapia oddechowa, wyrównywanie zaburzeń elektrolitowych, kwasowo-zasadowych, poziomu glikemii oraz hemoglobiny, zaburzeń hemostazy. Dla oceny stanu chorych podczas hospitalizacji była wykorzystana skala APACHE II.

Pacjenci byli podzieleni na 3 grupy. W przypadku, gdy liczba punktów wynosiła 30 i więcej, pacjentom przeprowadzano plazmaferezę, jak zaznaczono powyżej – terapię „rozpaczy”. Gdy stan pacjentów oceniono na 30 i mniej punktów w skali APACHE II, chorych losowo podzielono, przy pomocy programu komputerowego, na dwie grupy: kontrolną i doświadczalną.

Wyniki. U chorych na sepsę zaobserwowano nagły spadek wiążącej funkcji albumin. Zastosowanie hemosorbpcji z wykorzystaniem hemosorbentu „Ovosorb” odnowiło straconą funkcję albuminy, poprawiło stan chorego według skali APACHE II i zmniejszyło długość leczenia. Ponadto zauważono, że wykorzystanie plazmaferezy też zmienia wiążącą funkcję albuminy, ale w nieco mniejszym stopniu w porównaniu do sorbentu „Ovosorb”.

Wnioski. Plazmafereza polepsza funkcję wiążącą albuminy, jednak w porównaniu do hemosorbpcji efekt jest mniejszy. Pozwala to dojść do wniosku, że uzasadnionym jest wykorzystanie hemosorbpcji, która pozwala zachować białka i inne – nie mniej ważne dla organizmu – związki, zwłaszcza u chorych w bardzo ciężkim stanie, kiedy w ustroju gromadzą się autoprzeciwciała i toksyny, nieodwracalnie zmieniające funkcje transportu albuminy.

INTRODUCTION

Estimation data regarding United States recall 750 000 cases of sepsis per year, among which 215 000 were fatal (1).

Every year, the number of patients with sepsis increases all over the world and the discussion about the treatment is constantly raised.

Sepsis is a generalized inflammatory reaction, immunological mechanisms and biochemical mechanism of which have not been examined sufficiently and there are no specific markers for determination of those processes (2).

In sepsis pathogenesis, the important stage is human organism reaction to microorganisms activity inducing uncontrolled mediator reaction leading to generalized failure of internal organs (3). Bacteria lipopolysaccharides, cytokines and other mediators of inflammatory status influence functional properties of albumin in human blood serum (4). It is possible that in sepsis, albumin pathological changes, as a protein which serves as a transporter, as well as toxic substances accumulation lead to the impairment of metabolites elimination which have been created during severe generalized inflammatory reaction (5).

For a long period of time, in the evaluation of patient condition, quantitative biochemical indicators of albumin content in serum have been used. Research conducted in recent years revealed one more important fact: not only the amount of protein is important but also its quality which means its ability to bind and transfer different substances i.e. to transport and remove toxic metabolites, inflammatory mediators, free oxygen radical etc. from organism (6, 7).

Binding capacity of albumin in serum, availability of its centers binding low molecular weight ligands significantly change in critical state (4, 5). It has been determined that in case of sepsis and septic shock in patients with hypoproteinemia leukemia, albumin binding capacity of blood serum is decreased of 33% (8). It is possible that assay of protein binding function in case of sepsis deforms organism condition and efficiency of applied treatment.

In recent years, one of important directions in sepsis treatment is extracorporeal detoxification (9-12).

At the end of 20th century, in scientific journals, first information about plasmapheresis (PF) application in sepsis and septic shock treatment has appeared (11-18). In 1996, Stegmayr proved the efficiency of PF application in sepsis and septic shock treatment. In his study, he proved that PF may increase septic patients survival up to 75%. However, it eliminates from blood not only toxic substances but also many of those necessary for proper functioning which proves that the method is not completely safe (17, 18). Analysis of published by Stegmayr articles allows to state that PF appeared to be the therapy of “despair” in severe multiorgan dysfunction and disseminated intravascular coagulation syndrome which influences patients survival rate – up to 80% (15, 16).

In our country, hemosorbent “Ovosorb” has been tested. Beneficial influence of hemosorbition with “Ovosorb” removing from blood serum proteases (trypsin, chymotrypsin, elastase and others) is well known (10).

AIM

The aim of the study is the evaluation of functional properties of albumins in sepsis treatment.

MATERIAL AND METHODS

Study included 60 patients, among which 34 had pancreatitis, 12 – peritonitis, 10 – urinary tract inflammation, 2 – pneumonia, 2 – caries. In every case, the disease has been complicated with sepsis. All patients underwent preservative treatment: antibiotic therapy, intravenous infusions of crystalloids or colloids, immunotherapy, respiratory therapy, alignment of electrolyte and acid – base disturbances, glycemia and hemoglobin levels as well as hemostasis disorders. For evaluation of patients condition during hospitalization, APACHE II scale has been used.

Patients were divided into 3 groups. In case when the number o points was 30 and more, patients underwent plasmaphoresis, as it was stated above the therapy of "despair" (15, 16). When the condition of patients has been estimated for 30 points or less according to APACHE II scale, they were randomly divided by a computer software into two groups: examined and control.

Control group included 15 patients. This group underwent preservative treatment without extracorporeal detoxification. Average age of patients in this group was 39.2 ± 17.4.

Examined group consisted of 35 patients in which hemosorbition with "Ovosorb" (Belarus) using BP-742 ("Fresenius", Germany) pump has been applied. The blood passed through the gap with sorbent and then returned to the circulatory system. The speed of blood perfusion was 80-90 ml/min and the full time of the procedure – 60 minutes. In every patient in this group, 3 to 7 procedures have been performed; the average of patients was 47.3 ± 17.5.

The group of patients who underwent plasmaphoresis included 10 persons. The procedure has been conducted with AS.TEC 204 (Fresenius) device. The amount of removed plasma was 2500 ± 150 ml. In this group, 2 to 5 procedures have been performed, the average of patients was 45 ± 17.4.

In all patients during the admission and after intense treatment, leucocytic intoxication index was controlled according to Kalf-Kalif scale and patients condition according to APACHE II and SOFA scales.

Albumin binding function has been examined by determination of endogenic intoxication with thiazolidine (19). Obtained results have been presented in percentage relation to healthy donors. The method involves increase of metabolites and toxins concentration in pathological state and modification of functional groups of protein which lead to disorders in thiazolidine binding. Thiazolidine, usually after mixing with plasma, binds with plasma albumin and creates the compound of yellow color. Furthermore, optic density of plasma with thiazolidine has been measured in optic density units (D) on wave length 425 nm. For comparison, plasma diluted with water has been used. Optic density of diluted plasma has also been measured on wave length 280 nm (D₂₈₀), due to the fact that on this wave length optic density correlates with plasma proteins concentration – albumin. Quantitative evaluation of obtained results is presented on the graph D₄₂₅/D₂₈₀ and the

level of endogenic intoxication (percentage) is determined using comparison of D₄₂₅/D₂₈₀ of patients with D₄₂₅/D₂₈₀ of healthy donors. What is more, used graph D₄₂₅/D₂₈₀ indicates the concentration of albumin in blood and is an un-specific parameter suggesting severe condition of patient and reflects the reaction of the organism on pathological processes.

Optic density of thiazolidine solution with plasma in patients with endogenic intoxication is significantly lower than with the plasma of health individuals which indicates less amount of albumin free from toxins.

Parameters interesting for researchers have been examined before the procedure and after 1 hour within 2 days as well as after the whole course of extracorporeal detoxification. In control group, albumin binding function has been examined during the admission, after 2 days and after the whole course of preservative treatment. Albumin binding function has been presented in percentage relation to healthy donors.

Statistical analysis has been conducted with STATISTICA 5.5. software. Parametric and non-parametric test have been used during the calculation.

RESULTS

Obtained results of changes in albumin binding function in patients who did not undergo extracorporeal detoxification are presented in table 1.

Tab. 1. The dynamics of changes in albumin binding function in patients with sepsis in control group

Stage of the examination	Median (Me) during hospitalization, lower and upper quartile	Median (Me) after 2 days of hospitalization, lower and upper quartile	Median (Me) after the whole treatment, lower and upper quartile
Control group (N = 14) p (Wilkokson)	68.35% (47.8%; 74%)	45.3% (37.8%; 55%) 0.078*	38.05% (33.03%; 44.7%) 0.0499*

*p in comparison to the initial stage of examination

Obtained data suggest sudden decrease of albumin transportation of serum ability which has been developing during the whole stay in Intensive Care Unit which explains inclusion of extracorporeal detoxification to the treatment.

Obtained results of changes in albumin binding function with the application of "Ovosorb" hemosorbent are presented in table 2.

Tab. 2. The dynamics of changes in albumin binding function in patients with sepsis in examined group

Stage of the examination Examined group	During hospitalization	After the first hemosorption	After the second hemosorption	After the whole treatment
Mediane (Me), lower and upper quartile (N = 25) p (Wilkokson) p (Mann-Uitni – U)	54.52% (42.3%; 77.1%) 0.258**	70.0% (58.7%; 83.7%) 0.0179*	66.5% (62.4%; 97.2%) 0.035* 0.0002**	86.11% (75.4%; 87.2%) 0.0117* 0.00014**

*p in comparison to the initial stage of examination

**p in comparison to control group without extracorporeal detoxification

Tab. 4. The dynamics of changes in general condition of patients according to APACHE II and leucocytic intoxication index (LII) in patients with sepsis

Stage of examination	During hospitalization Mediane (Me), lower and upper quartile			After the whole treatment Mediane (Me), lower and upper quartile	
	Points in APACHE II	LII	Points in SOFA	LII	Points in SOFA
Control group (N = 15) p (Wilkokson)	14.2 (12; 17)	9.7 (5; 26.2)	4.1 ± 0.44	4.9 (3.9; 13.3) 0.046*	2.2 ± 0.54 0.00005*
Examined group (N = 35) p (Wilkokson) p (Mann-Uitni – U)	16.5 (11; 21) 0.6**	10.3 (6.6; 15.3) 0.87**	3.4 ± 0.3 0.14**	2.0 (1; 4.2) 0.002* 0.006**	0.28 ± 0.14 0.0001* 0.000001**
Plasmaphoresis group (N = 10) p (Wilkokson) p (Mann-Uitni – U)	35 (30; 40) 0.008**	24.1 (18; 28) 0.004**	6.5 (4; 9) 0.05**	12 (6; 14) 0.003* 0.004**	6 (2; 8) 0.00001**

*p in comparison to the initial stage of examination

**p in comparison to control group without extracorporeal detoxification

Application of hemosorption improves albumin binding function during the treatment.

Obtained results of albumin binding function using plasmaphoresis are presented in table 3.

Tab. 3. The dynamics of changes in albumin binding function in patients with sepsis with application of plasmaphoresis

Stage of the examination Plasmaphoresis group (N = 10)	During hospitalization	After the first procedure	After the second procedure	After the whole treatment
Mediane (Me), lower and upper quartile p (Wilkokson) p (Mann-Uitni – U)	15.5% (14.2%; 17.8%)	42% (40.3%; 46.7%) 0.0215*	33.5% (33.1%; 35.6%) 0.027* 0.002**	43.1% (41.4%; 49%) 0.022* 0.445**

*p in comparison to the initial stage of examination

**p in comparison to control group without extracorporeal detoxification

During the admission of patients in severe condition the binding function of albumin has been significantly decreased. After plasmaphoresis the function slightly increased which brought the improvement of general condition of patients.

Results of changes in patients condition according to APACHE II scale and leucocytic intoxication index (LII) of patients from 3 groups are presented in table 4.

DISCUSSION

In patients with sepsis, the decrease of albumin binding function is observed. During further development of pathological process and growing endotoxification, aforementioned disorders are developing and in patients with the most severe course of sepsis the index of albumin binding function is the lowest.

Using of hemosorbent “Ovosorb” allows to increase the binding function of albumin and changes the prognoses. In patients from examined group, general condition improved significantly according to SOFA scale in comparison to control group. What is more, the course of inflammatory processes changes; normalization of LII has been observed.

After application of plasmaphoresis, increase of albumin binding function has been observed, however,

in comparison to control group changes were not as significant. It may be caused by total removal of proteins from blood serum when the serum of donor or transferred albumins lost many important functions during preparation and preservation of preparates.

Comparing the duration of hospitalization of patients with sepsis it has to be mentioned that patients who underwent hemosorbition with “Ovosorb” stayed in the hospital for 7 days (p = 0.049 Mann-Whitney criterion) while those from control group – for 10 days.

Lethality of septic patients who underwent hemosorbition with “Ovosorb” – 12.5%, in control group – 22.5% (p = 0.03 Mann-Whitney criterion).

Using plasmaphoresis in sepsis treatment allowed to improve patients general condition, however, after its application, proper improvement of albumin function has not been observed which may be explained by the disorders caused by toxins. Lethality is 50%. Plasmaphoresis improved albumin binding function, however, in comparison to hemosorbition the effect is less visible. It brings a conclusion that application of hemosorbition is reasonable and allows to preserve proteins and other – less important – compounds especially in patients in severe condition when the body accumulates auto antibodies and toxins irreversibly changing albumin transport function.

RESULTS

1. Using thiazolidine for intrinsic intoxication determination enables fast diagnostics of albumin status in serum and control the dynamics of changes during the treatment due to its high sensitivity in severe sepsis.
2. It is reasonable to use extracorporeal detoxification in treatment of sepsis which is confirmed by positive dynamics of patients condition changes confirmed in laboratory tests.
3. Using hemosorbent “Ovosorb” in sepsis treatment is a method of choice which allows to increase albumin binding function and helps to preserve proteins in blood along with the removal of toxins.
4. Application of hemosorbition with “Ovosorb” allows to decrease the lethality of 10%.

5. Plasmaphoresis positively influences albumin transport function, however, in comparison with hemosorbition the effect is less visible.

CONCLUSIONS

Sepsis continues to be one of the most serious diseases in modern medicine. It is associated with changes in serum albumin qualities.

We've determined that albumin coupling capacity is decreased drastically with sepsis. Hemosorption with "Ovosorb" hemosorbent restores albumin functioning, improves condition status according to APACHE II and reduces general treatment time. Plasmapheresis also improves coupling capacity, but not so much as "Ovosorb" hemosorbent.

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