Perspectives of Plasmapheresis in the Treatment of Kidney Diseases

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Abstract: Many kidney diseases pose a serious threat to human health and even life. In some cases, they inevitably lead to hemodialysis and even the need for kidney transplantation. Almost all chronic kidney disease in varying degrees, are associated with disorders of the internal environment, mainly autoimmune nature. Drug therapy is not always effective and can lead to additional disorders. Pathogenetically justified is the use of plasmapheresis. The aim of this study was to analyze the modern world literature in order to identify the features of the pathogenesis and course of various forms of chronic kidney disease in terms of determining the possibility of using plasmapheresis and indications for it. With the help of plasmapheresis, a number of problems can be solved in urology, in particular in the treatment of pyelonephritis, prostatitis and even male infertility.

Keywords: Kidney Diseases, Autoimmunity, Plasmapheresis, Male Infertility

1. Introduction

Almost all chronic kidney diseases in varying degrees are associated with disorders of the internal environment of the body, mainly autoimmune nature. Moreover, the mechanisms of these disorders are very diverse. Therefore, we have analyzed a variety of pathological conditions, but united on the principle of homeostasis disorders, which can be treated using apheresis technology, mainly plasmapheresis.

2. Glomerulonephritis

As well as rheumatism, glomerulonephritis also most often is serious complication of a streptococcal infection when toxins on the way of removal distort anti-gene structure of glomerular cells of kidneys and provoke of the autoantibodies formation which are fixed on a basal membrane of a nefron with are irreversible the progressing damage of the last [1, 2]. Similarity of such succession of events to the aforesaid at rheumatism is confirmed by that in 25% of cases of glomerulonephritis really is combined with rheumatism. And the same as at rheumatism, here expediently perhaps earlier carrying out therapeutic apheresis – since the first signs of developing of this disease [3, 4], though often resort to a plasma exchange only at steroid-resistant forms of a glomerulonephritis [5]. However steroid therapy is followed by many complications and in severe cases of its opportunity are limited [6]. The same can be told also about cytostatics. So, it was described development of an acute severe liver failure after reception cyclophosphamide for which treatment over required carrying out a plasma exchange [7].

There was described the development of rapidly progressive glomerulonephritis associated with the acute endocarditis caused by Streptococcus. With the help of plasmapheresis it was also able to restore renal function [8].

The retrospective analysis of results of treatment of children with idiopathic quickly progressing glomerulonephritis, and also a kidney or not kidney vasculitis, subjected to plasma exchange courses against the previous inefficient treatment by corticosteroids and cytostatics, showed considerable improvement of kidneys function at the majority of patients and a lasting positive effect at all patients from vasculitis [9, 10]. At the same time
the double-filtration plasmapheresis finds application also [11].

And, it was noted considerably much more big efficiency of a plasma exchange in comparison with hormonal therapy [12]. The same results were reached at 18 patients with quickly progressing glomerulonephritis against a systemic lupus erythematosus, a hemorrhagic vasculitis, Wegener's granulomatosis and microscopic polyarteritis by means of courses from 5-10 procedures of a plasma exchange with removal a session of 1, 5-2 l of plasma [13]. It allowed to stabilize or improve the course of kidney process and to increase survival of patients.

Quite often develops rather malignant course of glomerulonephritis with severe kidney damage, requiring dialysis therapy. The inclusion of plasmapheresis significantly faster leads to the restoration of renal function with the abolition of hemodialysis [14, 15].

Glomerulonephritis can arise and during a pregnancy and the plasma exchange against high doses of steroids allowed to stop in 3 months manifestations of an illness [16].

Of course, it is necessary to consider that glomerulonephritis, as well as any other autoimmune pathology, finally it is impossible to cure and systematic carrying out courses of a plasma exchange throughout all life is required. In cases of interruption of such treatment patients inevitably become hemodialysis-dependent or demand transplantation.

2.1. Fibrillary Glomerulonephritis

The fibrillary glomerulonephritis characterized by the deposition of non-amyloid fibrillary proteins (immune complexes) along globular membranes is the most frequent reason of an idiopathic nephrotic syndrome [17], often leading to development of a chronic renal failure, despite the carried-out immunosuppressive therapy [18]. Carrying out three courses of a plasma exchange on 5-6 sessions each 3-5 months allowed to lower proteinuria degree from 7 g to 1 g a day [19].

2.2. Membranoproliferative Glomerulonephritis the II Type

It is a consequence of adjournment in a glomerular basement membrane of elements of a complement (Dense Deposite Disease) and meets most often at children. The course from 12 sessions of a plasma exchange with the subsequent purpose of an eculizumab provided permanent remission [20].

2.3. Nephrotic Syndrome

Inclusion of a plasma exchange at treatment of a glomerulonephritis against a nephrotic syndrome is especially indicated. It was applied thus equipment of a double-filtration plasmapheresis cycles on 3 sessions with introduction after the last Prednisolomon (300 mg/kg) and repetition of such courses monthly within a half year that allowed to reduce considerably degree of a proteinuria and permanently improve function of kidneys [21]. It was described a case when at treatment by steroids of a nephrotic syndrome at the patient who had hepatitis B the liver failure developed [22]. In the subsequent the cascade plasma exchange in the form of monotherapy to 9 sessions that led to decrease in level of a proteinuria from 9.2 g/day to 0.2 g/day was applied and such state kept and in 12 months. Also the combination of a cascade plasma exchange to immunoadsorption was effective [23].

Nevertheless, only timely removal of antibodies is capable to prevent or, at least, to reduce the scale of organic damage of kidneys parenchyma. The same tactics is justified also at the subsequent aggravations, even at already arisen manifestations of a renal failure, for a distance of prospect of transition to a chronic hemodialysis.

Use of a plasma exchange of patients in a conservative phase of a chronic renal failure when the glomerular filtration is still kept at the level of 10-15 ml/ (min • m²) leads to fast improvement of health with lowering of arterial pressure, disappearance of an itch, decrease in level of creatinine and urea, increase in a glomerular filtration. In such cases the plasma exchange allowed to remove the moment of the transfer of patients to a chronic hemodialysis.

3. Kidney Damage in Vasculitis

The kidneys are the target organ in a wide variety of autoimmune diseases, particularly such as systemic lupus erythematosus (lupus nephritis), Goodpasture's syndrome, purpura Henoch-Schönlein, Wegener's granulomatosis, polyarteritis nodosa, in which vasculitis is an important component of the pathogenesis. And application of a plasma exchange is here too justified [24, 25].

3.1. IgA Nephropathy

IgA nephropathy or Berger's disease is the form of a glomerulonephritis, most widespread in the world, and, at the same time, the leading reason of a terminal renal failure [26]. Its etiology includes increase of production of polymeric A1 immunoglobulin with abnormal composition of some carbohydrate chains. The increasing quantity of the circulating immune complexes erise and settle in the renal mesangium with subsequent inflammatory activation of mesangial cells, segmental sclerosis and interstitial fibrosis/tubular atrophy [27, 28, 29]. Current therapy is not sufficiently effective. Therefore in resistance cases to treatment and quickly progressing current also the plasma exchange can be used [10, 30]. The IgA-nephropathy can be followed by pulmonary bleedings, and the plasma exchange also helps to cope them, including in children [31, 32]. IgA-vasculitis is also characteristic of Henoch-Schönlein purpura, when glomerulonephritis can also develop like IgA-nephropathy with hematuria and proteinuria up to terminal kidney damage.

3.2. Thrombotic Microangiopathy

The thrombotic microangiopathy (TMA) is a serious
complication of the thrombotic thrombocytopenic purpura (TTP), as well as the hemolytic uremic syndrome (HUS) and hemolysis, elevated liver enzyme levels, low platelet count (HELLP), developing because of microvessels thrombosis associated with platelet thrombi [33, 34]. Thus system and kidney microvessels with development as anuries, and encephalopathies with damage and other vital organs. [35] The role and of a complement C5 activation is possible and the technique of release of a complement inhibitor – monoclonal antibodies anti-C5 is now developed, though efficiency and intensive courses of a plasma exchange is shown [36, 37, 38, 39]. The case of a thrombotic microangiopathy with the phenomena of an acute renal failure against an antiphospholipid syndrome with a favorable outcome after a plasma exchange with immunosupression is described also [40]. A case of gemcitabine-induced TMA is also described that has also demanded application of a plasmapheresis [41].

3.3. Periarteritis Nodosa

The most common periarteritis nodosa, which is a generalized autoimmune necrotizing inflammation of the endothelium and the middle layer of medium and small arteries as a result of antigen-antibody reactions. Emerging granulomatosis while sometimes called “rash” at vessels. The clinical picture depends on the primary lesion of any organ of the abdominal or thoracic cavity, brain, limbs. Renal artery aneurysms with expanded with thrombosis and ruptures, leading to heart attacks and kidney hemorrhage. In another form of the disease – “microscopic” polyarteritis (Horton's disease) – affects mainly small arteries with the development of necrotizing glomerulonephritis. Perhaps the development also renal amyloidosis with proteinuria and renal insufficiency. In the treatment of this disease, along with steroid therapy was used the plasmapheresis also [42].

3.4. ANCA-glomerulonephritis

ANCA-glomerulonephritis develops as a consequence of vasculitis, when activated neutrophils penetrate through the walls of blood vessels and, releasing toxic oxygen radicals and destructive enzymes, undergo apoptosis and necrosis along with the lesion and vascular wall. This is accompanied by necrotic vasculitis [43]. Similar in pathogenesis of syndromes of Goodpasture and Wegener, in addition to the kidney, accompanied by the lung destruction and bleeding that requires connecting plasmapheresis [44].

3.5. Diabetic Nephropathy

Kidneys also suffer from diabetes – diabetic nephropathy is the leading cause of end-stage renal disease in the world [45]. The most common complication of diabetes is damage to the walls of microvessels by secondary toxic metabolites that accumulate despite even maintaining glucose levels at an acceptable level. The final products of glycation are one of the toxic factors determining the development of vascular complications in diabetes [46]. Among them we can mention peralin (pyraline) arising from the interaction of glucose with amino groups of proteins. In addition, the level of circulating proinflammatory cytokines contributing to the progression of kidney damage is increasing [47]. The accumulation of uric acid and glycated hemoglobin, as well as oxidative stress with increased activity of the renin-angiotensin-aldosterone system is important [48, 49]. In this case, the thickening of the basal glomerular membrane, mesangial expansion, nodular glomerular sclerosis and tubulointerstitial fibrosis [50], immune disorders with infiltration of immune cells, mainly macrophages, and complement activation also play a role [51]. All this puts indications for the use of plasmapheresis, in particular, in diabetic ketoacidosis [52].

3.6. Lupus Nephritis

Lupus nephritis develops as a severe complication of SLE with a sufficiently large frequency. At the same time, circulating immune complexes are deposited in the renal vessels. Infiltration of renal parenchyma by T-lymphocytes, macrophages and dendritic cells occurs, which play a major role in the development of lupus glomerulonephritis leading to renal failure [53]. With the help of plasmapheresis it is possible to prevent the progression and fast enough to achieve remission [54]. It is possible to use immunoabsorption, which can be used to remove autoantibodies, but plasmapheresis removes activated complement components, clotting factors and cytokines [55]. The use of double-filtration plasmapheresis is also justified [56].

4. Metabolic Disorders

4.1. Amyloidosis

Kidney damage occurs in amyloidosis, when a clone of plasma cells secretes amyloidogenic light chains, which are deposited on the membranes of glomeruli, tubules and even microvessels. Severe nephrotic syndrome with proteinuria and progressive renal failure develops [57, 58, 59]. Moreover, amyloidosis can evolve on long-term hemodialysis, causing polyarthralgia and other organ lesions [57, 58].

4.2. Multiple Myeloma

Other types of monoclonal gammopathy, in particular multiple myeloma, carry the same risk to the kidneys [59]. The same can be said about cryoglobulinemia, leading to proteinuria, nephrotic syndrome and renal failure progression when plasmapheresis also helps to improve kidney function [60].

5. Kidney Disorders at Infection Diseases

5.1. Hemorrhagic Fever to a Kidney Syndrome

Kidneys suffer and at a number of infectious diseases. In particular, the combination of the hemorrhagic fever to a
plasmapheresis, including in children, can improve the progression of renal failure [69]. At the same time, it is often became clear by the end of such an epidemic in Europe in plasmapheresis also, promoting both removing viruses and presence of immunosuppressants allows for faster outcome of the disease [4].

5.2. Hemolytic Uremic Syndrome

The hemolytic uremic syndrome (HUS) is characterized by a triad of thrombocytopenia, microangiopathic hemolytic anemia, and acute kidney damage [61]. It is the most common cause of acute kidney damage in children and is divided into 2 groups – typical with diarrhea (dHUS) and atypical, not associated with it (aHUS). The most common cause of a typical form is Shiga-toxin produced by Escherichia coli type O157:H7 [62]. In such case, severe enterocolitis occurs with the development of dHUS with renal failure and high mortality. Antibiotics were thus powerless or, on the contrary, contributed to the growth of endotoxicosis. This became clear by the end of such an epidemic in Europe in 2010-2011, which forced even to abandon antibiotic therapy. The use of plasmapheresis in the early stages of the disease contributed to the fast healing [63, 64, 65] summarizing the experience of treatment of 631 patients in 84 hospitals in Germany, Sweden and the Netherlands, came to the same conclusion.

5.3. Kidney Damage at Viral Hepatitis C

Too most it is possible to tell and about viral hepatitis C at which the renal failure demanding a hemodialysis can develop too [66]. Hepatitis B can also lead to development of a secondary membranous nephropathy at which the plasma exchange renders medical effect [67, 68]. Therefore, in all these cases, plasmapheresis is a pathogenetically justified method of treatment and prevention of progression of kidney lesions [60]. Indeed, the use of plasmapheresis in the presence of immunosuppressants allows for faster stabilization of renal function with the cessation of progression of renal failure [69]. At the same time, it is often necessary to remove very massive amounts of plasma – up to 2-2.5 l, at first 3 such sessions every other day, then 2-3 sessions every 2 weeks [70]. It is used cascade plasmapheresis also, promoting both removing viruses and reduction of HCV-associated cryoglobulin-nephropathy [71].

6. Problems in Urology

6.1. Acute Pyelonephritis

At acute pyelonephritis quite often there is a process of generalization, up to sepsis and multiple organ insufficiency to a serious endotoxicosis which can be stopped only by means of an intensive plasmapheresis or a plasma exchange with replacing by donor plasma [72]. Pyelonephritis, both at the height of exacerbation, and with a sluggish course with frequent relapses, is also not always amenable to drug and antibacterial therapy. All this makes it shown and apheresis therapy – hemosorption, plasmapheresis with laser irradiation of the blood. The use of plasmapheresis in acute purulent pyelonephritis accelerates recovery, reduces the frequency of nephrectomy by 14% [73]. Physiological immunosuppression during pregnancy contributes to the exacerbation of chronic pyelonephritis, which contributes to the appearance of preeclampsia with endotoxicosis. Courses of plasmapheresis with laser irradiation of blood stop such exacerbation and provide the best conditions for the development of the fetus [74].

6.2. Chronic Pyelonephritis

For chronic pyelonephritis is characteristic periodic coming activation of inflammatory process against both local weakening of the immune defence, and the general immunosuppression. Thus by means of a plasma exchange in combination with it is possible to achieve both a detoxification, and immunocorrection that phototherapy will help to warn or soften episodes of aggravations in the future [75]. This is because plasmapheresis removes the "toxic press" from the immune system, which helps to restore its activity.

6.3. Prostatitis

It is quite widespread disease and, nevertheless, having the long and hardly giving in to therapy current. Most often in its etiology urogenital chlamydiosis and mycoplasmosis matter. One of the promoting factors of chronicization is the immunosuppressive state promoting such types of chronic infection. In such cases, with the help of plasmapheresis it is also possible to restore the immune response and stabilize such chronic inflammation.

6.4. Interstitial Cystitis

It is followed by pains and frequent desires on an urination perhaps has the autoimmune nature as about a half of these patients have the increased level of various autoantibodies [76]. It is impossible to exclude also allergic mechanisms, especially at a combination to allergic rhinitis and asthma [77]. Therefore the plasma exchange here too will be useful.

6.5. Priapism

In pathogenesis of such disease can play a role an anti-protein S antibodies leading to development of thrombosis in a cavernous body up to a necrosis of it and need of its removal. The plasma exchange is capable to prevent such complications [78].

6.6. Male Infertility

Among its reasons the essential role is played by autoimmune frustration when after quite often for a long time the forgotten injuries, an orchyepidimitis and even to the varicocele arise the autoantibodies against own spermatozoid which find in 8-21% of cases in men at suspicion on "man's" infertility [79]. They are capable to break both mobility of
spermatozoa, and ability of the last to get through an oocyte cover without what extracorporeal fertilization which success in such cases doesn't exceed 40% is impossible even. There are indications that antisperm antibodies can be caused by the use of immunosuppressants and cytostatic agents, anti-parasitic medicines, prostate-specific antigen (PSA). Play a role and the presence of men Chlamydia trachomatis, Ureaplasma urealyticum and Microplasma hominis [80, 81].

In addition to autoantibodies, the functional state of spermatozoa can be influenced by other toxic compounds of both exo- and endogenous origin, in particular – the generation of excess amounts of cytotoxic oxidants [82, 83]. In such cases, the sperm cells lose the genes for the oxidative phosphorylation [84]. Thus the autoantibodies maintenance of such in blood can increase to 3000-4000 units/ml (in norm of 75 units/ml) and to 500-2000 units/ml in an ejaculate (at the same norm) [85]. It is described the antispermal autoantibodies emergence also at men with the revealed viral (HSV1, CMV) infections (31.1%) or at their biocenosis from bacteria (61.4%) [86]. With systemic lupus erythematosus, spermatogenesis with the appearance of autoantibodies is disturbed and treatment is carried out with the help of cyclophosphamide [87].

Only by means of a plasma exchange it is possible to remove such antibodies and other toxic products out of an organism and to provide safe conditions for fertilization. So, it was noted increase of total of spermatozoa in an ejaculate for 46%, and quantities of mobile cells for 30-123% after a plasma exchange course at men thus that in 42% of cases also helps to restore erectile function [89].

6.7. Decrease in a Potentiality

Such problem can develop not only in old age, but also at younger (“reproductive”) age. And deterioration of cavernous bodies blood filling as a result of the occlusion processes in the arteries can be one of the reasons. It arises most often against of system vessels damages at autoimmune vasculitis, the Buerger disease, the obliterating endarteritis and a diabetic vasculopathy. And the plasma exchange in such cases also helps to restore erectile function [89].

7. Tactics of Treatment of Autoimmune Diseases

The most common they are based on two-component drug therapy – corticosteroids and cytostatics. They are designed to delay reproduction of auto-reactive T-and B-lymphocytes clones. However, such therapy doesn’t lack a large number of adverse reactions. Corticosteroids lead to cushingoid syndrome. Glucocorticoids, in particular, are diabetogenic hormones due to their suppression of glucose consumption by the tissues and increase of its production by the liver. Another complication of long-term glucocorticoid therapy is osteoporosis. It is believed that these hormones inhibit the proliferation and differentiation of osteoblasts and stimulate their apoptosis. There is also an indirect mechanism of bone resorption as a result of secondary hyperparathyroidism due to decreased calcium adsorption in the intestines. Cytostatics lead to significant metabolic disorders, including healthy organs and systems. Intravenous administration of large doses of immunoglobulins are often used, leading to a significantly decreased content of pathological autoantibodies and inhibitors, and this effect exceeds the life of these immunoglobulins, which indicates a more significant regulatory correction of pathological autoimmune processes in the patients. However, intensive intravenous administration of immunoglobulins is reported to have a great number of complications.

The most common cause of patients’ infection is said to be hepatitis G-viruses. Following such immunoglobulinoetherapy, acute renal failure may develop. It also describes and serious complications such as vasculitis and lupus due to the side effects caused by immunoglobulins administered along with related autoantibodies and circulating immune complexes, lethal hypersensitive myocarditis, not to mention transmission of hepatitis viruses C and D, etc. There is also a significant increase in blood viscosity associated with administration of high doses of immunoglobulins, which can create a number of problems in elderly patients, having vascular diseases, cryoglobulinemia, monoclonal gammopathy, and high levels of lipoproteins.

It should be taken into account that immunoglobulins are nothing but complexes of various antibodies. Among them there are not only useful antibodies against a variety of microbes and viruses, with which donors had to get into conflict during their lifetime, but also autoantibodies against their own structures antigens. And even if these donors are formally considered healthy, nevertheless, latent and not yet manifested symptoms of certain diseases are not excluded. In intensive immunoglobulins therapy immunoglobulin is simultaneously injected from many donors and the total number of certain autoantibodies can exceed the known critical mass and be manifested by additional pathology. This mass of immunoglobulins can turn from a "concentrate of health" into a "concentrate of diseases" [90].

In the recent years, treatment of autoimmune diseases with rituximab – chimeric monoclonal antibody to the CD20 antigen of B-lymphocytes – has also become widespread,
which is meant to reduce the autoantibodies production. However, complications of such treatment are described, resulting even in development of multi-organ failure [91]. Rituximab, cetuximab and panitumumab have direct nephrotoxic effect [92]. Eculizumab can lead to a severe damage of kidneys, up to anury associated with haemolytic uremic syndrome [93].

8. Hemodialysis - Opportunities and Complications

But even with a complete loss of kidney function, hemodialysis is not able to provide remove all pathological of compounds, particularly molecular weight of more than 1000 Daltons, ie, middle weight molecules, which do not pass through the dialysis membrane known, but cause a number of adverse metabolic disorders, among which more than just worried sick, itchy skin. In varying degrees, expressed it occurs in 60-90% of patients during hemodialysis. Its pathogenesis depends of many metabolic factors – hypercalcemia, hyperphosphatemia, secondary hyperparathyroidism, hypermagnesiemia, amyloidosis.

But even in the absence of metabolic disorders pruritus was significantly disturbed daily activity and nocturnal sleep [94]. In such cases, obviously, hemodialysis is simply not able enough to fully withdraw all products pathological metabolic and periodic addition of plasmapheresis can greatly improve the quality of life of these patients [95]. In particular, acute kidney failure with glomerulonephritis plasmapheresis in conjunction with hemodialysis facilitated more rapid relief of clinical symptoms and the achievement of stable remission. There is used also a "tandem method" simultaneous hemodialysis and plasmapheresis. At first the blood pass through the plasma filter, and then through the dialyzer [96].

In chronic hemodialysis often develop anemia, are not always amenable to erythropoietin administration and iron supplementation (Sorbifer). In such cases, periodic plasmapheresis helped stabilize hemoglobin levels and increased intervals between the infusions of packed red blood cells up to 6 months.

In essence, and any other form of renal parenchymal lesions (nephrosis or nephritis exo- or endotoxin genesis, lupus nephritis) therapeutic apheresis can prevent or reduce the disease occurred [97]. As it was already mentioned above, at a number of acute damages – poisonings, burns, severe injuries, a crush-syndrome, etc., timely removal of pathological products is capable to prevent organic damages of kidneys and will allow to avoid need of the subsequent hemodialyses.

Of course, not every acute renal pathology becomes chronic, but predict in advance such a situation is practically impossible, so even preventive perform in general completely safe procedure plasmapheresis seems justified, even in childhood. Especially when you consider that neither age nor body weight, have not additional restrictions for membrane plasmapheresis.

9. Plasmapheresis

This word comes from the Greek πλάσµα (liquid part of blood) and ἀφαίρεσις (removal). The picture of homeostasis disorders, leading to organ disorders increase, increasingly becomes clearer. In this case, many pathological products are accumulating, the molecules size of which does not allow them to be eliminated by the kidneys while the liver is also unable to destroy them. On the other hand, the fact of their accumulation suggests that no drugs are able to help them to be removed from the body [98, 99]. Therefore in all these cases the plasmapheresis is pathogenetic justified method of treatment and prevention of progressing of kidneys damages [60]. And it is valid, use of a plasma exchange against immunodepressants allows to stabilize quicker function of kidneys with the termination of a renal failure progressing [60]. Thus, removal of very massive volumes of plasma – up to 2-2.5 l (1 CPV), in the beginning 3 such sessions every other day, then 2-3 sessions every 2 week often is required [13].

10. Conclusion

The provided findings show real dangers and serious complications of many kidney diseases, which not always can be prevented by drug therapy. This is because many large-molecular substances accumulate – antibodies, immune complexes and other pathological metabolites that cannot be excreted by the kidneys. On the other hand, the kidneys themselves are damaged due to their deposition in the microvessels, glomeruli, tubules, which causes an impairment of their functions, up to fatal disorders that require hemodialysis and even the need for transplantation of donor kidneys. Drug therapy itself can be dangerous due to serious side effects and not always provides a favorable outcome. Therefore, the question raises of physical removal of these accumulated pathological products together with the liquid part of the blood – plasma, which occurs in plasmapheresis. With the help of plasmapheresis, much better treatment results can be achieved, more stable remission with a lower level of drug support.

References


