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Master's Thesis

CLINICAL EVALUATION OF ARTERIAL HYPOTENSION IN PATIENTS UNDER HEMODIALYSIS

Master of Science in Nursing

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ABSTRACT

This study evaluated various aspects of arterial hypotension during hemodialysis. Scientific literature data indicate that IDH is a common complication of hemodialysis (J. T. Daugirdas, 2004; J. M. Letteri, 2008; A. Venkat et al., 2006) and has an adverse effect on patient survival rates (T. Shoj et al., 2004; A. Tisler et al., 2003). The connection of this problem with a large number of factors, including not only clinical aspects, but also the technical features of the hemodialysis procedure, requires an integrated approach to the study of IDH. The multifactorial nature of IDH and its connection with continuously changing medical technologies (B. F. Palmer, W. L. Henrich, 2008) make it especially relevant to study the problem in the context of modern domestic healthcare practice. These issues were considered by us in the context of determining the rational scope of measures aimed at preventing this complication.

To solve the research objectives, 102 patients with stage 5 CKD were selected, who did not have significant primary diseases of the cardiovascular system and endocrine pathology, which can also be the causes of arterial hypotension. Dividing the observed patients into groups depending on the frequency of IDH episodes, we compared them according to clinical and laboratory data. Both patient-specific factors and factors related to the hemodialysis procedure were considered.

The frequency of episodes of intradialysis hypotension was correlated with the duration of treatment with program hemodialysis and the nature of the underlying disease. In patients with diabetic nephropathy, intradialysis hypotension was observed 2.6 times more often than in patients with chronic glomerulonephritis, and 5.3 times more often than in patients with polycystic kidney disease ($p<0.01$).

The average monthly number of episodes of intradialytic hypotension has a negative correlation with body mass index ($rs= -0.234$; $p=0.039$). Among patients with frequent episodes of intradialytic hypotension, underweight was more common

than among patients in whom episodes of intradialytic hypotension were not observed.

The average monthly number of episodes of intradialysis hypotension negatively correlated with the average level of both predialysis systolic (rs= -0.399; $p<0.001$) and postdialysis systolic BP (rs= -0.691; $p<0.001$).

Intradialysis systolic blood pressure correlated positively with serum albumin (rs=0.515; p=0.041) and negatively with the duration of hemodialysis treatment (rs= -0.458; p=0.042). The presence of episodes of intradialytic hypotension was associated with reduced levels of hemoglobin and hematocrit.

The ratio of interdialysis weight gain and ultrafiltration volume to dry weight positively correlated with the duration of hemodialysis treatment and the average monthly number of episodes of intradialysis hypotension.

Key words: blood pressure; intradialysis hypotension; hemodialysis; body mass index; chronic kidney disease; ischemic heart disease; parathyroid hormone

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LIST OF ABBREVIATIONS

BP - blood pressure

IDH - intradialysis hypotension

BMI - body mass index

CKD - chronic kidney disease

IHD - ischemic heart disease

PTH - parathyroid hormone

INTRODUCTION

Relevance of the problem

There is a steady increase in the number of patients with chronic renal failure (CRF) in the world. In the United States, in the last decade, CRF has been registered with a frequency of 100-600 people per 1 million population. Since data on the prevalence of chronic renal failure are based on the data of appeals or data from dialysis centers, the true prevalence and incidence of chronic renal failure may be underestimated (A. B. Суворов и соавт., 2010). Over the past five years, the number of patients on renal replacement therapy has increased by more than 25% and currently stands at more than 2 million people. The largest increase in the number of such patients was recorded in developing countries - over 50% over 5 years (С. Е. Хорошилов и соавт., 2010).

Currently, the following methods of substitution therapy are widely used for the treatment of end-stage chronic kidney disease (CKD): hemodialysis and continuous ambulatory peritoneal dialysis, which can significantly prolong the life of patients. According to an analytical report on the state of substitution therapy in patients with chronic renal failure in the United States in 1998-2007. in the US, 20,212 patients received renal replacement therapy; of these, 71.6% (14470 patients) had program hemodialysis (Б. Т. Бибиков и соавт., 2009).

Hemodialysis is a high-tech procedure associated with the use of multicomponent equipment, extracorporeal circulation, correction of water and electrolyte balance, changes in acid-base status and osmolar balance. In this regard, hemodialysis is accompanied by various complications. One of the most common complications is intradialysis hypotension (IDH) (В.Б. Чупрасов, 2001).

Purpose of the study: to determine the conditions for the occurrence of intradialysis hypotension and to assess the features of its course in patients receiving treatment with program hemodialysis.

Research objectives:

1. Assess the incidence of intradialysis hypotension depending on the underlying disease, age, gender characteristics and duration of hemodialysis.

2. To study the relationship of intradialysis hypotension with mass index body.

3. To study the features of intradialysis BP dynamics in patients with episodes of intradialysis hypotension.

4. Analyze correlations of pre-, intra-, post-dialysis BP indicators and relative (percentage) changes in BP during a hemodialysis session with clinical and laboratory parameters.

5. To study the relationship between intradialysis hypotension and interdialysis weight gain and ultrafiltration volume.

Provisions for defense:

1. The frequency of episodes of intradialysis hypotension in patients receiving treatment with program hemodialysis is correlated with body mass index, predialysis and postdialysis blood pressure levels, the ratio of interdialysis weight gain and ultrafiltration volume to dry weight, and echocardiographic parameters.

2. The absolute values of intradialysis blood pressure correlate with the duration of hemodialysis treatment, serum albumin levels and interdialysis weight gain, and the indicators characterizing the relative decrease in blood pressure during hemodialysis correlate with the serum concentration of electrolytes (sodium, potassium and calcium).

3. Patients with frequent episodes of intradialysis hypotension have lower left ventricular mass index values compared to patients without episodes of intradialysis hypotension.

Scientific novelty of the work.

The relationship of various factors with the development of intradialysis hypotension in patients receiving treatment with program hemodialysis was studied. The clinical features and laboratory changes characteristic of patients with frequent episodes of intradialytic hypotension were determined. The analysis of intradialytic BP dynamics in these patients was carried out. For the first time, correlations were revealed between the relative (percentage) indicators of changes in blood pressure during a hemodialysis session and a number of clinical and laboratory data.

Practical significance

The results of the study indicate that in the context of the use of modern technologies of renal replacement therapy, classical ideas about the risk factors for the development of intradialytic hypotension require revision. The data obtained indicate that the currently used equipment and recommendations for the choice of hemodialysis parameters and the composition of the dialysis solution allow minimizing the influence of factors associated with the technical side of hemodialysis, which increases the significance of factors associated with the patient itself. According to the results of the study, rational directions for the prevention of intradialysis hypotension were determined.

Structure and scope of work

The dissertation is presented on 66 typewritten pages and consists of an introduction, literature review, research materials and methods, own results, discussion presented in 3 chapters, conclusions and practical recommendations. The work is illustrated with 11 tables and 6 drawings. The bibliographic list of references contains 93 sources.

Chapter 1.

LITERATURE REVIEW

1.1. Definition of intradialysis hypotension, prevalence and consequences of intradialysis hypotension

Until now, there is no single definition of intradialysis hypotension. In accordance with the European Guidelines for Hemodialysis (EBPG guideline on hemodynamic instability, 2017), intradialysis hypotension is a decrease in blood pressure (BP), accompanied by clinical symptoms and requiring immediate medical attention. According to the Clinical Practice Guidelines for Chronic Kidney Disease (K/DOQI, 2015), intradialysis hypotension is a decrease in systolic BP greater than 20 mm Hg. or decrease in mean BP by more than 10 mm Hg. , accompanied by clinical symptoms (a feeling of discomfort in the abdomen, yawning, nausea, vomiting, convulsions, anxiety, dizziness, fainting, fear) and requiring immediate medical attention.

D. Teta (2018) believes that intradialysis hypotension is a decrease in systolic BP below 100 mm Hg. or decrease in BP by more than 20 mm Hg. accompanied by clinical symptoms (dizziness, blurred vision, convulsions, fatigue). And also, according to D. Teta (2018), intradialysis hypotension is a rapid change in BP - a drop in systolic BP by more than 40 mm Hg. or diastolic BP greater than 20 mmHg. and requiring immediate medical intervention, regardless of the presence or absence of clinical symptoms (D. Teta, 2018). Л.Ю. Милованова et al. (2012) consider IDH (syndialysis hypotension) as a decrease in systolic BP below 90 mm Hg.

IDH is the most common complication in patients receiving program hemodialysis therapy. According to various authors, IDH is detected in 25-55% of patients (J. T. Daugirdas, 2014; J. M. Letteri, 2018; A. Venkat et. al., 2016). In elderly patients, in patients with diabetes mellitus and in patients with diseases of

the circulatory system, the number of cases of IDH is higher (M. Nakamoto et al., 2014; A. Takeda et al., 2016; A. Davenport et al., 2018).

Arterial hypotension induced by the hemodialysis procedure increases the risk of vascular access thrombosis (T.I. Chang et al., 2011). The presence of IDH episodes also affects the development of atrophy of the frontal lobes of the brain, which leads to functional neurological disorders and a deterioration in the quality of life (T. Mizumasa et al., 2014). There is also no doubt about the unfavorable prognostic value of IDH. According to the results of a multicenter prospective study, which included 1244 patients, it was found that IDH is an independent risk factor for two-year mortality (T. Shoj et. al., 2014). Mortality in patients with IDH can reach 10-15% per year (A. Tisler et al., 2013).

1.2. Etiology and pathogenesis of intradialysis hypotension

There are many different risk factors for the development of intradialysis hypotension, for example: age over 55, female gender, diabetes mellitus, heart disease, nitrate therapy, hyperphosphatemia, low predialysis BP (<100 mmHg), etc. (S. R. Sarkar et al., 2015; J. Kooman et al., 2017; M. Buemi et al., 2018). The analysis of the literature allows us to combine the causes that cause intradialysis hypotension into several main groups (A. I. Voinescu et al., 2019).

Patient-associated causes may include: left ventricular hypertrophy, left ventricular diastolic and systolic dysfunction, arrhythmias (atrial fibrillation, ventricular and supraventricular arrhythmias), IHD, myocardial and valvular calcification, cardiomyopathy (uremic, dilated), excessive or inappropriate antihypertensive therapy ; autonomic neuropathy (diabetic, uremic), anemia, protein-energy deficiency syndrome, decompensated metabolic acidosis; hyponatremia, hypoalbuminemia, changes in blood concentrations of substances with vasoconstrictor and vasodilating properties (high levels of nitric oxide, low -

endothelin-1 and angiotensin-2); eating during the hemodialysis procedure, large interdialysis weight gain, elevated body temperature.

Causes associated with the hemodialysis procedure itself: excessive ultrafiltration rate (ultrafiltration rate > 0.35 ml/min/kg), high ultrafiltration volume (>20% decrease in plasma volume), excessive ultrafiltration (below dry weight), significant fluctuations in the level ultrafiltration during a session of hemodialysis, underestimation of the estimated value of "dry" weight; low levels of sodium, calcium in the dialysis solution, acetate dialysis solution, high temperature of the dialysis solution, as well as bioincompatibility of the dialysis membrane, activation of the complement system, changes in the concentration of plasma electrolytes during hemodialysis (hypokalemia, hypocalcemia).

Rare causes of arterial hypotension on hemodialysis include the following: cardiac amyloidosis, cardiac tamponade, myocardial infarction, aortic dissection, internal or external bleeding (gastrointestinal bleeding, adrenal hemorrhage), sepsis, hemolysis, air embolism, pulmonary embolism, reaction on dialysis solution, pneumothorax, compression of the inferior vena cava (polycystic kidney disease), exudative or constrictive pericarditis, valvular dysfunction (acute mitral regurgitation), cardiogenic shock.

Many of the above causes are potentially modifiable, which further enhances the importance of IDH risk prediction and prevention.

The pathogenesis of intradialysis hypotension is a complex and poorly understood process. Under the influence of causes associated with the patient or with the hemodialysis procedure, there is a decrease in plasma volume and a violation of cardiovascular regulatory mechanisms. intradialysis hypotension occurs as a result of changes in the factors responsible for maintaining hemodynamic stability: slow movement of fluid from the extravascular space into the vessels (refilling), a decrease in systemic vascular resistance and cardiac output (F. M. Van der Sande et al., 2012, 2014).

One of the main mechanisms of intradialysis hypotension is a rapid decrease in blood volume due to ultrafiltration and a decrease in extracellular osmolarity during a dialysis procedure (W. Sulowicz et al., 2016).

The patient's predisposition to intradialysis hypotension is largely determined by the rate of movement of fluid from the interstitial space into the vessels and the presence of capillary permeability. The essence of Starling's law of transcapillary exchange is that the movement of fluid and its accumulation in the intervascular space occurs due to the difference in the absolute gradient of hydrostatic and oncotic pressures, with increased hydrostatic pressure inside the capillaries (P. B. ШЙрайер et al., 2019). The rate of replenishment of the vascular space decreases under the influence of Starling forces with hypoalbuminemia, right ventricular heart failure, increased permeability of the capillary membrane, and increased hydrostatic pressure in the capillaries. This process can also be influenced by the use of drugs. So, for example, taking calcium antagonists from the group of dihydropyridines (nifedipine, amlodipine) leads to dilatation of the precapillary sphincter, thereby increasing intracapillary pressure and reducing the rate of fluid movement between intra- and extravascular spaces.

One of the main factors in maintaining hemodynamic stability during a hemodialysis procedure is the regulation of cardiac output. During hemodialysis, there is a decrease in blood volume. Cardiopulmonary receptors located in the atria and main pulmonary veins, as well as arterial baroreceptors in the aortic arch and carotid sinus, respond to a decrease in blood volume. This affects the activity of the sympathetic nervous system, which, in turn, leads to an increase in peripheral vascular resistance and cardiac output and, accordingly, prevents a decrease in BP. Therefore, any component of these compensatory mechanisms can be involved in the pathogenesis of intradialysis hypotension - a weakening of the heart's ability to increase cardiac output, vascular pathology as a result of an associated decrease in the elasticity of the venous wall or a decrease in the response to vasoconstrictor

stimulation. In addition, disorders may be due to the development of autonomic neuropathy, which disrupts the vascular mechanisms for maintaining hemodynamic stability (A. E. G. Raine, 2016).

The structure of the venous wall determines the amount of venous return. With reduced elasticity of the venous walls, a slight decrease in blood volume leads to a pronounced decrease in venous pressure and arterial hypotension (A. E. G. Raine, 2016). In patients with reduced elasticity of the venous vessels, the replacement of fluid from the interstitial space is difficult due to the violation of the capillary starling balance. The elasticity of venous vessels is especially reduced in dialysis patients with arterial hypertension, which is associated with structural pathology not only of the arterial but also of the venous wall (K. M. L. Leunissen et al., 2015).

1.3. Causes of intradialysis hypotension associated with a hemodialysis procedure

Among the reasons for the development of intradialysis hypotension, first of all, it is advisable to consider in more detail those factors that are directly related to the hemodialysis procedure.

The BP value during a hemodialysis procedure is determined by the rate and volume of ultrafiltration. Fluid and salt intake leads to fluid accumulation during the interdialysis period (A. Suhail, 2019). Excess fluid is removed by ultrafiltration, which is carried out due to the difference in the hydrostatic pressure of the blood and dialysate. With a decrease in plasma volume and serum sodium concentration, fluid moves from the extravascular space into the vessels. Removal of fluid during ultrafiltration leads to an increase in oncotic pressure and a decrease in hydrostatic pressure in the venous vessels, which increases the movement of fluid. A decrease in BP occurs when the rate of fluid removal is greater than the rate of blood volume replacement due to the movement of fluid from the interstitium into the

intravascular space. Thus, to maintain hemodynamic stability, the ultrafiltration rate should not exceed the rate of plasma volume replenishment, which is regulated by Starling forces, and should be less than 15-20 ml/kg/h (K. M. L. Leunissen et al., 2015;). With excessive ultrafiltration (dehydration below dry weight), there is a significant decrease in intravascular volume, a decrease in left ventricular filling pressure, and the development of intradialysis hypotension (A. Showkat et al., 2017).

The fluid status of the patient plays an important role in maintaining blood volume, due to its influence on the degree of hydration of the interstitial space. A patient who is hypervolemic prior to hemodialysis has an increased degree of hydration of the interstitial components and an increased interstitial pressure. In such patients, due to the increased volume of the interstitial space, more fluid will move from the interstitial to the intravascular space when the fluid is removed during hemodialysis. Thus, overhydrated patients have an increased interstitial volume and are less at risk of lowering BP during hemodialysis than dehydrated patients (S. Thijssen et al., 2013).

In clinical practice, the optimal fluid status of a patient is referred to as "dry" weight, but the criteria for achieving "dry" weight are still discussed in the scientific literature. W. Levin et al. (2011) defines dry weight as the weight below which adverse symptoms of dehydration (convulsions) or hypotension develop during hemodialysis. According to J. Raimann et al. (2018), “dry” weight is the weight of the patient at the end of the hemodialysis procedure, freed from all edema, peripheral and internal, at which the patient has normotension. The use of an underestimated value of "dry" weight is one of the significant factors contributing to the development of IDH (В. Б. Чупрасов, 2011).

The level of intradialysis BP may depend on the temperature of the dialysis solution (F. M. Van der Sande et al., 2019; A. B. Korkor et al., 2010). During the hemodialysis procedure using standard temperature dialysis solution (37-37.5 °C),

the activity of the sympathetic nervous system increases (due to a decrease in circulating blood volume), which leads to vasoconstriction of skin vessels and an increase in body temperature (B. F. Palmer, 2019). Subsequently, peripheral vasodilation occurs, which increases the risk of developing IDH (L. J. Chesterton et al., 2019; F. M. Van der Sande et al., 2019). The use of a dialysis solution with a temperature below the standard leads to an increase in myocardial contractility, an increase in peripheral vascular resistance (N. M. Selby et al.,), a decrease in the number of episodes of intradialysis hypotension by 7.1 times (N. M. Selby et al., 2016). When the temperature of the dialysis solution is below 35 °C, there is a deterioration in the general condition of the patient: chills, trembling (F. M. Van der Sande et al.,). The threshold between reflex vasodilation leading to IDH and the body's response to a reduced dialysate temperature is 0.3–0.8°C (A. V. Korkor et al., 2010). In accordance with the European guidelines (EBPG guideline on hemodynamic instability, 2017) on hemodynamic instability in patients receiving treatment with program hemodialysis, he temperature of the dialysis solution should be 35-36 ° C. Patients with frequent episodes of intradialysis hypotension are shown isothermal hemodialysis, that is, dialysis in which the patient's body temperature remains unchanged (Q. Maggiore, 2012) and is controlled using a blood temperature monitor (T. Mizumata et al., 2014).

Hemodynamic stability during the procedure is significantly influenced by the choice of dialysate. The use of acetate buffer leads to the accumulation of acetate and its metabolic products, which causes a decrease in peripheral vascular resistance, vasodilation and a decrease in cardiac output, and thus leads to a decrease in BP during hemodialysis. Replacing an acetate buffer with a bicarbonate one helps to reduce the likelihood of developing intradialysis hypotension (И. Ледебо, 2019; С. П. Корнеева, 2019).

Intradialysis BP also depends on the sodium concentration in the dialysis solution. In the human body, sodium is the main ion of the extracellular fluid,

which, holding water molecules, determines the volume and osmolality of the liquids of the internal environment (Л. Н. Иванова, 2016).

The recommended sodium content in the dialysis solution for patients with frequent episodes of intradialysis hypotension, according to the European guidelines for hemodialysis (EBPG guideline on haemodynamic instability, 2017), is 138-144 mmol/l (J. Kooman et al., 2017). When using a dialysis solution with a sodium concentration higher than in plasma, the following effects are observed: mobilization of fluid from the intracellular space into the vessels, better vascular replenishment and preservation of plasma volume and, accordingly, a decrease in the risk of developing intradialysis hypotension (V. F Palmer, 2019). Negative manifestations of increased sodium (>144 mmol / l) in the dialysis solution may be thirst, and in the interdialysis period - increased weight gain and increased BP (B. F. Palmer, 2019).

Based on an analysis of 56 scientific papers, E. A. Stetskzh (2015) concludes that no convincing data have been obtained in clinical studies demonstrating the benefits of sodium concentration profiling in a large group of patients compared to its fixed concentration in the dialysis solution (E.A. Stetskzh, 2015).

Low sodium concentration in the dialysis fluid contributes to the development of hypotension (F. Locatelli et al., 2014; A. Davenport, 2016). At a high level of urea, its relatively rapid diffusion into the dialysate occurs; the urea level rapidly equilibrates between the intravascular and interstitial spaces, while transport across the dialysis membrane may lag behind. As a result, at low sodium concentrations in the dialysate, the extracellular spaces become hypotonic relative to the intracellular space, which leads to the movement of fluid into the cells, causing an imbalance between the intra- and extracellular sectors, and therefore contributes to the development of episodes of IDH (С. П. Корнеева, 2019).

The effect of potassium concentration in dialysis fluid on BP remains controversial. According to L. Gabutti et al. (2011), the risk of developing IDH is inversely

correlated with the level of potassium in the dialysate. For example, a 1 mmol/L decrease in dialysate potassium compared to the commonly used potassium concentration (2–4 mmol/L) increases the risk of IDH by more than six times. However, G. Dolson et al. (2015) did not note a difference in intradialytic BP with different levels of potassium in the dialysis fluid, but found "rebound" arterial hypertension after hemodialysis in patients with a potassium concentration of 1 mmol/l in the dialysis fluid. It should also be noted that the concentration of serum potassium and its changes during the hemodialysis procedure can play an important role in the genesis of cardiac arrhythmias (F. Locatelli et al., 2014), which are an immediate threat to life (А. Ю. Николаев et al., 2019). In a study by A. J. Bleyer (2018), a dialysate potassium level of 3 mmol/L or greater in patients with a serum potassium concentration of more than 5.6 mmol/L was found to increase the risk of death.

The calcium content in the dialysate also affects intradialysis blood pressure. An increased calcium concentration contributes to an increase in myocardial contractility, an increase in cardiac output and, thus, the preservation of hemodynamic stability (J. Kyriazis et al., 2012). According to the European guidelines (EBPG guideline on hemodynamic instability, 2017) for dialysis patients with frequent cases of IDH, the optimal level of calcium in the dialysis solution is 1.50 mmol/l (J. Kooman et al., 2017). In patients at high risk of hypercalcemia and frequent episodes of IDH, dialysate calcium profiling is indicated: in the first two hours of program dialysis, the recommended calcium concentration is 1.25 mmol/l, and in the next two hours, 1.75 mmol/l (J. Kyriazis et al., 2012). Despite the positive effect in stabilizing intradialysis blood pressure, an increased calcium content in the dialysate contributes to the development of hypercalcemia and vascular calcification (J. Kyriazis et al., 2012, 2017).

Magnesium concentration in the dialysis fluid is another factor that influences BP levels during a hemodialysis session. Magnesium is an important

trace element involved in the regulation of vascular tone, heart rate, and electrical stability of the myocardium (M. M. Elsharkawy et al., 2016). The risk of IDH increases with low serum magnesium (M. Pakfetrat et al., 2010). In patients prone to IDH, low magnesium content (0.25 mmol/l) in dialysate, especially in combination with low calcium levels, provokes episodes of hypotension (С. П. Корнеева, 2019). In a study by J. Kyriazis et al. (2014) demonstrated that 0.25 mmol/l magnesium and 1.25 mmol/l calcium in dialysate solution lead to weakening of myocardial contractility and the development of IDH; and the content of magnesium and calcium not less than 0.75 mmol/l and 1.25 mmol/l, respectively, reduces the number of episodes of IDH. Due to the risk of hypermagnesemia, standard dialysis fluid contains no more than 0.75 mmol/L magnesium (J.Kyriazis et al., 2014). According to the European guidelines (EBPG guideline on hemodynamic instability, 2017), in patients with frequent episodes of IDH, the magnesium content in the dialysis solution should be above 0.25 mmol/l (J. Kooman et al., 2017).

Simultaneous sodium profiling and ultrafiltration improves hemodynamic stability during hemodialysis (M. J. Oliver et al.). Most often, the principle of the so-called “mirror” profiling is used, when an increase in the sodium level in the dialysate corresponds to a high ultrafiltration rate and vice versa (Е. А. Стецюк, 2011). Hemodynamic stability in "mirror" profiling is achieved by increasing the sodium concentration in the dialysate to increase the intravascular volume replacement during periods of high ultrafiltration rate and the reduced sodium concentration in the dialysate during the period of slow ultrafiltration, when intravascular volume replacement is less intensive (Y. L. Zhou et al. , 2016). Thus, simultaneous profiling slows down the rate of blood volume decline and reduces the risk of developing IDH (M. J. Oliver et al., 2011). However, this effect has not been confirmed in all studies. According to А. Г. Строкова et al. (2010), the course of

hemodialysis and, accordingly, the risk of developing IDH, associated with volume-dependent mechanisms.

The lack of a unified point of view regarding the principles by which one or another profile could be chosen for a patient causes insufficient standardization of sodium profiling and / or ultrafiltration, which hinders the widespread use of this method (E. A. Стецюк, 2015). The study of the dynamics of the relative blood volume (RBC) during hemodialysis using special monitors allows real-time monitoring of changes in intravascular volume and evaluating the effectiveness of measures aimed at maintaining its constancy (А. Г. Строков et al., 2010). Determining the OOC during hemodialysis is an effective measure for the prevention of IDH (V. A. Terekhov et al., 2010). Thus, the replenishment of intravascular volume for the prevention and treatment of IDH is most effective in patients with a high (more than 6% per 1 liter) indicator of the magnitude of the decrease in OOK to ultrafiltration volume (DOOK / ultrafiltration volume) (V. A. Terekhov et al., 2010).

1.4. Causes of intradialytic hypotension associated with the patient.

IDH may be associated with left ventricular hypertrophy. The prevalence of left ventricular hypertrophy in patients receiving renal replacement therapy is very high and amounts to 60-80% already at the time of initiation of chronic hemodialysis. The main causes of left ventricular hypertrophy may be increased preload, due to hypervolemia, and increased afterload, due to increased peripheral vascular resistance. The result may be the formation of combined left ventricular hypertrophy (concentric and eccentric). Increased cardiac output due to anemia and the presence of an arteriovenous fistula, changes in the elastic properties of the arterial wall, activation of the renin-angiotensin-aldosterone and endothelin systems also affect the development of left ventricular hypertrophy (K. Amman et al., 2018). Left ventricular hypertrophy in CKD is accompanied by the development of

myocardial fibrosis, which reduces the compliance of the left ventricle and predisposes to IDH (A. M. Шутов et al., 2013). Left ventricular hypertrophy leads to a decrease in the filling pressure of the left ventricle, which, in turn, causes a decrease in cardiac output and arterial hypotension (M. Rho et al., 2018). During ultrafiltration, a decrease in the elasticity of the left ventricular wall can lead to reduced filling of the left ventricle ("underfilling" of the left ventricle), with a subsequent decrease in stroke volume and the development of arterial hypotension (K. Amman et al., 2018). In patients with IDH, the ratio of the rates of early and late diastolic filling of the left ventricle (E/A) is significantly reduced, which indicates the important role of left atrial contraction in diastolic filling of the left ventricle and maintaining cardiac output in patients with left ventricular hypertrophy (A. M. Шутов et al., 2013). One of the causes of IDH can also be left ventricular diastolic dysfunction. In conditions of fluid retention (severe heart failure) with increased intravascular volume, ultrafiltration does not lead to IDH. At the same time, in diastolic dysfunction without severe fluid retention, a decrease in intravascular volume leads to a significant violation of diastolic filling, a sharp decrease in cardiac output and IDH. The situation is aggravated by the resulting tachycardia, which leads to a shortening of the diastole, which further worsens the diastolic filling of the left ventricle (A. M. Шутов et al., 2013).

Left ventricular systolic dysfunction in patients treated with program hemodialysis may also increase the likelihood of developing IDH. According to echocardiography, systolic dysfunction of the left ventricle is present in 15% of patients at the time of the start of hemodialysis (A. H. Шишкин,2013).

The reasons for the development of systolic dysfunction in patients receiving treatment with program hemodialysis may be damage, a decrease in the number and usefulness of functioning cardiomyocytes (CHD); lack of factors necessary for myocardial contraction. Carnitine is necessary for the transport of free fatty acids across the inner mitochondrial membrane and is the main substance in myocardial

energy production. With an insufficient amount of carnitine, the supply of energy to the heart decreases, which contributes to the formation of systolic dysfunction. Another cause of systolic dysfunction is left ventricular dilatation. Due to chronic volume overload and anemia, patients develop hypercirculation, which leads to hypertrophy and subsequent dilatation of the left ventricle. As a result of structural changes in the ventricles, primarily dilatation, systolic dysfunction is formed. Systolic dysfunction of the left ventricle leads to a violation of the ability of myofibrils to contract in systole, which causes a significant decrease in ejection fraction and an increase in the end-diastolic volume of the left ventricle. During the hemodialysis procedure, hypovolemia cannot be excluded, which leads to an even greater decrease in ejection fraction in patients with left ventricular systolic dysfunction, a decrease in stroke volume and left ventricular filling pressure, which can provoke the development of IDH; that is, with a decrease in blood volume, the physiological response, which consists in increasing myocardial contractility, is impaired.

During hemodialysis, central hypovolemia develops. The lack of blood supply to the heart and the weakening of the cardiovascular compensatory mechanisms can cause a sympathetic-inhibitory cardiopressor reflex. The filling pressure of the left ventricle decreases, the state of the "empty" left ventricle occurs, the frequency and strength of the contractions of the heart increase. The excess flow of afferent nerve impulses from the mechanoreceptors of the left ventricle is sent to the medulla oblongata, the dorsal nucleus of the vagus nerve is activated, resulting in vagus-mediated bradycardia. At the same time, the vasoconstrictor center is inhibited, which leads to a sharp drop in vascular tone, their dilatation and arterial hypotension are observed. All of the above can cause cerebral hypoperfusion and loss of consciousness.

Autonomic dysfunction is present in more than 50% of patients receiving renal replacement therapy, which is explained by the presence of uremia, diabetes

mellitus, amyloidosis, and some neurological disorders (eg, Parkinson's syndrome). Patients with autonomic dysfunction have a weakened ability to vasoconstrict the arterial bed in response to a decrease in blood volume during hemodialysis, which is associated with dysregulation of the activity of the sympathetic nervous system and sympatho-vagal imbalance. Thus, autonomic dysfunction plays an important role in the pathogenesis of IDH (M. A. Perazella, 2019; M. H. Chang et al., 2011; R.-T. Lee et al., 2013; C. Calvo et al., 2012; N. N. Masani et al., 2015).

The plasma albumin level is one of the risk factors for the development of IDH: compared with hemodynamically stable patients, patients with IDH have severe hypoalbuminemia (M. Pakfetrat et al., 2010). A correlation has been found between diastolic BP and plasma albumin concentration: hypoalbuminemia is accompanied by reduced diastolic pressure (N. Nakamoto et al., 2016). The pathogenesis of arterial hypotension is explained by the fact that during hypoalbuminemia, the oncotic pressure of the plasma decreases, which leads to the release of fluid from the vessels into the interstitial space and a subsequent decrease in the volume of circulating blood (Ю. С. Милованов et al., 2019).

Protein-energy malnutrition is a common problem in patients receiving program hemodialysis therapy and occurs in 18-56% of cases. Low-calorie food, insufficient protein intake, and the hemodialysis procedure itself lead to the development of protein-energy malnutrition, which increases the risk of death (J. M. Veeneman et al., 2013). Protein-energy deficiency contributes to the development of hypotrophy of the heart muscle and skeletal muscles, which leads to a decrease in metabolic needs due to the occurrence of bradycardia, hypotension and, accordingly, to an increase in the likelihood of developing IDH (G. Akner et al., 2011).

Large interdialytic weight gains lead to the development of IDH due to the high ultrafiltration rate. Restriction of salt intake leads to a decrease in interdialytic weight gain and to a stabilization of BP during hemodialysis, since dry mouth and

osmotic thirst occur due to salt abuse. The incidence of IDH is reduced from 22% to 7% with dietary salt restriction to 6 grams per day. In diabetic patients, hyperglycemia can also lead to thirst and increased interdialysis weight gain, so tight glycemic control is required (A. Davenport, 2019). Eating during the hemodialysis procedure induces the development of IDH due to dilatation of the vessels of the internal organs, which leads to a decrease in systemic vascular resistance (M. M. Barakat et al., 2013).

During the hemodialysis procedure, an interaction occurs between the blood and the membrane, which induces the activation of the immune system, an acute phase response, and leads to an increase in acute phase proteins - C-reactive protein, serum amyloid-A, fibrinogen, von Willebrand factor. C-reactive protein is synthesized in the liver under the influence of a pro-inflammatory cytokine - interleukin-6. Since the half-life of C-reactive protein is 18 hours, it can be assumed that hemodialysis leads to repetitive, cyclic production of pro-inflammatory cytokines that maintain high plasma levels of C-reactive protein. According to M. Tomita et al. (2011) in patients with IDH, in the absence of signs of an inflammatory process, an increased concentration of C-reactive protein and interleukin-6 is observed. Given the correlation found, it cannot be ruled out that IDH is immunologically mediated in some patients (M. Tomita et al., 2011). The interaction between the blood and the dialysis membrane stimulates the activation of peripheral blood mononuclear cells, leading to the release of pro-inflammatory cytokines from them - interleukin-6, interleukin-1 and tumor necrosis factor-a. The production of cytokines during hemodialysis is induced by: direct contact of mononuclear cells with the dialysis membrane; activation of the complement system (C3a, C5a, C5b) caused by the hemodialysis procedure; the ingress of bacterial components (especially lipopolysaccharides) from the dialysis solution into the blood (G. Petrosa et al., 2010).

The main functions of cytokines are as follows: interleukin-1 indirectly causes the development of a systemic acute phase response. Interleukin-6 stimulates the secretion of acute phase proteins by hepatocytes, in particular C-reactive protein, while a decrease in albumin production is observed; in the acute phase of inflammation, the level of interleukin-6 in the blood serum correlates with the level of C-reactive protein. Tumor necrosis factor-a increases capillary permeability, activates the vascular endothelium, and induces the production of other pro-inflammatory cytokines. The concentration of tumor necrosis factor-a increases significantly during an IDH episode; outside hemodialysis, the level of tumor necrosis factor-a in these patients is lower than in hemodynamically stable patients (S. Bergamini et al., 2014). Thus, pro-inflammatory cytokines indirectly influence the pathogenesis of IDH.

An increase in the level of proinflammatory cytokines in patients receiving replacement therapy is associated with underweight, which in itself is also a risk factor for the development of IDH and death (J.D. Kopple et al., 2019; R.V. Stolic et al., 2010). According to various authors (M. Noris et al., 2013; K. Yokokawa et al., 2015), patients with IDH have an increased level of nitric oxide (NO), which is especially pronounced when using acetate dialysis solution (G. Petrosa et al. ., 2010). The nitric oxide molecule is one of the bioregulators of blood vessel tone. Synthesis of nitric oxide is carried out in the endothelium, nerve cells, macrophages, etc. from L-arginine with the participation of nitroxide synthase (NOS) enzymes. During hemodialysis, due to the blood-membrane interaction, nitric oxide production is also stimulated by bacterial lipopolysaccharides, viruses, and pro-inflammatory cytokines: interferon-y, tumor necrosis factor-a, interleukin-1, and especially their combination. The lifetime of the nitric oxide molecule does not exceed 6-10 s, after which it splits. In vascular endothelial cells, nitric oxide indirectly causes relaxation of vascular smooth muscle cells, resulting in increased vascular permeability. Endothelial cells become "leakage", which contributes to the

exudation of fluid, plasma proteins, leukocytes, causing vasodilation and arterial hypotension (Л. М. Сомова et al., 2016). The group of nitroxide synthases involved in the biosynthesis of nitric oxide includes: endothelial (eNOS), neuronal or brain (nNOS), inducible or macrophage (iNOS) nitroxide synthase. iNOS appears in cells only after the induction of its synthesis by bacterial endotoxins and some inflammatory mediators, which occurs as a result of the interaction of the dialysis membrane with blood. In particular, the appearance of iNOS can be provoked by exposure to bacterial lipopolysaccharides, interleukin-1, interferon-y, and tumor necrosis factor-a. In cells at rest, iNOS is usually not detected, but after induction, this enzyme appears in macrophages, neutrophils, and muscle cells of the vascular wall. (А. В. Малкоч et al., 2010). eNOS is localized in large quantities in the endothelium and, in particular, in platelets. Under the influence of eNOS, small amounts of nitric oxide are constantly formed, which mainly carry out local regulation. In erythrocytes, eNOS activation is induced by the extracorporeal blood circulation during hemodialysis, leading to increased nitric oxide synthesis, vasodilation, and arterial hypotension (U. M. Fischer et al., 2017). The change in blood volume during hemodialysis enhances the expression of the gene encoding eNOS, which causes arterial hypotension by increasing the production of nitric oxide by endothelial cells (M. Uematsu et al., 2015; M. Tomita et al., 2011).

The role of vasopressin in the pathogenesis of IDH cannot be excluded. Vasopressin, or antidiuretic hormone, is produced by neurosecretory cells in the hypothalamus. This is the main hormone that regulates the osmolarity of the internal environment: it ensures the constancy of blood volume, regulates the volume of cells by maintaining a constant osmotic pressure of the pericellular. Vasopressin stimulates water reabsorption by the distal renal tubules; by increasing the permeability of the tubules, it contributes to the reabsorption of water and a decrease in diuresis. Vasopressin is a vasoconstrictor that is involved in the regulation of BP through baroreceptors and direct myotropic action on arterioles

and capillaries, causing an increase in BP. The role of vasopressin in the pathogenesis of IDH is supported by the following facts. First, due to the decrease in fluid volume during hemodialysis, an increase in the concentration of vasopressin is expected; however, the concentration of vasopressin is reduced. Second, therapy aimed at preventing the fall in osmolarity (vasopressin levels) during hemodialysis, including a high concentration of sodium in the dialysis solution, improves hemodynamic stability. Third, the administration of low-dose vasopressin during hemodialysis stabilizes blood pressure. Thus, reduced vasopressin synthesis during hemodialysis contributes to the development of IDH (A. M. Thompson et al., 2019).

1.5. Importance of the hemodiafiltration method in the prevention of intradialysis hypotension

Among the technological advances that reduce the risk of hypotension during hemodialysis, hemodiafiltration deserves special attention.

There are several advantages of hemodiafiltration compared to conventional hemodialysis:

1. Due to the combination of diffusion and convection, a better purification of the blood from a number of substances is provided: p-cresol, homocysteine, advanced glycation end products, inflammatory mediators.

2. When using hemodiafiltration, greater hemodynamic stability is observed: in response to fluid removal, peripheral resistance increases adequately to maintain blood pressure; while during hemodialysis, peripheral resistance, on the contrary, decreases. Accordingly, hemodiafiltration reduces the number of IDH episodes.

3. With regular sessions of hemodiafiltration, the level of blood phosphorus decreases, resistance to the action of erythropoietin is eliminated, and the nutritional status is restored (A.V. Smirnov, 2011).

4. Compared with conventional (standard) hemodialysis, regular sessions of highly effective hemodiafiltration (convection exchange > 15 liters per session) lead to a 35% reduction in the relative risk of death (A. B. Смирнов, 2011).

The latest modification of hemodiafiltration is online hemodiafiltration, which allows preparing a replacement solution directly during the procedure, from the so-called “reverse osmosis water” and dialysate, super-purified with an additional filter (Г. Х. Дамдинова et al., 2011; J. E. Tattersall). According to some authors, online hemodiafiltration provides greater hemodynamic stability during the dialysis procedure and makes it possible to better control BP (C. Ronco et al., 2016; Canaud B., 2016). In a multicenter, open, randomized controlled trial, F. Locatelli et al. (2010) demonstrated that the use of online hemodiafiltration in predilution reduces the frequency of IDH episodes by 54%. Due to the peculiarities of the online hemodiafiltration technique, it is possible to prevent IDH, increasing hemodynamic stability at a higher ultrafiltration rate. The positive effect of online hemodiafiltration is also associated with a more pronounced peripheral vasomodulatory effect, which is determined by the negative heat balance and a number of other factors, including the intensive removal of vasodilating mediators (J. T. Daugirdas et al., 2017).

Hemofiltration also has a stabilizing effect on hemodynamics (И. Ледебо, 2019). Hemofiltration is a method of blood purification by filtering it through artificial highly permeable membranes with simultaneous replacement of the removed filtrate with a special solution. Unlike hemodialysis, blood purification during hemofiltration is carried out due to the convective movement of substances dissolved in plasma through a semipermeable membrane under the action of transmembrane pressure, similar to how it occurs in the renal glomeruli (A. B. Бердников et al., 2014). With hemofiltration, the ultrafiltration rate is very high, and the resulting fluid removal is approximately the same as in hemodialysis (I. Ledebo, 2019). However, the removal of fluid during hemofiltration causes a

sympathetic response, and the released noradrenaline leads to an increase in total peripheral vascular resistance, which compensates for the decrease in cardiac output and maintains hemodynamics. However, clinical trial data published in recent years do not reveal significant benefits of hemofiltration over hemodialysis and hemodiafiltration in cases of IDH. Serious technical difficulties and the high cost of the procedure, due to the need to use large volumes (up to 40-45 liters) of a sterile, pyrogen-free replacement solution for each procedure, limit the use of hemofiltration in everyday practice (Н. Я. Губарь, 2018).

The above data demonstrates the complexity and ambiguity of the IDH problem. The regulation of BP during hemodialysis is simultaneously influenced by a large number of interrelated factors, including fluid status, electrolyte balance, oncotic pressure, inflammation, the state of the autonomic nervous system, heart, vascular wall, etc. There is no doubt that IDH is associated with the continuously evolving technologies of hemodialysis and the standards of management of patients receiving renal replacement therapy. In this regard, a number of classical IDH risk factors may lose their significance, and, conversely, the role of other factors may increase. Thus, the study of risk factors and features of the course of IDH in modern conditions is of both scientific and practical interest.

Chapter 2.
MATERIALS AND METHODS OF RESEARCH

2.1. General characteristics of the examined patients

We examined 102 patients with stage 5 chronic kidney disease. The study was conducted at hemodialysis units Fresenius Medical Care Niles Chicago, IL, USA.

Inclusion criteria for the study were the presence of stage 5 chronic kidney disease according to the US National Kidney Foundation classification (NKF: K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease, 2002) and renal replacement therapy with program hemodialysis for 1 year or more.

The exclusion criteria were:

1. Postponed acute myocardial infarction or acute cerebrovascular accident, paroxysmal cardiac arrhythmias.

2. Acute pyoinflammatory and infectious diseases.

3. Diseases of the thyroid gland and adrenal glands.

4. Erosive and ulcerative lesions of the gastrointestinal tract and an indication of acute blood loss in history.

The scope of the examination corresponded to the accepted standards for the management of nephrological patients.

We studied in detail the clinical and anamnestic data. We analyzed the features of the hemodialysis procedure that may affect the likelihood of developing IDH (frequency and duration of hemodialysis sessions, composition of the dialysis solution, type of dialyzer, blood flow velocity, ultrafiltration volume, etc.). BP was measured before the start of the hemodialysis session, during the session and after it. IDH episodes were defined as a decrease in systolic BP below 100 mm Hg. or more than 20 mm Hg. compared to pre-dialysis levels in case of clinical symptoms.

Retrospectively, the maximum number of IDH episodes per 1 month and their average monthly number over the previous 12 months.

We also evaluated conventional 12-lead electrocardiography data (to identify exclusion criteria).

All patients underwent clinical and biochemical blood tests, additional instrumental studies and specialist consultations to exclude gastrointestinal diseases, endocrinological diseases and other possible causes of secondary arterial hypotension. When conducting a biochemical blood test, serum levels of creatinine, urea, total protein, albumin, C-reactive protein, electrolytes (potassium, sodium, calcium, phosphorus, chlorine), parathyroid hormone (PTH).

The development of chronic renal failure was due to: chronic glomerulonephritis - in 51.0%, diabetic nephropathy - in 13.7%, polycystic kidney disease - in 8.8%, hypertension - in 6.9%, congenital kidney dysplasia - in 5, 9%, chronic pyelonephritis - in 3.9%, other diseases (amyloidosis of the kidneys, gouty nephropathy, bilateral stenosis of the renal arteries, chronic tubulointerstitial nephritis, unspecified causes) - in 9.8% of patients.

The age of the patients ranged from 24 to 78 years. The mean age was 50.3±2.4 years ($p=0.05$). Among the examined patients there were 57.8% women and 42.2% men.

The duration of treatment with program hemodialysis ranged from 12 to 288 months, with an average of 86.8±12.7 months.

Patients were divided into 3 clinical groups depending on the frequency of IDH episodes.

Group 1 included 39 patients with relatively infrequent episodes of IDH (mean, less than 2 episodes per month over 1 year of follow-up).

Group 2 included 32 patients with frequent episodes of IDH (mean, 2 or more episodes per month over 1 year of follow-up).

Group 3 (control group) consisted of 31 patients without episodes of IDH during 1 year of follow-up.

Characteristics of patients by mean age, gender, as well as the average frequency of IDH episodes are presented in Table 1.

Table 1.

Main characteristics of clinical groups

	Group 1	Group 2	Control Group
Average age, years	54,6±4,3	49,0±4,2	48,1±4,4
% of men	33,4	45,6	64,5
% women	66,7	54,5	35,5
Average monthly number of IDH episodes	0,87±0,15	6,59±0,87	0,00±0,0

2.2. Research methods

2.2.1. General clinical examination

When questioning patients, we paid special attention to the clinical manifestations of hemodialysis complications (arterial hypotension, anemia, hormonal and electrolyte disorders, infectious and hemorrhagic complications). Anamnestic data were studied in detail, taking into account the specifics of the underlying disease. The duration of treatment with program hemodialysis, its tolerance, the nature of drug therapy (especially cardiotropic and antihypertensive) were assessed. We also took into account the complaints of patients, their compliance with the prescribed diet and water-salt regimen.

The body mass index (BMI) was calculated based on the dry weight values. Determination of the degree of obesity by BMI was carried out in accordance with the WHO classification (1997), presented in table. 2.

Table 2

BMI classification of obesity

Body mass types	BMI (кг/м^2)
Underweight	<18,6
Normal body weight	18,4-24,8
Overweight (preobesity)	25,1-29,9
Obesity I degree	30,1-34,8
Obesity II degree	35,0-39,8
Obesity III degree	>40

2.2.2. Assessment of blood pressure and factors associated with the hemodialysis procedure

BP was assessed before the hemodialysis session, during the session (with an interval of 1 hour) and after its completion. The average values of the corresponding indicators for 1 month of observation were calculated. In addition, we calculated the relative (percentage) reduction in systolic and diastolic BP at 1, 2, 3, 4 hours and for the entire hemodialysis session.

Pulse BP was defined as the difference between systolic and diastolic BP. Average BP was calculated using the formula:

Mean BP = (systolic BP + 2 x diastolic BP)/3

An IDH episode was defined as a fall in systolic BP below 100 mm Hg. or more than 20 mm Hg. compared with the pre-dialysis level in case of clinical symptoms (dizziness, fainting, convulsions, yawning, blurred vision).

After analyzing the data for 12 months of follow-up, we determined the average and maximum number of IDH episodes in 1 month.

I n studying the factors associated with the hemodialysis procedure, we assessed the patient's treatment regimen (frequency and duration of sessions). The patients observed by us received hemodialysis treatment from 3 hours 2 times a week to 5 hours 3 times a week.

The association of IDH frequency with interdialysis weight gain and ultrafiltration volume (both in absolute value and as a percentage of dry weight) was analyzed. The average indicators of the volume of ultrafiltration and interdialysis weight gain were calculated for 1 month of observation.

We evaluated the volumetric blood flow velocity during the hemodialysis procedure. The values of this indicator varied from 200 to 370 ml per minute.

The relationship between the frequency of IDH and the composition of the dialysate was analyzed. The minimum and maximum concentrations of substances in the solutions used are given in Table. 3.

Table 3

The concentrations of the main components of the used dialyzers solutions

Dialysate component	Concentration, mmol/l	
	From	To
Sodium	135,0	145,0
Potassium	2,0	3,0
Calcium	1,5	1,75
Bicarbonate	26,0	35,0
Glucose	0,0	6,0

2.2.3. Assessment of hematological parameters

In our study, in patients receiving treatment with program hemodialysis, the indicators of a clinical blood test were evaluated. Since it is known that anemia and infectious and inflammatory diseases can increase the risk of developing intradialysis hypotension, we paid special attention to red blood parameters (hemoglobin, hematocrit, erythrocyte count), leukocyte count, leukocyte formula and ESR. The studies were performed on an automatic hematological analyzer "SYSMEX XT-20001". Reference values of the main indicators are presented in table. 4.

Table 4

Reference values of the main indicators of a clinical blood test

Indicator	Reference value
Hemoglobin	130-160 g/l (men) 120-150 g/l (women)
Erythrocytes	4,5-5,5x10^{12} /л (men) 3,8-5,3x10^{12} /л (women)
Hematocrit (Ht)	40-45 % (men) 36-42 % (women)
Leukocytes	4,0-9,0x10^{9}/л
Platelets	180-320x10^{9}/l
ESR	2-10 mm/hour (men) 2-15 mm/hour (women)

2.2.4. Determination of biochemical parameters

When performing a biochemical blood test in patients receiving treatment with program hemodialysis, serum levels of total protein and albumin (colorimetric method), glucose (glucose oxidase method), creatinine and urea (colorimetric method), as well as C-reactive protein (immunoturbidimetry method) were assessed.

The studies were carried out on automatic analyzers "Architect 12000". Reference values are presented in table. 5.

Table 5

Reference values of biochemical parameters

Indicator	Reference value
Total protein	65-85 g/l
Albumen	35-55 g/l
Glucose	3,3-6,0 mmol/l
C-reactive protein	< 6 mg/l

2.2.5. Assessment of water and electrolyte balance

In order to study the relationship between fluid and electrolyte balance and the frequency of IDH episodes, we assessed the levels of electrolytes in the blood serum of patients, as well as the serum concentration of PTH by enzyme immunoassay. Reference values are presented in table. 6.

Table 6

Reference values for fluid and electrolyte balance and PTH

Indicator	Reference value
Potassium	3,8-5,5 mmol/l
Sodium	135-145 mmol/l
Chlorine	98-107 mmol/l
Calcium total	2,15-2,60 mmol/l
Phosphorus	0,87-1,45 mmol/l
PTH	16-62 pg/ml

2.2.6. Methods of statistical data processing

Statistical processing of the obtained data was carried out using the software package for applied statistical analysis IBM SPSS Statistics (version 19.0) and Microsoft Excel (version 14.0).

When carrying out statistical processing, methods of parametric and nonparametric statistics were used. The methods of descriptive (descriptive) statistics included the estimation of the arithmetic mean and standard error of the mean for features with a continuous distribution, as well as the frequency of occurrence for features with discrete values.

To assess intergroup differences in the values of features with a continuous distribution, the Student's t-test and the Mann-Whitney U-rank test were used.

The analysis of the relationship between the features was carried out by calculating the Spearman correlation coefficient (r_s). The severity of correlations was assessed by the value of the correlation coefficient: strong - at values of more than 0.7, moderate - from 0.3 to 0.7, weak - less than 0.3. The direction of the links was estimated by the sign of the correlation coefficient. The critical confidence level of the null hypothesis (the absence of significant differences or factorial influences) in our study was 0.05.

Chapter 3.
RESEARCH RESULTS

3.1. Clinical characteristics of patients with episodes of intradialysis hypotension

Of the 102 patients included in the study, episodes of IDH were observed within 1 year in 71 patients.

The average number of IDH episodes in 1 month was up to 11.67. Their maximum number for 1 month of observation ranged from 0 to 13. 8 patients (7.8%) had up to 13 episodes of IDH per month, that is, they developed this complication during each hemodialysis session for 1 month or more.

Differences in the average monthly number of IDH episodes in clinical groups were statistically significant. The mean values were: in group 1 — 0.87±0.14, in group 2 — 6.59±0.87, in the control group — 0.00±0.00 ($p<0.05$ when comparing any two groups).

The average monthly number of IDH episodes in women and men is shown in Fig. 1. As can be seen from the presented data, in men the average was lower than in women (2.2 and 3.8 for 1 month, respectively), but the differences were not statistically significant ($p>0.05$). The observed trend could be related to a number of other clinical factors. In particular, male patients had higher dry weight values compared to women — 74.6±2.2 and 62.0±1.7 kg, respectively ($p<0.001$). In addition, we noted that women treated with program hemodialysis were more likely to experience hypochloremia. The mean values of serum chlorine concentration were: in men — 102.3±0.8 mmol/l, in women — 99.9±0.8 mmol/l ($r_s=2.06$; $p=0.044$).

Our study assessed the relationship between the age of patients and the average monthly number of IDH episodes. Frequent episodes of decreased BP were observed both in a number of young patients and in some elderly patients. However, it should be noted that the nosological structure of stage 5 CKD differed significantly in certain age groups. Thus, the majority of patients with type 1 diabetes mellitus were younger than

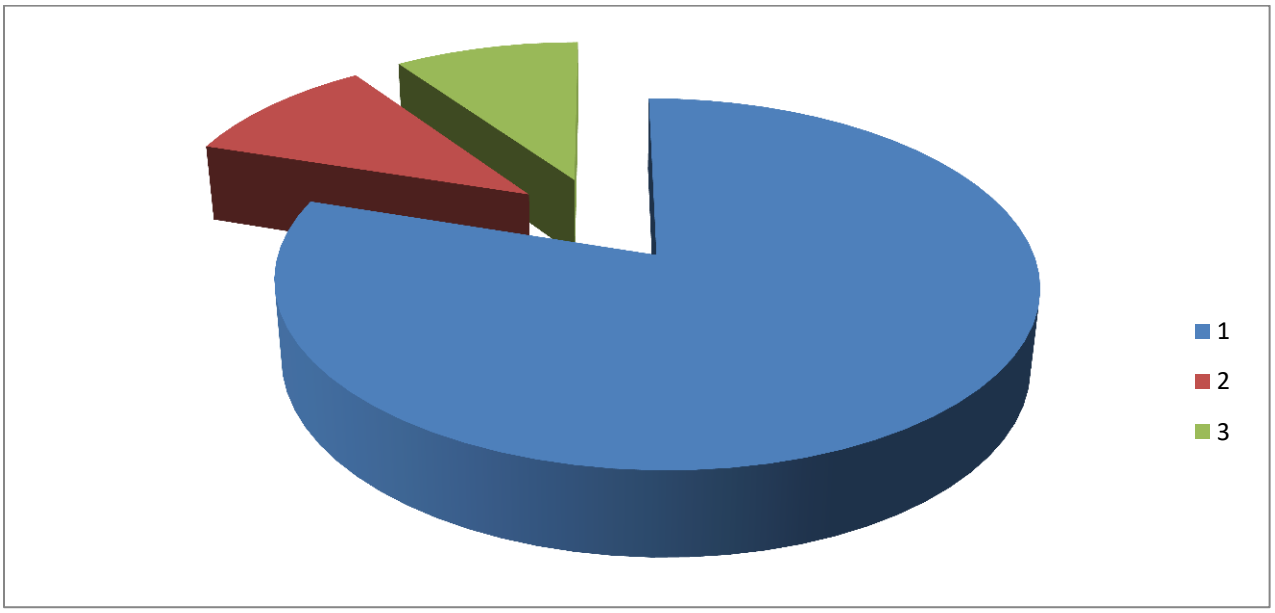
40 years of age and had frequent episodes of IDH. Having analyzed separately the largest nosological subgroup of patients with chronic glomerulonephritis (n=52), we found in it a positive correlation of moderate strength between the average monthly number of IDH episodes for 1 year of observation and the age of patients.

In the study of anamnestic data, we also assessed the duration of treatment with program hemodialysis. This indicator varied from 12 to 288 months. The mean duration of hemodialysis treatment was maximal in patients with frequent episodes of IDH in group 2 (111.9±12.6 months) and minimal in the control group (70.5±14.8 months). Differences between these groups were statistically significant (t=2.14; p=0.041). The mean duration of hemodialysis treatment in group 1, with relatively infrequent episodes of IDH, was 83.7±10.6 months.

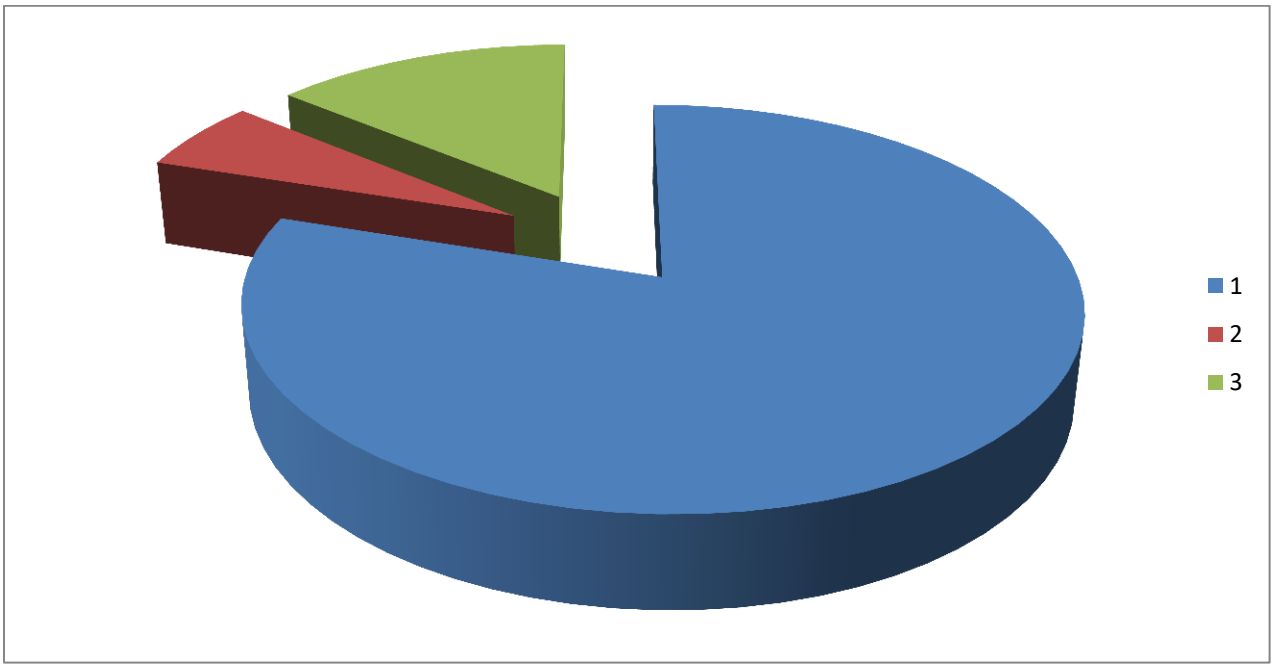
3.2. Body Mass Index Results

We also analyzed BMI values calculated based on dry weight. The majority of patients (56.9% of the total) had normal body weight. The proportion of patients with normal body weight, pre-obesity (overweight), obesity and underweight in each of the clinical groups is shown in Fig. 1 and 2. The presented diagrams show that among the patients in the control group there were no patients with underweight. At the same time, among patients with episodes of IDH, BMI values <18.5 kg/m^2 were often detected. In the control group, the average BMI value was 26.4±1.2 kg/m^2. Differences with group 1 (22.5±0.8 kg/m^2) and group 2 (23.1±0.9 kg/m^2) were statistically significant (t=-2.44 and t=-2.08, respectively; p<0.05).

Correlation analysis revealed a weak negative correlation between BMI and the average monthly number of IDH episodes (r_s= -0.234; p=0.039). No statistically significant correlation was found between BMI and maximum IDH episodes per month.



Pic. 1. The proportion of patients with normal body weight, underweight and obesity in the group with relatively rare episodes of IDH (group 1). 1- Patients with normal body weight and preobesity. 2- Patients with obesity. 3- Patients with underweight.



Pic. 2. The proportion of patients with normal body weight, underweight and obesity in the group with relatively rare episodes of IDH (group 2). 1- Patients with normal body weight and preobesity. 2- Patients with obesity. 3- Patients with underweight.

Correlation analysis revealed a weak negative correlation between BMI and the average monthly number of IDH episodes (r_s= -0.234; p=0.039). No statistically significant correlation was found between BMI and maximum IDH episodes per month.

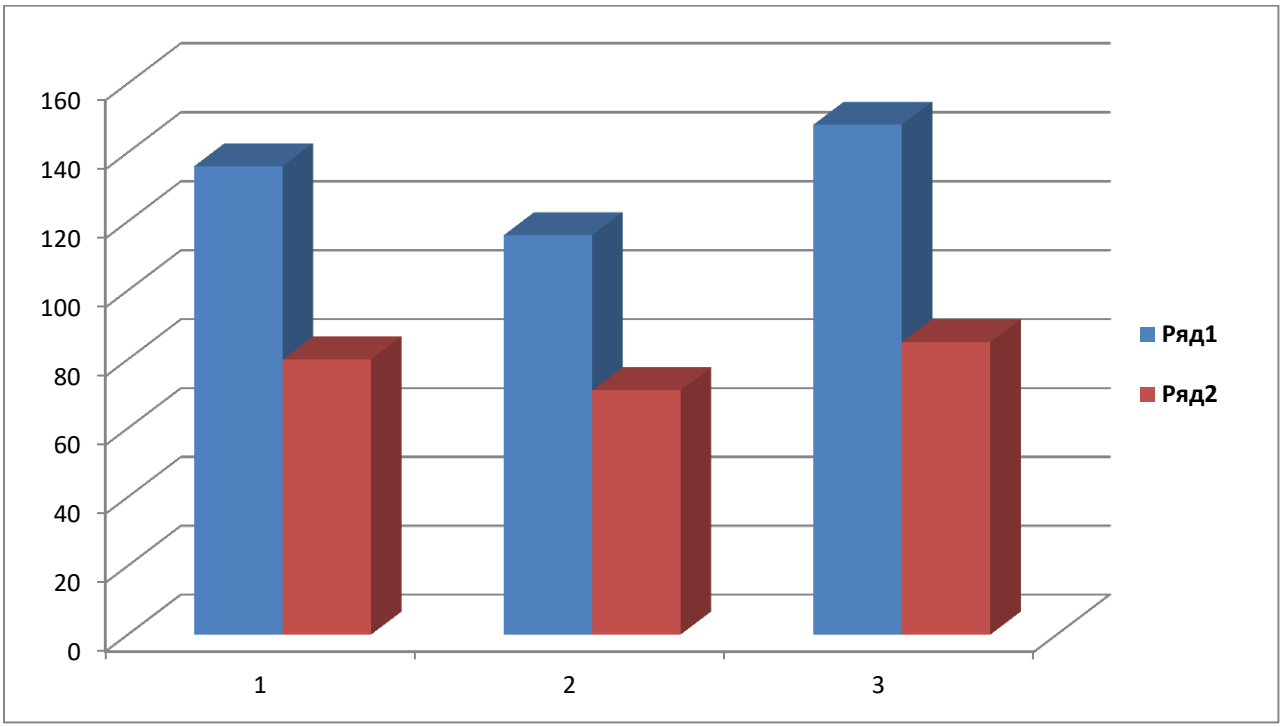
The effect of BMI on the risk of developing IDH was probably not independent, as BMI was also correlated with other possible predictors of BP reduction during the hemodialysis procedure. We found a weak negative correlation between BMI and the duration of treatment with program hemodialysis (r_s= -0.249; p=0.029). In addition, BMI was positively correlated with serum albumin (r_s=0.480; p=0.041).

3.3. The results of the assessment of blood pressure levels.

Our study assessed pre-, intra- and post-dialysis BP levels. On the basis of the data obtained during the observation of patients in dynamics, the corresponding average indicators for 1 month were calculated.

On Pic. 3 shows mean levels of pre-dialysis systolic and diastolic BP over 1 month of follow-up. In group 1, they were 136.8±3.2 and 79.7±1.8 mm Hg. in group 2 — 116.7±4.4 and 70.8±2.4 mm Hg. in the control group -148.5±6.3 and 84.6±3.1 mm Hg. respectively. Between group 2 and the control group showed statistically significant differences both in the level of systolic (t= -3.83, p<0.001) and in the level of diastolic BP (t= -3.11, p=0.003).

Predialysis BP figures corresponded to arterial hypertension in 28.2% of patients in group 1, 15.6% in group 2, and 54.8% in the control group. Among these patients, 71.4% had systolic hypertension, 28.6% had systolic-diastolic hypertension, and 5.7% had diastolic arterial hypertension. In most cases, hypertension of the 1st degree was observed.



Pic. 3. Average levels of pre-dialysis systolic diastolic BP in clinical groups. 1-Group 1. 2-Group 2. 3- Control Group. Series 1- Pre-dialysis systolic blood pressure. Series 2- Pre-dialysis diastolic blood pressure

When conducting a correlation analysis, we found that the average level of predialysis BP was negatively correlated with the duration of hemodialysis treatment and the average monthly number of IDH episodes (Table 7). Correlations with systolic BP were more pronounced than with other indicators (diastolic, pulse and mean BP). In addition, we have identified the relationship between predialysis BP values and echocardiographic data, which will be discussed in detail below in the corresponding section. There were no significant correlations with BMI, dry weight, and interdialysis weight gain.

We analyzed episodes of IDH in patients from groups 1 and 2 (one case was studied in detail in each patient, the first during the observation period).

Table 7

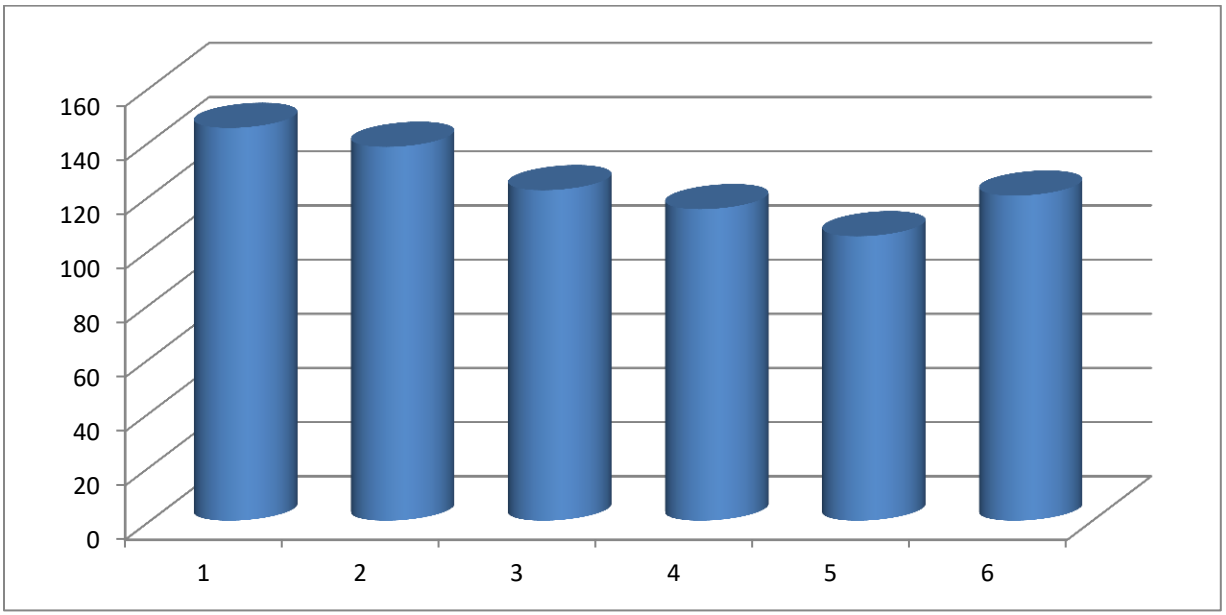
Correlations of predialysis BP with duration of hemodialysis and mean monthly number of IDH episodes

	Duration of hemodialysis treatment		Average monthly number of IDH episodes	
	r_8	P	r_5	P
Systolic BP	-0,241	0,018	-0,398	<0,001
Diastolic BP	-0,149	>0,05	-0,359	0,001
Pulse blood pressure	-0,205	0,042	-0,367	0,001
Average blood pressure	-0,234	0,018	-0,384	<0,001

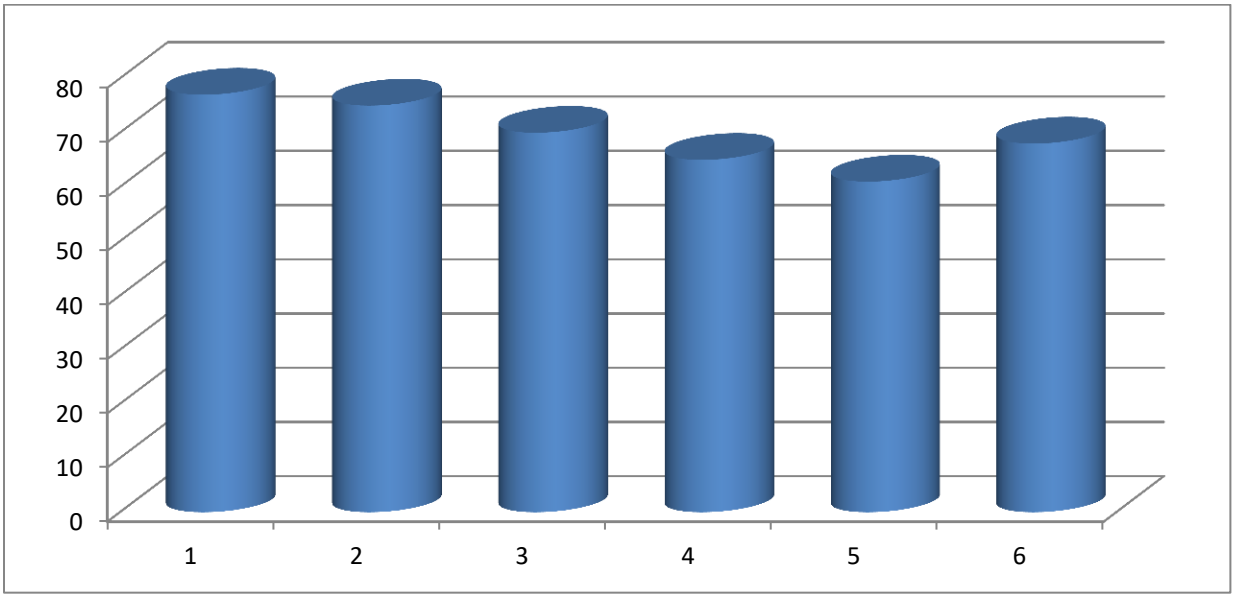
The development of IDH was noted: 1 hour after the start of hemodialysis - in 5.6%, after 2 hours - in 21.1%, after 3 hours - in 32.4%, after 4 hours - in 38.0% of patients (out of the total number of patients with IDH episodes). The duration of the episode in 60.6% of cases did not exceed 1 hour, in 18.3% it was from 1 to 2 hours, in 5.6% it was from 2 to 3 hours, in 7.0% it was more than 3 hours.

On Pictures 4 and 5 show the average dynamics of BP during the hemodialysis procedure.

The mean values of systolic and diastolic BP at 1 hour and 2 hours after the start of the hemodialysis procedure did not differ significantly from the corresponding indicators of pre-dialysis and post-dialysis BP. Average systolic BP at 3 hours (112.3±4.1 mm Hg) and 4 hours (103.8±2.6 mm Hg) after the start of hemodialysis, as well as post-dialysis BP (117.0± 4.2 mm Hg), were significantly lower than the predialysis level — 145.0±4.7 mm Hg. ($p<0.01$).



Pic 4. Average dynamics of systolic BP during the hemodialysis procedure. 1- Before hemodialysis. 2- After 1 hour. 3- After 2 hours. 4- After 3 hours. 5- After 4 hours. 6-After hemodialysis.



Pic 5. Average dynamics of diastolic BP during the hemodialysis procedure. 1- Before hemodialysis. 2- After 1 hour. 3- After 2 hours. 4- After 3 hours. 5- After 4 hours. 6-After hemodialysis.

The average values of diastolic BP at 3 hours (62.4±1.8 mm Hg) and 4 hours (60.0±1.5 mm Hg) after the start of the procedure were also below the pre-dialysis level — 76.3±2 .3 mmHg ($p<0.001$).

Based on the data of hourly BP measurement during hemodialysis sessions for each patient, we calculated the average (by the hour) intradialysis indicators of systolic and diastolic blood pressure. Correlation analysis showed the presence of statistically significant relationships between intradialysis systolic BP and the duration of hemodialysis treatment, interdialysis weight gain, and serum albumin levels Table 8

Table 8

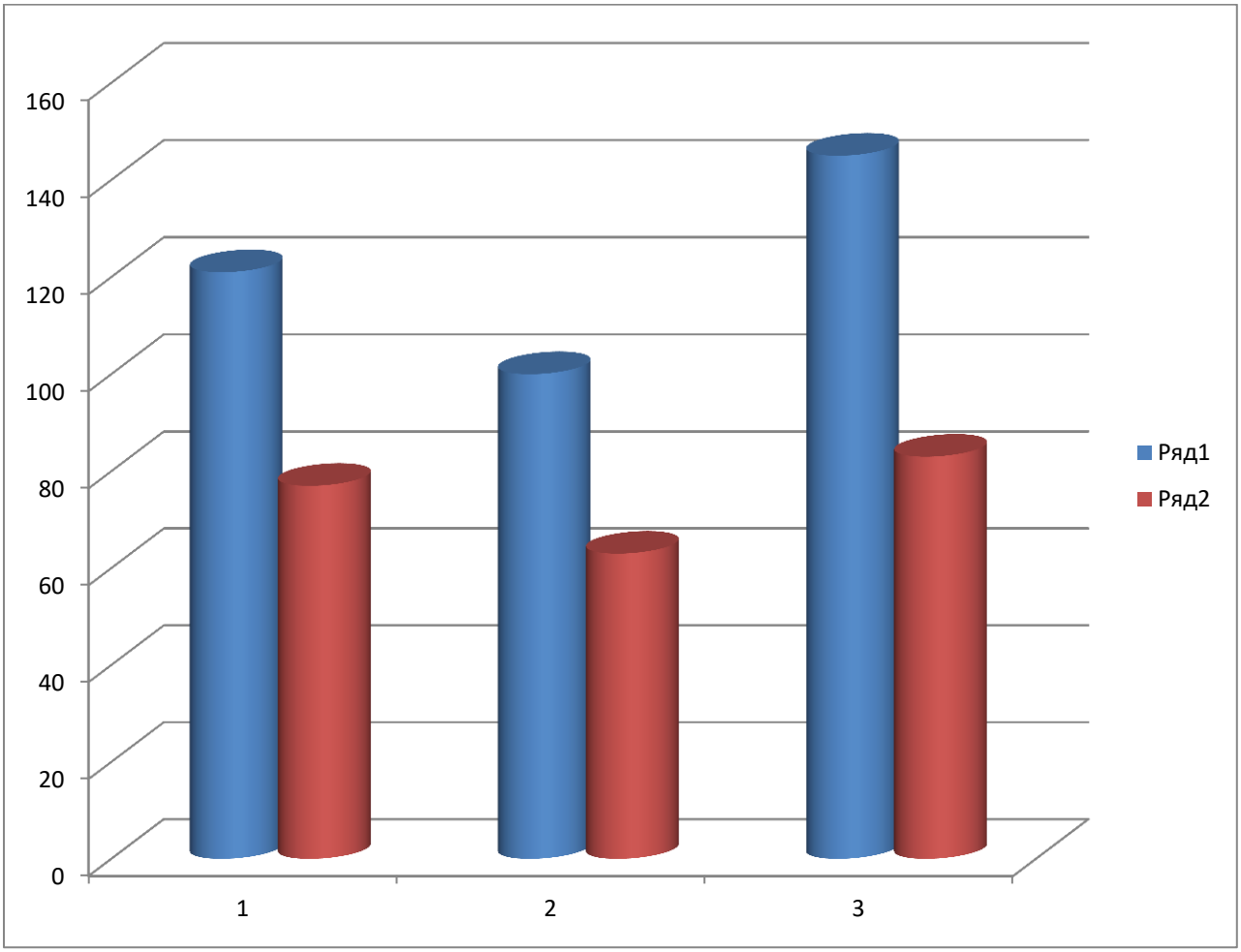
Correlations of intradialysis BP with duration of hemodialysis, interdialysis weight gain, and albumin levels.

	Average intradialytic systolic BP		Average intradialytic diastolic BP	
	r_s	P	r_s	P
Duration of hemodialysis	-0,458	0,044	-0,338	>0,1
Interdialytic weight gain	-0,469	0,037	-0,301	>0,1
Serum albumin level	0,517	0,043	0,469	0,066

When conducting a correlation analysis, it was found that the indicators of relative changes in blood pressure, in contrast to the absolute values of blood pressure, do not have a statistically significant relationship with such factors as the duration of hemodialysis treatment, BMI, and the average monthly number of IDH episodes. At the same time, relative indicators correlated with serum concentrations of electrolytes (calcium and sodium), and after 1 hour and after 2 hours of hemodialysis session,

correlations with calcium levels had a moderate strength, and after 3 hours of the procedure, correlations with sodium levels. Changes in systolic and diastolic blood pressure after 4 hours of hemodialysis session relative to the predialysis level did not significantly correlate with any of the clinical and laboratory parameters assessed in our study.

On Pic.6 shows mean post-dialysis systolic and diastolic BP levels at 1 month of follow-up. In group 1, they were 121.±3.6 and 73.1±1.7 mm Hg. in group 2 —



Pic. 6. Average levels of post-dialysis systolic diastolic BP in clinical groups. 1-Group 1. 2-Group 2. 3- Control Group. Series 1- Pre-dialysis systolic blood pressure. Series 2- Pre-dialysis diastolic blood pressure

100.2±3.9 and 63.3±2.6 mm Hg. in and control group — 145.4±3.3 and 83.1±1.7 mm Hg. respectively. The level of systolic BP was significantly higher in the control group compared to group 1 (t= -4.96, p<0.001) and group 2 (t= -9.77, p<0.001). Differences in diastolic BP were also statistically significant (t= -3.51, p=0.001 and t= -7.09, p<0.001, respectively).

The level of post-dialysis BP, as well as pre-dialysis, correlated with the duration of hemodialysis treatment and the average monthly number of IDH episodes. The corresponding correlation coefficients are presented in Table. 9.

Table 9.

Correlations of postdialysis BP with duration of hemodialysis and mean monthly number of IDH episodes

	Duration of hemodialysis treatment		Average monthly number of IDH episodes	
	r_8	P	r_5	P
Systolic BP	-0,264	0,011	-0,692	<0,001
Diastolic BP	-0,298	0,004	-0,628	<0,001
Pulse blood pressure	-0,196	>0,05	-0,634	<0,001
Average blood pressure	-0,271	0,008	-0,679	<0,001

Thus, pre-, intra- and post-dialysis levels of blood pressure, as well as indicators of relative changes in blood pressure during a hemodialysis session, are associated with a large number of correlations with various clinical and laboratory factors. The most significant decrease in blood pressure, as a rule, occurs 3-4 hours after the start of the hemodialysis session. Patients with frequent episodes of IDH have lower pre- and post-dialysis BP than patients without IDH. Patients with

relatively infrequent IDH episodes have comparable pre-dialysis BP values but lower post-dialysis BP values compared to patients without IDH episodes.

3.5. The results of the assessment of hematological and biochemical parameters

In our study, clinical analysis scores were assessed to identify factors contributing to the development of IDH. There were significant intergroup differences in hemoglobin and hematocrit levels. Anemia was detected: in group 1 — in 59.0%, in group 2 — in 65.6%, in the control group — in 38.7% of patients. Indicators of red blood in clinical groups are presented in Table10. Significant intergroup differences in MSI, MSU, the number of leukocytes, platelets and ESR were not found in our study.

Table 10

Red blood values in clinical groups

Parameter	Group 1	Group 2	Control group
Hemoglobin, g/l	108,4±2,3 *	107,3±3,2 *	117,1±2,3
Hematocrit, %	31,6±0,7 *	31,8±0,8 *	34,7±0,9
Quantity erythrocytes, 10^{12} /l	3,78±0,08	3,66±0,13	3,86±0,18

* $p<0.05$ compared to the control group

We also evaluated the biochemical parameters of patients under observation. Average indicators are presented in table 11. There were no intergroup differences in the level of total protein and albumin. Differences in the concentration of C-reactive

Table 11

Average values of biochemical parameters in clinical groups

Parameter	Group 1	Group 2	Control group
Total protein, g/l	73,8±0,8	72,7±1,2	74,4±1,1
Albumin, g/l	37,9±0,7	37,3±0,8	36,2±0,8
C-reactive protein, mg/l	9,4±3,3	34,6±17,6*	8,2±4,7

* $p<0.05$ compared to the control group

protein in the clinical groups were also not statistically significant, although patients in group 2 (with frequent episodes of IDH) showed a tendency to higher levels of C-reactive protein.

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Chapter 4.
DISCUSSION OF THE OBTAINED RESULTS

This study evaluated various aspects of arterial hypotension during hemodialysis. Scientific literature data indicate that IDH is a common complication of hemodialysis (J. T. Daugirdas, 2004; J. M. Letteri, 2008; A. Venkat et al., 2006) and has an adverse effect on patient survival rates (T. Shoj et al., 2004; A. Tisler et al., 2003). The connection of this problem with a large number of factors, including not only clinical aspects, but also the technical features of the hemodialysis procedure, requires an integrated approach to the study of IDH. The multifactorial nature of IDH and its connection with continuously changing medical technologies (B. F. Palmer, W. L. Henrich, 2008) make it especially relevant to study the problem in the context of modern domestic healthcare practice. These issues were considered by us in the context of determining the rational scope of measures aimed at preventing this complication.

To solve the research objectives, 102 patients with stage 5 CKD were selected, who did not have significant primary diseases of the cardiovascular system and endocrine pathology, which can also be the causes of arterial hypotension. Dividing the observed patients into groups depending on the frequency of IDH episodes, we compared them according to clinical and laboratory data. Both patient-specific factors and factors related to the hemodialysis procedure were considered.

Among the 71 patients with IDH episodes, there were 32 with frequent IDH episodes (mean, 6.59 ± 0.87 per month) and 39 with relatively infrequent IDH episodes (mean, 0.87 ± 0.14 per month). The control group included 31 patients without episodes of IDH. Differences in the frequency of IDH in men and women were not statistically significant, however, the absence of episodes of lowering blood pressure during hemodialysis was more often observed in men. This fact can be partly associated with higher values of "dry" weight in men. Accordingly, the average duration of hemodialysis sessions in men was also longer. The clinical and prognostic

significance of the duration of sessions (dose) of hemodialysis has been and remains a topical issue in nephrology (J. T. Daugirdas, 2013). In addition, this issue is relevant to the relationship between IDH risk and body weight, which will be discussed below, and, in general, to the problem of complications of renal replacement therapy in underweight individuals.

We did not find a significant statistical relationship between the average monthly frequency of IDH and the age of patients, which is consistent with the data of the study by A. Capuano et al. (1990). However, there is no doubt that the decrease in blood pressure during hemodialysis is of particular danger to elderly patients who have a high risk of cardiovascular events, neurological disorders and other complications (M. Buemi et al., 2008). We also hypothesized that the results obtained may be related to the dissimilar etiological structure of CKD in young and old people. Having analyzed separately a subgroup of 52 patients with chronic glomerulonephritis, we found in it a positive correlation of moderate strength between the average monthly number of IDH episodes for 1 year of observation and the age of patients (r_s=0.342; p=0.028).

The results of our study showed that the most frequent episodes of IDH occur in patients with diabetic nephropathy. If we take the average monthly number of IDH episodes in these patients as 1, then the relative number of similar events in patients with chronic glomerulonephritis will be 0.38, and in patients with polycystic kidney disease - 0.19. These data are consistent with other studies that have shown that diabetes is one of the independent factors that increase the risk of developing IDH (A. Takeda et al., 2006; A. Davenport et al., 2008). The main mechanism contributing to the decrease in blood pressure during hemodialysis sessions in patients with diabetes mellitus is considered to be dysregulation of vascular tone due to the development of autonomic diabetic neuropathy (M. Nakamoto et al., 1994).

According to our data, frequent episodes of IDH are associated with a longer duration of renal replacement therapy. In patients of group 2 (with frequent episodes of IDH), the average duration of hemodialysis treatment was 111.9 ± 12.6 months, in

patients of group 1 (with relatively rare episodes of IDH) - 83.7 ± 10.6 months, in patients of the control group - 70.5±14.8 months. The differences between Group 2 and the control group were statistically significant. In the scientific literature, this factor is not given significant importance, probably due to the fact that it is not modifiable.

In our study, a weak negative correlation was found between BMI and the average monthly number of IDH episodes (rs = -0.234; p = 0.039). Most of the patients under observation had normal BMI values. All patients with deficiency body weight (BMI<18.5 kg/m) had more or less IDH episodes. BMI values were the highest in the control group (26.4±1.2 kg/m). Differences with group 1 (22.5±0.8 kg/m) and group 2 (23.1±0.9 kg/m) were statistically significant (t=-2.44 and t=-2.08, respectively; p<0.05). The tendency to hypotension in underweight patients may be closely related to a range of causes, including inflammation and atherosclerosis with its characteristic changes in the cardiovascular system (Q. Yao et al., 2004). The clinical significance of the combination of these pathological processes allowed P. Stenvinkel et al. (1999) combine them under the name "MIA syndrome" (Malnutrition, Inflammation, Atherosclerosis). These pathogenic relationships should be taken into account in the treatment and prevention of IDH in underweight patients.

One of the main objectives of the study was to evaluate pre-, intra- and post-dialysis BP parameters in patients receiving hemodialysis treatment.

The mean levels of pre-dialysis systolic and diastolic blood pressure for 1 month of follow-up were: in group 1 (with rare episodes of IDH) — 136.8±3.2 and 79.7±1.8 mm Hg. in group 2 (with frequent episodes of IDH) — 116.7±4.4 and 70.8±2.4 mm Hg. in the control group (without episodes of IDH) — 148.5±6.3 and 84.6±3.1 mm Hg. respectively. Between group 2 and the control group there were statistically significant differences in the level of systolic (t= -3.83, p<0.001) and diastolic blood pressure (t= -3.11, p=0.003). In the majority of patients in the control group, predialysis BP values corresponded to arterial hypertension (mainly systolic). When conducting a correlation analysis, we found that predialysis systolic BP correlated negatively with the duration of hemodialysis treatment (r_s= -0.240; p=0.017) and the

average monthly number of IDH episodes (r_s= -0.399; p<0.001). Similar, but less strong, correlations were found for diastolic, mean, and pulse predialysis BP. Thus, we believe that predialysis BP (primarily systolic) is an important factor in determining the risk of developing IDH. At the same time, however, it is known that pre-dialysis BP indicators do not allow to adequately judge the level of BP between hemodialysis sessions and have less prognostic value compared to the values recorded during outpatient BP monitoring in the interdialysis period (A. I. Pe1ho1: et a1. , 2000; B. A. Добронравов et al., 2009). It should also be noted that there were no correlations between predialysis BP and interdialysis weight gain in our study.

Analyzing intradialysis BP indicators, we found that in most patients, IDH episodes developed 3-4 hours after the start of hemodialysis, which is consistent with data on intradialysis BP dynamics obtained by other authors (B. A. Добронравов et al., 2009). The duration of the episode in 60.6% of cases did not exceed 1 hour, in 18.3% it was from 1 to 2 hours, in 5.6% it was from 2 to 3 hours, in 7.0% it was more than 3 hours.

The average values of systolic and diastolic blood pressure at 1 hour and 2 hours after the start of the hemodialysis procedure did not differ significantly from the corresponding indicators of pre-dialysis and post-dialysis blood pressure. Average systolic BP 3 hours (112.3±4.1 mm Hg) and 4 hours (103.8±2.6 mm Hg) after the start of hemodialysis, as well as post-dialysis BP (117.0±4 .2 mm Hg), were significantly lower than the predialysis level — 145.0±4.7 mm Hg. (p<0.01). The mean values of diastolic blood pressure after 3 hours (62.4±1.8 mm Hg) and 4 hours (60.0±1.5 mm Hg) after the start of the procedure were also below the average pre-dialysis level — 76.3± 2.3 mmHg (p<0.001). Postdialysis diastolic blood pressure did not differ significantly from predialysis.

Averaged (according to the data of hourly measurements) intradialytic blood pressure indicators correlated positively with the serum albumin level (r_s=0.515; p=0.041), negatively with the duration of hemodialysis treatment (r_s= -0.458; p=0.042) and interdialysis weight gain (y=-0.469; p=0.037). Comparing the results of our study

with the data of scientific literature, it can be noted that in the work of M. Rakfetrat et al. (2010) found that the serum level of albumin in patients with IDH is lower than in patients with normal blood pressure during hemodialysis, and in the work of C.-T. Lee et al. (2005) found a negative correlation between albumin levels and serum concentrations of C-reactive protein and interleukin-6. Interdialysis weight gain is currently considered as one of the main factors influencing intradialysis BP parameters (А.Ю.Николаев, Ю. С. Милованов, 2011). Results of A. Davenport et al. (2008) indicate that patients with diabetic nephropathy have higher rates of interdialysis weight gain, higher values of pre- and post-dialysis BP and, at the same time, are more prone to developing IDH compared to patients with kidney damage of other etiologies.

Since the level of predialysis BP in individual patients with stage 5 CKD can differ significantly and correspond to both hyper- and normo- or hypotension, and multidirectional intradialytic dynamics cannot be adequately reflected by averaged absolute BP values, it was of interest to us to study the relative changes in BP in during hemodialysis. The charts presented in Chapter 3 demonstrate that patients may have different intradialysis BP profiles. In some patients, the minimum values of systolic and diastolic blood pressure were achieved 2 hours after the start of a hemodialysis session, after which there was a tendency to normalize and even increase blood pressure. In other cases (more often), the decrease in blood pressure occurred gradually over 3-4 hours of hemodialysis. At the same time, the relative decrease in both systolic and diastolic blood pressure sometimes reached 40-50% of pre-dialysis indicators, which, as a rule, was accompanied by the development of severe clinical symptoms. This issue has not been adequately covered in the scientific literature. From our point of view, its study seems promising, since the detection of significant fluctuations in blood pressure during hemodialysis and the analysis of related factors can be essential for the primary prevention of IDH (before the occurrence of this complication).

It is noteworthy that in our study, the indicators of the relative change in blood pressure during a hemodialysis session had correlations that differed from the correlations of absolute blood pressure levels. It was found that serum calcium

concentration positively correlated with the relative change in systolic blood pressure for 1 hour (r_s=0.425; p=0.049) and 2 hours (r_s=0.484; p=0.002) of a hemodialysis session, and serum sodium concentration positively correlated with the relative change in systolic blood pressure. BP for 3 hours of hemodialysis session in relation to the pre-dialysis level (r_s=0.508; p=0.010). Thus, patients with hyponatremia and hypocalcemia are more prone to a pronounced decrease in blood pressure at different periods of the hemodialysis session. The results of our study are consistent with those of Kaue et al. (1998), in which it was shown that a decrease in the concentration of ionized calcium during a hemodialysis session leads to a decrease in blood pressure.

The mean levels of postdialysis systolic and diastolic blood pressure were: in group 1 — 121.3.6 and 73.1±1.7 mm Hg. in group 2 — 100.2±3.9 and 63.3±2.6 mm Hg. in the control group — 145.4±3.3 and 83.1±1.7 mm Hg. respectively. The level of post-dialysis BP was negatively correlated with the duration of hemodialysis treatment and the average monthly number of IDH episodes. Correlation coefficients for systolic blood pressure were r_s= -0.262 (p=0.011) and r_s= -0.691 (p<0.001), for diastolic blood pressure — r_s= -0.297 (p=0.004) and r_s= -0.629 (p<0.001).

Thus, it can be stated that pre-dialysis and post-dialysis BP parameters have similar correlations with the duration of hemodialysis treatment and the average monthly number of IDH episodes. According to the scientific literature, however, neither pre-dialysis nor post-dialysis BP values have significant prognostic value (R. Agarwal, 2010).

When examining laboratory data, patients in group 1 (with relatively infrequent episodes of IDH) and group 2 (with frequent episodes of IDH) were found to have lower hemoglobin levels compared to patients in the control group who did not develop IDH (108.3 ±2.4, 107.2±3.1 and 117.0±2.2 g/l, respectively). Similar differences were also characteristic of the hematocrit level (31.5±0.8, 31.9±0.7 and 34.6±0.8%, respectively). According to the scientific literature, the early use of erythropoietin preparations for the correction of anemia (if necessary, already at the pre-dialysis stage of treatment) improves the morphological and functional parameters

of the cardiovascular system and reduces the risk of developing IDH (JI. Ю. Милованова et al., 2004).

There were no significant intergroup differences in mean serum concentrations of total protein, albumin, and C-reactive protein. The level of C-reactive protein varied significantly (from 2.0 to 149.7 mg/ml), as a result of which the comparison of average values is uninformative. Despite the absence of intergroup differences, the serum albumin level had a moderate positive correlation with the mean intradialytic systolic BP (r_s=0.515, p=0.041). The association of IDH with hypoalbuminemia was also demonstrated in a study by M. Pakfetrat et al. (2010).

Thus, our study showed the presence of a large number of correlations between the frequency of IDH, as well as the actual pre-, intra- and post-dialysis levels of blood pressure with various clinical and laboratory data. The analysis of the obtained results made it possible not only to identify some general trends, but also to demonstrate the significance of individual characteristics. As shown, for the relative values of intradialysis changes in blood pressure (taking into account its predialysis level), interdialysis weight gain and ultrafiltration volume (taking into account the "dry" weight of the patient), correlations are characteristic that differ from the correlations of the corresponding absolute parameters. Taking into account the results of the study and data from the scientific literature, we believe that the prevention of IDH should be comprehensive and individualized. Prospects for solving the problem of IDH are inextricably linked with the technological side of hemodialysis (wider introduction of hemodiafiltration and various types of profiling). Further improvement of IDH prevention measures, in our opinion, is one of the most significant directions in the development of renal replacement therapy.

CONCLUSIONS

1. The frequency of episodes of intradialysis hypotension was correlated with the duration of treatment with program hemodialysis and the nature of the underlying disease. In patients with diabetic nephropathy, intradialysis hypotension was observed 2.6 times more often than in patients with chronic glomerulonephritis, and 5.3 times more often than in patients with polycystic kidney disease ($p<0.01$).

2. The average monthly number of episodes of intradialytic hypotension has a negative correlation with body mass index ($r_s= -0.234$; $p=0.039$). Among patients with frequent episodes of intradialytic hypotension, underweight was more common than among patients in whom episodes of intradialytic hypotension were not observed.

3. The average monthly number of episodes of intradialysis hypotension negatively correlated with the average level of both predialysis systolic ($r_s= -0.399$; $p<0.001$) and postdialysis systolic BP ($r_s= -0.691$; $p<0.001$).

4. Intradialysis systolic blood pressure correlated positively with serum albumin ($r_s=0.515$; $p=0.041$) and negatively with the duration of hemodialysis treatment ($r_s= -0.458$; $p=0.042$). The presence of episodes of intradialytic hypotension was associated with reduced levels of hemoglobin and hematocrit.

5. The ratio of interdialysis weight gain and ultrafiltration volume to dry weight positively correlated with the duration of hemodialysis treatment and the average monthly number of episodes of intradialysis hypotension.

PRACTICAL RECOMMENDATIONS

1. Patients with frequent episodes of intradialytic hypotension require correction of malnutrition and control of serum albumin levels.

2. Patients who have more than 2 episodes of intradialytic hypotension per month should be given special attention. attention to the correction of anemia and dyselectrolytemia.

3. When assessing risk factors for intradialysis hypotension, one should take into account the relative indicators of interdialysis weight gain and ultrafiltration volume (the ratio of their absolute values to "dry" weight).

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