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Personalized prevention and treatment strategies for hypotension patients during maintenance hemodialysis

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Abstract: Hemodialysis (HD) is the most common renal replacement therapy for patients with end-stage renal disease. Intradialytic hypotension (IDH) is a serious complication during dialysis. It is mainly related to hypovolemia, resulting in premature interruption of dialysis, and insufficient clearance of fluid and solute, which eventually causes a variety of adverse clinical outcomes such as decline in quality of life, inadequate dialysis, vascular access embolism, loss of residual renal function, cardiovascular events and death, seriously threatening the life and health of patients. Despite its clinical significance, the early prediction of IDH remains a challenge. In recent years, the discovery of some new biomarkers and the use of volume assessment devices, hemodialysis equipment, biofeedback systems, new drugs and artificial intelligence early warning models have provided great help in the early identification and treatment of IDH. In view of the clinical heterogeneity of blood pressure changes in hemodialysis patients, it has become an inevitable trend to shift from standardized management to personalized nursing. This article mainly reviews the best strategies for personalized prevention and treatment of IDH.

1. Introduction

Hemodialysis (HD) is the most common renal replacement therapy for patients with end-stage renal disease. Intradialytic hypotension（IDH）is the most common serious complication in the process of hemodialysis. The occurrence of intradialytic hypotension is the final result of the interaction between ultrafiltration rate (UFR) and cardiac output and arteriolar tension during hemodialysis. Dialysis hypotension is related to a variety of adverse clinical outcomes, such as decreased quality of life, inadequate dialysis, vascular embolism, cardio-cerebrovascular accidents and death, which seriously threaten the life and health of patients. In recent years, the further deepening of dialysis treatment research and the progress of science and technology have provided us with many new ideas for hemodialysis treatment. Dialysis is undergoing a series of fundamental clinical changes-from standardized management to personalized nursing. Subtle differences in dialysis prescriptions and methods may affect the risk of death and quality of life. Therefore, it is urgent to develop personalized prevention and treatment strategies for each patient.

2. The Emergency Treatment of IDH

IDH is the decrease of effective circulating blood volume caused by fluid discharge during dialysis. Therefore, the basis of emergency treatment of IDH is to reduce ultrafiltration, supplement blood volume, increase plasma osmotic pressure, increase cardiac output and maintain organ perfusion. Including reducing ultrafiltration rate and blood flow, placing patients in Trendelenburg position, inhaling oxygen, or stopping dialysis treatment immediately. In addition, intravenous infusion of normal saline, hypertonic saline, hypertonic glucose water, albumin, dextran, 6-hydroxyethyl starch, mannitol and other solutions to supplement blood volume, or the use of vasoactive drugs such as dopamine and midodrine to increase cardiac output and central venous pressure.

3. Intervention during Dialysis

3.1 Setting an Appropriate Dry Weight

Accurate evaluation of dry weight is very important for dialysis patients. The assessment of patients' volume status by clinicians is often based on the clinical features of patients, such as vital signs, peripheral edema signs, jugular vein dilatation, pulmonary auscultation and so on. In recent years, with the development of clinical research and technology, some new tools to objectively evaluate the fluid status of patients have been increasingly used by clinicians, including bioimpedance spectrum[1], lung ultrasound[2,3], inferior vena cava ultrasound, echocardiography and other devices. These modern technologies and analytical tools help clinicians adjust ultrafiltration and dialysis prescriptions in a more precise and personalized manner to ensure that patients get the best volume condition, thus helping to minimize the risk of IDH.

3.2 Develop Personalized Dialysis Prescriptions

The different effects of heterogeneity of dialysis prescriptions on patients' clinical outcomes have been confirmed by many studies. Personalized dialysate with high sodium concentration [4], high magnesium concentration, high calcium concentration and low temperature [5] all have potential benefits in reducing the risk of IDH. For patients at high risk of IDH, it is recommended to limit the ultrafiltration rate to 12ml/kg/h or to use hemodiafiltration [6,7].

3.3 Drugs for Prevention and Treatment of IDH

Studies have found that intravenous albumin infusion before the beginning of dialysis can reduce the onset and severity of IDH in patients with hypoalbuminemia, and is better than normal saline[8]. For patients who are ineffective to emergency treatment of IDH with normal saline, mannitol and albumin can be considered as alternative treatment. Long-term use of loop diuretics (rather than aldosterone receptor antagonists)[9] and rational selection of antihypertensive drugs (choosing antihypertensive drugs with high dialysis clearance and high receptor selectivity)[10] may help to reduce the morbidity, all-cause mortality and cardiovascular mortality of IDH in maintenance hemodialysis patients. Sertraline may have potential benefits in reducing the discomfort symptoms of patients with frequent IDH, but it does not decrease the incidence of IDH. Razeghi et al. found that sertraline has a positive effect on the prevention of IDH only in non-diabetic patients [11]. Hormones may be an effective drug to prevent the occurrence of IDH. It has been reported that the use of fluorocortisone before dialysis can improve the drop of blood pressure during dialysis in patients with recurrent IDH after treatment with midodrine [12]. A small sample study also found that intravenous injection of hydrocortisone 30 minutes before the start of dialysis significantly reduced the number of recurrent IDH in patients with previous IDH [13]. Taking midodrine before dialysis seems to be a safe and effective treatment for IDH in the short term, but it may lead to an increase in long-term mortality and hospitalization. Some studies have found that intravenous injection of L-carnitine before and after dialysis is beneficial to reduce the incidence of IDH [14], but its efficacy is still controversial. Other traditional Chinese medicine, such as Dushen decoction, Scutellaria baicalensis, intravenous injection of Lishen, Shengmai, Shenfu and other drugs, or the use of traditional Chinese medicine acupoint therapy (HAT), intra-dialysis acupuncture and other treatment methods have a certain preventive and therapeutic effect on IDH. In addition, studies have shown that 1 hour after hemodialysis, injection of adenosine receptor antagonist FK352 may be helpful in improving IDH [15], but more prospective studies are needed to further assess the benefits and potential risks of various treatments.

3.4 Diet and Exercise

Eating during dialysis may increase systolic blood pressure variability, increase the incidence of uncomfortable symptoms during dialysis, and reduce dialysis adequacy, even if you take a high-protein diet. Therefore, routine use of nutritional supplements during dialysis is not recommended. For patients with poor nutritional status, eating a high-protein diet one hour before dialysis may be an intervention strategy to stabilize hemodynamics and improve dialysis adequacy [16]. The occurrence of IDH is often accompanied by fatigue after dialysis and a long time for symptom recovery, so patients' physical activity may be limited. Proper physical activity exercise during or between dialysis may help to improve the occurrence of symptomatic hypotension during dialysis.

4. Intervention in Interdialysis

Strengthening the health education of dialysis patients and urging them to manage the volume during dialysis interval is the key to patient management. Individual health management programs should be made according to the basic disease status of patients. Actively treat the primary disease, improve the dietary composition and structure of patients, correct the state of malnutrition, and control the weight gain during dialysis. It includes standardizing the use of diuretics and antihypertensive drugs, and if necessary, prophylactic use of some potentially effective drugs for patients at high risk of IDH.

5. Prediction of IDH

5.1 Biomarkers and potential predictors

Some studies have found potential predictors of IDH, such as TNF- α, IL-1 β [17], propeptide level (Δ Prot) [18], Δ OER (oxygen uptake rate) [19], coronary artery calcium score (CACS) [20] and so on. Studies have shown that Δ OER > 19% 15 minutes after the start of dialysis or > 36% final increment at the end of dialysis can help identify high-risk IDH patients with hemodynamic instability, but this method can only be applied to patients with permanent central venous catheters [19].

5.2 Hemodialysis Equipment

Some new devices also show the feasibility of early prediction of IDH [21-25]. The non-invasive continuous blood pressure system can identify the hemodynamic changes of patients during dialysis in real time and adjust the ultrafiltration rate according to the trend of volume change during dialysis. ClearSight, developed by Edward Life Sciences Company of the United States, can identify the volume state of HD by analyzing the data of mean arterial blood pressure (MAP), heart rate (HR), stroke volume index (SVI), cardiac index (CI) and calculated systemic vascular resistance index (SVRI), and help dialysis patients to set the best volume management strategy [21]. Photoacoustic (PA) imaging can monitor changes in blood pressure during dialysis by detecting changes in local perfusion during dialysis [22]. Non-invasive venous waveform analysis (NIVA) uses a piezoelectric sensor connected to the skin to dynamically obtain the peripheral vein waveform during dialysis and quantify it into Niva value by algorithm, thus reflecting the intravascular volume state during dialysis [23]. Sudocan ®is a device that quantifies autonomic nervous dysfunction by measuring electrochemical skin conductance (ESC) of the hands and feet and can be used to identify the risk of IDH early [24]. Optical coherence tomography angiography (OCT-A) can perform risk stratification of short-term IDH by measuring the baseline central concave vessel density and choroidal thickness of superficial capillary plexus (SCP) and deep capillary (DCP) in dialysis patients [25].

5.3 Biofeedback System

In recent years, with the development of science and technology, some personalized biofeedback systems with real-time online monitoring equipment began to appear in the field of dialysis. Blood volume biofeedback, body temperature biofeedback, blood pressure biofeedback, sodium concentration biofeedback [26] are the most commonly used clinical applications. The biofeedback system of blood volume is suitable for volume management of patients with hypotension tendency and significant weight gain during dialysis. The hemodynamic stability can be maintained by identifying the decreasing trend of blood volume during dialysis and continuously adjusting the ultrafiltration rate and the conductivity of dialysate. Body temperature biofeedback control can be used in patients with poor regulation of peripheral vascular resistance and frequent IDH. By feeling the blood temperature during dialysis and adjusting the dialysate temperature or the energy flow rate of cardiopulmonary bypass to maintain constant temperature, it can improve the compensatory response of cardiovascular system to hemodynamic instability during dialysis, improve the dialysis tolerance of hypotension susceptible patients and reduce the incidence of IDH. Blood pressure biofeedback is suitable for patients whose cardiovascular system does not respond adequately to changes in blood volume and peripheral vascular resistance. The sodium concentration biofeedback system can provide real-time electrolyte prescriptions for dialysis patients, make up for individual and intra-individual differences in serum sodium levels, and improve hemodynamic stability during dialysis, reduce the occurrence of intradialytic hypotension and adverse reactions during dialysis without causing interdialysis weight gain. Therefore, for patients tend to occur hypotension, excessive weight gain during dialysis or cardiovascular regulation dysfunction, the use of biofeedback system will bring great benefits.

5.4 Intelligent System

With the advent of big data and the era of artificial intelligence, artificial intelligence has been applied to health care to help doctors make medical decisions. Some researchers have applied machine learning algorithms to develop intelligent early warning systems to predict the occurrence of IDH and provide personalized medical advice in time [27]. Artificial intelligence model shows better prediction ability than traditional logistic regression model, and the accuracy, authenticity and extensiveness of data sets are the key to the development of repeatable prediction model. Therefore, for patients with high risk of IDH, AI modeling can help them formulate personalized dialysis treatment prescriptions and improve hemodynamics during dialysis.

6. Prospect

So far, evidence-based medicine has not provided nephrologists with accurate advice on the best strategies for individual dialysis patients. A single dialysis technology, procedure or equipment can not achieve the comprehensive management of dialysis patients. Therefore, it is suggested that personalized management strategies should be formulated according to the heterogeneity of dialysis patients, based on their main complications, clinical characteristics and parameters related to dialysis prescription, so as to minimize the adverse consequences of dialysis. So that every patient can get the best quality of life and higher survival rate. More new large-scale trials are needed to customize dialysis prescriptions based on the personal characteristics of uremic patients and to assess their impact on quality of life, family burden and long-term survival.

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