

Evidence-Based Strategies for the Prevention and Management of Intradialytic Hypotension in Maintenance Hemodialysis Patients

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Abstract: Objective: To summarize evidence on the prevention and management of intradialytic hypotension in maintenance hemodialysis patients, providing reference for clinical practice. Method: Chinese and English databases, guideline websites, and professional society websites were systematically searched for literature on intradialytic hypotension guidance, including clinical decisions, guidelines, evidence summaries, systematic reviews, and expert consensuses, from database inception to October 1, 2024. Evidence was extracted after literature quality evaluation. Results: A total of 11 publications were included: 2 clinical decisions, 7 guidelines, 1 systematic review, and 1 expert consensus. 38 pieces of evidence were summarized across 4 themes: pre-dialysis assessment and prevention, monitoring and management during dialysis, medication use, and patient self-management. Conclusion: The best evidence for prevention and management of intradialytic hypotension in maintenance hemodialysis patients is scientific and comprehensive. Healthcare professionals are advised to apply this evidence judiciously in conjunction with clinical realities to ensure patient safety.

Keywords: Hemodialysis; Intradialytic hypotension; Evidence summary; Evidence-based nursing

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1. Introduction

Intradialytic hypotension (IDH) is the most common acute complication in maintenance hemodialysis (MHD) patients, with an incidence of 20-40% ^[1, 2]. Currently, most studies recognize the definition of IDH in The European Best Practice Guidelines (EBPG): a decrease in systolic blood pressure of ≥ 20 mmHg (1 mmHg = 0.133 kPa) and a decrease in mean arterial blood pressure of ≥ 10 mmHg on dialysis with symptoms of hypotension,

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which requires the administration of interventions ^[3,4].IDH causes clinical symptoms such as nausea and vomiting, muscle cramps, dyspnea, and transient syncope ^[5,6], which not only results in inadequate dialysis, decreased residual renal function, and occlusion of endovascular fistulae, but also causes cardiovascular and cerebral vascular diseases, and even leads to the death of patients ^[7,9]. At present, there is a lack of standardized and systematic guidance on the prevention and management of hypotension in MHD patients on dialysis in China. This study summarizes the evidence on the prevention and management of IDH in MHD patients, aiming to provide an evidence-based basis for clinical healthcare professionals to develop management programs.

2. Materials and methods

2.1. Literature retrieval strategy

Following the "6S" pyramid model, top-down searches are performed on BMJ Best Practice, UpToDate, Cochrane Library, JBI, National Institute for Health and Clinical Excellence (NIHCE) (UK), Ontario Nursing Association (Canada), International Guidelines Collaboration (IGCC), DynaMed Evidence-Based Knowledge Base, U.S. National Guidelines Repository, Scottish Interhospital Guidelines Network, American College of Physicians Guidelines Repository, Nursing Practice Guidelines Web site, American Society of Diagnostic Interventional Nephrology, National Kidney Foundation, and the British Society of Nephrology Web sites, the websites of professional societies, such as the European Renal Association-European Dialysis and Transplantation Association, the Japan Dialysis Society, and the Chinese Society of Medicine Nephrology Section [10]. Supplementary searches are performed on databases such as PubMed, Embase, Medline, CINAHL, Web of Science, China Biomedical Database, CNKI, Wanfang Database, VIP Database, and Yimaitong. Chinese keywords such as "hemodialysis / renal dialysis /hemodialysis purification /hypotension in dialysis /complications" and "systematic evaluation / systematic review /evidence-based /guidelines /summary of evidence /recommendations /consensus /statements". English keywords included "renal dialysis /maintenance hemodialysis /maintained hemodialysis /hemopurification /HD /haemodialysis /blood purification" and "hypotension /IDH /adverse events in dialysis /intradialytic hypotension /low blood purification." The search was performed from the time of construction to October 1, 2024. This study is registered with the Center for Evidence-Based Nursing at Fudan University under registration number on ES20257587.

2.2. Literature inclusion and exclusion criteria

2.2.1. Inclusion criteria

- (1) Publicly available literature in Chinese and English
- (2) The study subjects are MHD patients
- (3) The study is on the prevention, treatment, and care of IDH
- (4) The type of study is on clinical decision making, guideline, evidence summary, systematic evaluation, and expert consensus

2.2.2. Exclusion criteria

- (1) Full text is not available
- (2) Guidelines and expert consensus that had been updated
- (3) Research proposal or report, abstract

(4) Low quality evaluation, incomplete information, duplicate publication, or translated version

2.3. Literature quality evaluation

- (1) Guideline evaluation is performed using the appraisal of guidelines for research and evaluation II, AGREE II [11].
- (2) Expert consensus is evaluated using the JBI expert consensus evaluation tool [12].
- (3) Systematic evaluations are evaluated using the measure tool to assess systematic reviews, AMSTAR 2 [13].
- (4) Critical appraisal for summaries of evidence (CASE) to evaluate the quality of inclusion in clinical decision making [14].

2.4. Evidence extraction, integration, and evaluation

The evaluation of guidelines is done independently by four researchers, and the rest of the literature is done independently by two researchers. In case of disagreement, it was discussed and adjudicated by the research team. When evidence from different sources conflicted, the inclusion of evidence followed the principle of prioritizing the most recently published, authoritative sources, and evidence-based evidence [15]. Inclusion is done using the JBI Evidence Pre-grading and Evidence Recommendation Level System (2014) to evaluate the inclusion of evidence and categorize it into levels 1 to 5, where 1a is the highest level and 5c is the lowest level [16].

3. Results

3.1. General characteristics of the included literature

A total of 690 documents were retrieved, and 38 documents were obtained after initial screening by deemphasizing, reading titles and abstracts, and further re-screened by reading the full text and quality evaluation, and finally 11 documents were obtained, including 2 clinical decision-making, 7 guidelines, 1 systematic evaluation, and 1 expert consensus [17–25, 26, 28]. The basic characteristics of the literature are shown in **Table 1**.

Table 1. Basic characteristics of included literature (n = 11)

Literature	Publication time (year)	Literature sources	Document type	Subject		
Jennifer et al. [17]	2023	Uptodate	Clinical decision	Intradialytic hypotension in an otherwise stable patients		
Thomas et al. [18]	2022	Uptodate	Clinical decision	Emergency hemodialysis prescription		
Kooman et al. [19]	2007	European Renal Association European Dialysis and Transplantation Association	Guide	Guidelines for the management of patients with hemodynamic instability		
National Kidney Foundation [20]	2015	Cochrane	Guide	KDOQI Clinical practice guidelines for hemodialysis adequacy: 2015 update		
Ashby et al. [21]	2019	British Renal Association Network	Guide	Hemodialysis Clinical Practice Guidelines		
Watanabe <i>et al</i> . [22]	2015	Uptodate	Guide	Dialysis prescription for maintenance hemodialysis		
Hirakata et al. [23]	2012	Japanese Society for Dialysis Therapy	Guide	Guidelines for Management of Cardiovascular Diseases in Patients on Chronic Hemodialysis		

Table 1 (Continued)

Literature	Publication time (year)	Literature sources	Document type	Subject		
Chen XM [24]	2021	Pulse of Medicine (TCM)	Guide	Standard Operating Procedures for Blood Purification		
Liu WH et al. [25]	2015	Wanfang (China)	Guide	Clinical Practice Guidelines for Hemodialysis Adequacy in China		
Mustafa et al. [26]	2016	PubMed	Systematic review	Dialysate temperature reduction for intradialytic hypotension for people with chronic kidney disease requiring haemodialysis		
Li WG et al. [28]	2022	Wanfang (China)	Expert consensus	Expert consensus on prevention and treatment of hypotension in hemodialysis		

3.2. Results of literature quality evaluation

Two clinical decisions were included in this study, all of which were evaluated as "yes" except for the entry "whether potential bias was avoided", which was evaluated as "partially yes" [17, 18]. Seven guidelines were recommended at grade B or higher [19–25]. Two systematic evaluations were evaluated in this study, one of which was included in the literature, and one of which was traced back to the original literature through clinical decision-making derived from UpToDate [26, 27]. Literature was rated as "yes" for all entries except entry 4, "Systematic evaluation of whether authors used a comprehensive search strategy", which was rated as "partially yes"; and literature was rated as "partially yes" except for entry 4 evaluated as "partially yes" and entry 10 "Systematic evaluation of whether authors reported funding sources for individual studies" evaluated as "no", all other entries in literature were evaluated as "Yes" for all entries [26, 27]. One expert consensus was included, and all entries were evaluated as "yes" [28].

3.3. Summary of evidence

Through evidence extraction and integration, 38 pieces of evidence were summarized and formed in 4 areas: predialysis assessment and prevention, monitoring and management, medication use, and patient self-management, as shown in **Table 2**.

Table 2. Summary of the best evidence for the prevention and management of hypotension in hemodialysis patients during dialysis

Category of evidence	Content of evidence	Level of evidence	
Assessment	1.It is recommended that the target weight be assessed once a month and again when the clinical situation changes ^[17,21-22,28]		
and prevention	2. The use of objective measurements is recommended to supplement the assessment of the patient's fluid status after an ambiguous clinical assessment or after the occurrence of a complication ^[17,21-24]		
	3.Evaluate patient's cardiac function and maintain patient's cardiac status ^[17,19,23-24,28]	1a	
	4.Evaluate primary causes of hypotension e.g. pericardial effusion, amyloidosis, systemic infection, air embolism ^[17,24]	1a	
	5.It is recommended that the ultrafiltration rate be controlled at or below 13 ml/kg-h in dialysis ^[23, 28]	2a	
	6.Reduction of IDH using a simple ultrafiltration model ^[28]	2b	
	7.Ultrafiltration programs (curves) are not recommended to prevent IDH ^[17-19,28]	3b	
	$8. In \ patients \ with \ frequent \ IDH, \ a \ dialysate \ with \ a \ calcium \ concentration \ of \ no \ less \ than \ 1.5 \ mmol/L \ is \ recommended^{[18-19,24]}$	2b	
	9.Avoid magnesium dialysate ≤0.25 mmol/L, especially in combination with low-calcium dialysates ^[19]		
	10.It is not recommended to increase the sodium concentration to reduce the incidence of hypotension in dialysis, and if it is needed, it is not recommended to set the dialysate with a sodium concentration of >144 mmol/L and try not to increase the sodium concentration 1 h before going off the machine ^[28]		
	11.Use of low-temperature dialysis fluid, dialysis fluid temperature \leq 36 °C and \geq 35 °C ^[17-20,23-24,26-28]		
	12.Recommendations for prolonging dialysis duration and/or increasing dialysis frequency ^[17-20,23-24,28]	2b	
	13.In patients with frequent IDH or IDH that is not easily corrected, a change in dialysis modality, such as hemodialysis filtration, peritoneal dialysis, daily dialysis, or nocturnal dialysis, is recommended ^[17,19,23-24,28]		
	14.The use of dialysis devices with continuous blood pressure monitoring and biofeedback mechanisms and automatic ultrafiltration control is recommended for the prevention of IDH. [28]	3c	
	15.Automated Volume Control Feedback Can Be Tried as a Second-Line Option for Patients with Refractory IDH ^[17,19]		
and of IDH ^[19]	16.It is recommended that blood pressure and heart rate should be measured frequently during dialysis to predict the onset of IDH ^[19]	5c	
	17.Reduce ultrafiltration rate or stop ultrafiltration ^[17,19,24,28]	1a	
	18.Reduced blood flow <200 ml/min and dialysate flow rate <350 ml/min ^[24]	2a	
	-	1a	
	20.Recommended 50% dextrose injection 40~100ml IV, isotonic/hypertonic saline 100~200ml rapid IV infusion ^[17,23-24,28]	1a	
	21. For those whose blood pressure has not recovered, a rapid intravenous infusion of 100-200 ml of 20% mannitol solution and a rapid infusion of 100 ml of hydroxyethyl starch solution (succinyl gelatin) are recommended [23-24,28]		
	22.Human albumin transfusion is recommended for those whose blood remains unrecovered [23-24,28]		
	23.Oxygen therapy is recommended ^[17,28]	2a	
	24.Cardiac monitoring is recommended, and blood pressure should be rechecked every 5 min. [28]	1a	
	25.Use of antihypertensive drugs (intravenous pumping of vasoactive drugs or orthostatic inotropic drugs) for those with hypotension despite adequate fluid intake ^[24,28]		
	26.Early termination of dialysis if treatment for severe hypotension is ineffective ^[24,28]	2a	
Drug use	27.It is recommended that antihypertensive drugs should be discontinued/reduced prior to dialysis in patients with a tendency to develop hypotension on dialysis ^[17,19,24,28]		
	28.It is recommended that patients with residual urine output be given an oral diuretic to increase urine output, preferably a tab diuretic [17,27]		
	29.It is recommended to give 2.5~5.0mg of midodrine hydrochloride 15~30min before dialysis ^[17-18,28]	2a	
	30.L-carnitine supplementation is recommended ^[17,19,24,28]	2a	
	31.In elderly or comorbid diabetic patients, 20-40 ml of 50% dextrose can be given after 2 hours of dialysis to stabilize hemodynamics ^{19,23}]	3a	

Table 2 (Continued)

Category of evidence	Content of evidence	Level of evidence
Patient self-	$32. Improve nutritional \ status, correct \ hypoproteinemia, recommend \ serum \ Alb \ge 35 g/L, \ serum \ Alb \ge 40 g/L \ if \ available^{[23-25,28]}$	2a
management	33.Correct anemia and recommend maintaining Hb levels at $110g/L \sim 130g/L^{[19-20,23-25]}$	2a
	34.Control of weight gain during the interdialytic period should be prioritized by controlling sodium intake, with recommended daily salt intake of <3 to 6 g (less than 3 g is preferred) ^[17,19-20,24-25,28] 35.Recommended weight gain between dialysis <5% of target weight (3% or less preferred) ^[25,28]	
	36. Water intake should include not only liquids but also water in food ^[20,25]	2b
	37.Recommended pre-dialysis systolic blood pressure <160 mmHg (with medication) ^[25]	5a
	38.In hypotensive dialysis patients and those with a tendency to hypotension on dialysis, fasting should be done during dialysis [17,19-21,24-25,28]	2a

4. Discussion

4.1. Regular assessment of target weight and cardiac function

Target weight is the weight a dialysis patient wishes to achieve at the end of dialysis under normal equilibrium conditions ^[29]. Studies have shown that patients with MHD have lower all-cause mortality using target weight assessment compared to assessment through clinical performance ^[30]. Pre-existing cardiovascular disease in the end-stage renal disease population as well as dialysis complications lead to systolic or diastolic dysfunction of the heart, increasing the risk of IDH ^[19, 28]. Evidence 1–2 gives clear guidance on the frequency and manner of assessment of target body weight, recommending that it should be assessed using objective measures such as bioimpedance techniques, blood volume monitoring, and inferior vena cava or lung ultrasound. Evidence 3–4 states that patients' cardiac functional status should be assessed regularly and that primary causes of hypotension should be treated aggressively. Therefore, it is recommended that healthcare professionals enhance the comprehensive assessment of dialysis patients' volume status through multidisciplinary cooperation and the combined application of multiple methods.

4.2. Setting the appropriate ultrafiltration mode and rate

The application of ultrafiltration mode and rate is described in Evidence 5–7. The main mechanism of IDH occurrence is the reduction of effective circulating blood volume caused by ultrafiltration, and in order to alleviate the loss of blood volume, pure ultrafiltration is used to remove water from the body in order to minimize the change of plasma osmolality. Ultrafiltration modes can adjust the rate of ultrafiltration to influence blood volume changes. The most commonly used ultrafiltration curves are characterized by an initial high ultrafiltration rate, an intermediate linear decrease in ultrafiltration rate or intermittent ultrafiltration pulses, and finally a minimal ultrafiltration cycle. Guidelines state that controlling the ultrafiltration rate in dialysis to 13 ml/kg-h or less is effective in reducing the incidence of IDH in patients [28]. Taken together, these recommendations suggest that the pattern and goals of individualized ultrafiltration should be carefully observed and set in dialysis.

4.3. Reasonable Dialysate Concentration and Temperature

Evidence 8–11 gives guidance on the concentration, type, and temperature of dialysate. Changes in the concentration of ionized calcium can affect myocardial contractility during dialysis. Therefore, enhancing cardiac

contractile function by elevating dialysate calcium concentration is also an effective means of preventing IDH; however, high-calcium dialysate may have short-term adverse effects on atherosclerosis and cardiac diastolic properties, and should be used with caution [19]. It has been noted that elevating the sodium concentration of dialysate can maintain plasma osmolality [17, 28]. However, the use of higher sodium concentrations for dialysis can affect sodium balance, leading to patient thirst and weight gain between dialysis sessions. Therefore, several guidelines do not recommend increasing sodium concentration to reduce the incidence of IDH, and national studies supporting the attitude are applying adjustable sodium in combination with other means, such as temperature or ultrafiltration mode to prevent IDH [17–19, 28]. Studies have shown that dialysis with dialysate below body temperature can help prevent the development of IDH [26–28]. A Cochrane systematic evaluation concluded that lowering the temperature of the dialysate, while reducing IDH, also increases patient discomfort [31]. Several guidelines recommend that dialysate temperature should be $\leq 36^{\circ}$ C and $\geq 35^{\circ}$ C [19–21]. Therefore, dialysate temperature settings should be individualized.

4.4 Changing dialysis modality

Evidence 12–13 comes from expert panel opinions, which are not yet supported by high-quality studies, and therefore are not considered as the preferred measure to prevent IDH [32]. Evidence 14–15 recommends the use of biofeedback to predict the occurrence of IDH. Hemodialysis is a treatment based on blood purification equipment, and modern dialysis equipment with biofeedback technology correlates with treatment through continuous monitoring of blood pressure and blood volume to improve hemodynamic stability in hemodialysis and achieve prevention of IDH, with some efficacy in clinical trials.

4.5 Timely and effective treatment

Evidence 16 states that enhanced blood pressure and heart rate monitoring during dialysis can predict the occurrence of IDH ^[20]. Evidence 17–26 gives a step-by-step management plan for IDH based on the degree of hypotension and clinical symptoms. The occurrence of hypotension is often accompanied by reduced blood perfusion to tissues and organs and decreased oxygen delivery. Therefore, it is recommended that the hypoxic state of tissues and organs can be appropriately improved by timely oxygenation and cardiac monitoring. Clinical staff should be proficient in the management process of IDH to avoid more serious complications in patients caused by IDH, such as endocardial thrombosis ^[33].

4.6. Standardizing the use of medications

Evidence 27–31 summarizes the management of medications in IDH-prone populations, including the use of antihypertensives, diuretics, and midodrine hydrochloride. Evidence 30–31 give references to the dosage of midodrine hydrochloride and 50% dextrose, and medical staff adjust the dosage of related medications in a timely manner according to the patient's blood pressure changes in the clinic, as well as monitor the effects of the medications and the adverse effects of long-term use.

4.7. Improving patient self-management

Evidence 32–38 places demands on patients, but requires healthcare professionals to provide guidance on nutrition, anemia and blood pressure management, control of fluid growth, and eating during dialysis [34]. Improving the nutritional status of patients and actively correcting anemia may reduce the incidence of IDH by improving cardiac function. Blood glucose and blood pressure should be monitored during dialysis, individualized dietary guidance

should be implemented, fasting should be done for patients at risk of hypotension during dialysis, and eating should be encouraged for patients at risk of hypoglycemia [35].

5. Conclusion

This study summarizes the current best evidence on the prevention and management of hypotension in maintenance hemodialysis patients on dialysis for healthcare professionals. The evidence mostly comes from the more authoritative guidelines and clinical decision-making at home and abroad in the past 5 years, and the overall quality is high, so it is recommended that clinical workers still need to combine the specific clinical situation and patients' wishes to apply the evidence judiciously in the process of selecting and applying the evidence.

Disclosure statement

The authors declare no conflict of interest.

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