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INCIDENCE OF INTRADIALYTIC HYPOTENSION IN HEART TRANSPLANT RECIPIENTS WITH ACUTE KIDNEY INJURY TREATED BY ACETATE-FREE HEMODIAFILTRATION

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Introduction. Intradialytic hypotension (IDH) is a common complication of renal replacement therapy (RRT) sessions and may be a particularly detrimental factor in heart recipients. **Objective:** to investigate the incidence of IDH in heart recipients with acute kidney injury (AKI). **Patients and Methods:** Two groups of recipients were compared – the study group (SG), n = 313, in which 49 patients required intermittent RRT (IRRT) and in which online hemodiafiltration (OL-HDF) sessions were performed using acetate-free hydrochloric acid-based dialysate fluid; and control group (CG) n = 387, in which 88 patients required IRRT, where standard dialysate with an acetate ion content of 3 mmol/L was used for OL-HDF. **Results.** There was a significantly lower incidence of IDH in the SG compared to the CG: 10.46% *vs* 20.47% ($p < 0.05$). **Conclusions.** In heart recipients for whom IDH can be considered as a significant adverse factor, the use of acetate-free dialysis fluid can significantly reduce the incidence of this complication.

Keywords: heart transplantation, acute kidney injury, renal replacement therapy, hemodialysis, intradialytic hypotension, acetate-free hemodiafiltration.

INTRODUCTION

Heart transplantation (HTx) is the only curative option for patients with end-stage heart failure. The number of HTx is increasing annually; 310 such operations were performed in the Russian Federation in 2022, 212 of them alone at our center, Shumakov National Medical Research Center of Transplantology and Artificial Organs (Shumakov Center) [1]. By the first 10 months of 2023, Shumakov Center had already performed 200 such interventions. One of the most frequent and serious complications after cardiac surgery is postoperative acute kidney injury (AKI), requiring renal replacement therapy (RRT). In a number of cases, this need turns out to be quite prolonged. After patients' condition has been stabilized, intermittent RRT methods replace permanent ones. In such a complex category of patients, ensuring adequate dialysis treatment requires careful attention to all its components, including the composition of the dialysate.

Modern technology for the preparation of bicarbonate dialysate in the proportional mixing system of hemodialysis units involves the use of two-component concentrate, with one component being a sodium bicarbonate solution and the other containing the main electrolytes – sodium, potassium, calcium and magnesium in the form of chlorides. To stabilize the dialysate, prevent precipitation of hardness salts and give it a physiological pH, acid is added to the second component of the concentrate. In the practice of hemodialysis, acetic acid or its substitute, sodium diacetate, is traditionally used, which results in the presence of acetate ion in the dialysate at a concentration of 3–6 mmol/L. The negative effect of acetate ion on the tolerance of dialysis sessions and the incidence of complications, primarily IDH is known. In this regard, elimination of this component from the composition of dialysis fluid can have a beneficial effect on treatment outcomes, especially in patients prone to hemodynamic disorders.

Citric, succinic, and hydrochloric acids are used as alternative acids in dialysate concentrate. Hydrochloric acid is the most appropriate, since replacing acetic acid with hydrochloric acid does not require changes in the routine practice of the hemodialysis center and does not increase the cost of treatment. However, literature data on experience with acetate-free dialysate are limited and fragmentary.

The purpose of this study was to determine the effect of acetate ion replacement in a dialysate composition on IDH incidence in heart transplant survivors with AKI.

PATIENTS AND RESEARCH METHODS

The presented study retrospectively analyzed data from 313 recipients who underwent HTx between January 1, 2022 and June 1, 2023 (study group, SG) and a comparable cohort of 387 recipients who underwent

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HTx between January 1, 2016 and June 1, 2018 (control group, CG), when the switch to hydrochloric acid-based dialysate concentrate was made.

SG was represented by 313 heart transplant recipients, CG by 387 recipients; male patients predominated in both groups; the age composition of the groups did not differ. Among recipients in both groups, patients with dilated cardiomyopathy (DCM) predominated; the number of retransplantations was higher in SG. The proportion of patients with urgent indications for transplantation was also higher in SG, 35.5% UNOS 1B, compared to 12.4% in CG, and the number of patients with UNOS score 2 – 34.0% in SG compared to 57.4% in CG. The baseline characteristics of patients in the two groups are summarized in Table 1.

Intermittent renal replacement therapy (IRRT) was used after the recipients' condition was stabilized on continuous renal replacement therapy (CRRT). Online hemodiafiltration (OL-HDF) sessions in postdilution mode with dialysate/substitute of the following composition was used as IRRT: Na^+, 132–142; K^+, 2.0–4.0; Ca^{++}, 1.5–1.75; Mg^{++}, 0.5; Bic, 30–36; CH_3COO^-, 0–3.0 (mmol/L). Electrolyte composition and bicarbonate concentration were selected individually depending on the electrolyte composition of the patient's plasma and acid-base state parameters. Anticoagulation was performed in the form of dosed administration of unfractionated heparin under the control of activated clotting time. High-flow double-lumen central venous catheters were used as vascular access.

The IDH recorded in treatment session reports was evaluated as a decrease in systolic blood pressure by more than 20 mmHg with the development of clinical symptoms of hypotension and the need for intervention by medical personnel, including increased doses of cardiotonic drugs.

The obtained results were processed using statistical package Biostat; the t-test was used to establish the significance of differences, taking into account the Bonferroni correction. Differences were considered significant at $p < 0.05$ (EpiInfo 5.0, statistical package recommended by WHO).

RESULTS

The need for RRT in the two groups was not significantly different, 33.5% in SG and 34% in CG (Table 2). At the same time, the duration of CRRT, which was performed in the intensive care unit (ICU) immediately after HTx, was significantly longer in SG, 9.85 ± 0.73 days versus 4.57 ± 0.38 in CG ($p < 0.001$). Apparently, longer CRRT was associated with a significantly lower need for IRRT in SG, 15.7% versus 22.7% in CG. IRRT in SG was longer, 20.56 ± 4.9 days versus 13.14 ± 2.03 days in CG, but this difference did not reach statistical significance ($p = 0.163$). A statistically non-significant trend for longer duration of IRRT in SG was observed both when analyzing IRRT duration in ICU, 15.61 ± 8.42 days in SG versus 8.42 ± 1.16 days in CG ($p = 0.122$), and for IRRT duration in the ward, 25.34 ± 8.62 versus 19.70 ± 3.29 ($p = 0.54$).

The main characteristics of IRRT sessions are summarized in.

The number of sessions per week, session duration, ultrafiltration volume (excluding injected fluids), replacement volume (convection volume), and session efficiency according to the Kt/V coefficient did not differ significantly between the two groups. The significance of the differences in the average duration of OL-HDF session and convection volume is determined by many

Table 1

Main characteristics of recipients in the two groups

Indicators	Control group	Study group
Follow-up period	01.01.2016–01.06.2018	01.01.2022–01.06.2023
N (men/women)	387 (341/46)	313 (277/36)
Mean age (m/w)	49.2 (78–13) / 41.7 (70–11)	47.0 (69–12) / 41.1 (62–11)
Pre-HT diagnosis		
DCM	221	195
ICM	154	104
Graft dysfunction	6	11
LVA	4	1
HCM	–	2
RCM	1	–
ACM	1	1
UNOS distribution		
1a	30.2%	30.5%
1b	12.4%	35.5%
2	57.4%	34.0%

Note. DCM, Dilated cardiomyopathy; ICM, Ischemic cardiomyopathy; LVA, Left ventricular aneurysm; HCM, Hypertrophic cardiomyopathy; RCM, Restrictive cardiomyopathy; ACM, Arrhythmogenic cardiomyopathy.

observations. The frequency of IDH episodes was significantly and statistically significantly lower in SG compared to CG, 10.46% vs. 20.47% ($p < 0.05$).

DISCUSSION

The main finding in this study was a significant reduction in IDH incidence during acetate-free OL-HDF sessions in heart recipients with AKI compared with OL-HDF using standard bicarbonate dialysate containing 3 mmol/L acetate ion.

IDH is one of the most frequent complications occurring during hemodialysis sessions [2]. This complication not only reduces treatment effectiveness and prevents adequate ultrafiltration, but also impairs coronary blood flow [3, 4], which can be a particularly unfavorable factor in heart recipients in need of IRRT. One of the mechanisms contributing to the development of IDH may be the influence of acetate ion, which has cardiosuppressive, vasodilatory, and proinflammatory effects [5]. It has been shown that plasma acetate ion levels when using standard bicarbonate dialysate can exceed physiological values by dozens of times, accordingly, its elimination can have a favorable effect on tolerance to IRRT sessions [6].

Most publications concerning the use of acetate-free hemodialysis techniques are devoted to acetate-free biofiltration [7], but this technique requires the use of sterile sodium bicarbonate solution, and the convection volume obtained during the therapy session does not reach the current efficiency criteria. Studies of the effect of acetate-free dialysate on IDH incidence are limited to small groups of patients with end-stage renal failure undergoing program treatment [8, 9]. A Russian study by a group led by T.V. Mukhoedova reported a significant 3.8-fold decrease in the incidence of complications, including IDH, when performing sustained low-efficiency dialysis (SLED) in patients after cardiac surgery [10]. Our study, which included a larger number of heart transplant survivors, revealed a similar relationship. In our study, high-efficiency OL-HDF was performed, duration of sessions was somewhat shorter, and ultrafiltration volume was significantly greater than in the above-mentioned study. It should also be noted that the follow-up period of patients in our study was significantly longer, and recipients with prolonged need for IRRT in some cases were treated as outpatients. Nevertheless, analysis of the entire data set showed a very significant reduction in IDH incidence.

It is worth mentioning that hydrochloric acid used to produce acetate-free concentrate is more aggressive than acetic acid. This should be taken into account both when preparing the concentrate and when using it. In our practice, the steel activator blades in the concentrate mixer were destroyed and the concentrate centralized pump failed (Fig.).

Table 2

RRT need and duration in the two groups

Parameters	Control group		Study group
Needed CRRT	34% (132)		33.5% (105)
CRRT duration (days on avg.)	4.57 (1–19) ± 0.38	$p < 0.001$	9.85 (2–37) ± 0.73
Needed IRRT	22.7% (88)	$p < 0.05$	15.7% (49)
IRRT duration (days on avg.)	13.14 ± 2.03 (1–112), n = 129	NS $p = 0.163$	20.56 ± 4.9 (1–267), n = 63
IRRT duration in ICU (days)	8.42 ± 1.16 (1–67), n = 68	NS $p = 0.122$	15.61 ± 4.46 (1–102), n = 31
IRRT duration in the hemodialysis unit	19.7 ± 3.29 (3–112), n = 61	NS $p = 0.54$	25.34 ± 8.62 (1–267), n = 32

Note. CRRT, Continuous renal replacement therapy; IRRT, Intermittent renal replacement therapy.

Table 3

Main characteristics of OL-HDF sessions in the two groups

Parameters of IRRT sessions (OL-HDF)	Control group	Study group	P
Average number of RRT sessions per week	5.2 ± 0.06	5.06 ± 0.07	NS $p = 0.13$
Average duration of IRRT session (minutes)	300.7 ± 1.35	295.5 ± 1.57	$p = 0.012$
Mean UF volume (ml)	2373 ± 23	2311 ± 24	NS $p = 0.09$
Average replacement volume (l)	15.44 ± 0.08	15.81 ± 0.10	$p = 0.04$
Average Kt/V	1.49 ± 0.05	1.54 ± 0.06	NS $p = 0.42$
Frequency of hypotensive episodes (%)	20.47	10.46	$p<0.05$

Note. UF, ultrafiltration; Kt/V, efficacy of an IRRT session determined by ionic dialysance.

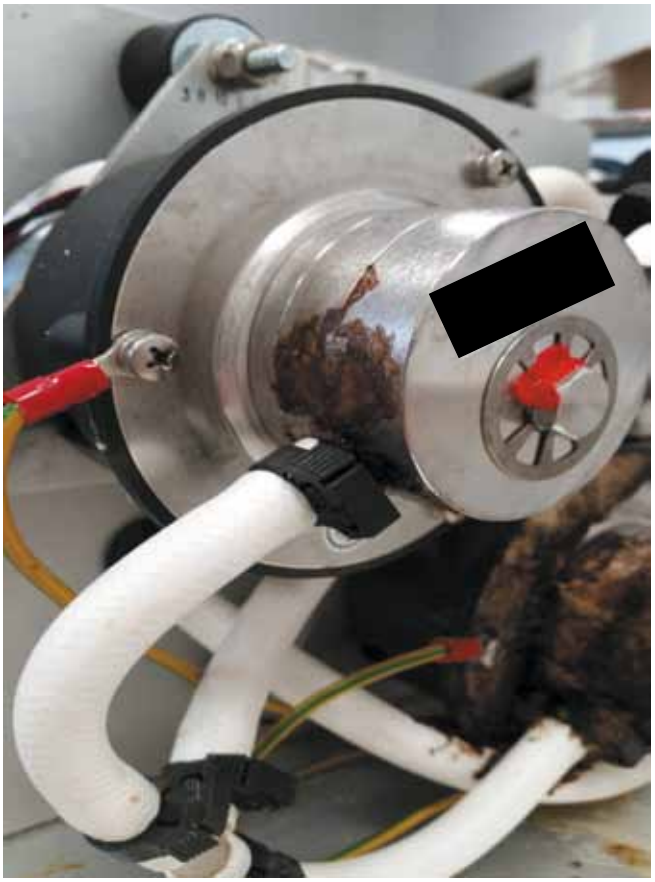

Fig. Corrosion of the central concentrate pump by hydrochloric acid

CONCLUSION

Despite its retrospective nature with uncontrolled collection of clinical data, the large size of the study, which included about 137 heart recipients and about 1700 OL-HDF sessions, allows for the following conclusion: when using an acetate-free hydrochloric acid-based dialysate fluid, treatment of OL-HDF heart transplant recipients is complicated by IDH half as often as when using standard bicarbonate dialysate containing 3 mmol/L acetate ion.

The authors declare no conflict of interest.

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