Renal Replacement Therapy

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Sodium zirconium cyclosilicate hydrate reduces medical expenses compared with hemodialysis in patients with acute hyperkalemia

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Abstract

Background Sodium zirconium cyclosilicate (SZC) has recently emerged as a therapeutic option for the management of acute hyperkalemia. Nevertheless, the relative effectiveness, safety, and financial considerations of SZC therapy versus conventional hemodialysis therapy remain uncertain.

Methods In this retrospective study, we embarked upon a comparative analysis encompassing the financial aspects, safety profiles, and efficacy metrics associated with SZC therapy and hemodialysis in patients grappling with acute hyperkalemia. No patients had systemic congestion or uremia.

Results A total of 21 patients (median 81 years old, 14 men) were included; 14 received SZC therapy and seven underwent hemodialysis. Acute hyperkalemia improved immediately within several days without any procedure-related adverse events, regardless of therapeutic interventions ($p < 0.05$ for both). Total medical expenses were significantly lower in the SZC group than in the hemodialysis group (55,596 [43,652, 69,761] vs. 419,768 [354,270, 514,700] Japanese yen, $p < 0.001$).

Conclusions In the realm of acute hyperkalemia management, SZC therapy emerges as an economically judicious alternative, while upholding parity in terms of safety and effectiveness when compared with the conventional hemodialysis paradigm—unless complicated by systemic congestion or uremia. The pressing task at hand revolves around the discernment of the optimal patient demographic for SZC therapy within the ambit of acute hyperkalemia.

Keywords Chronic kidney disease, Potassium binder, Medical cost

Introduction

Individuals afflicted by chronic kidney disease (CKD) frequently grapple with the intricacies of acute hyperkalemia, a condition stemming from the progression of renal dysfunction, metabolic acidosis, and the utilization of renin–angiotensin system inhibitors [1]. Acute hyperkalemia requires urgent intervention because it is associated with fatal arrhythmias such as complete atrioventricular block [2].

Various therapeutic modalities have been explored to confront acute hyperkalemia, encompassing potassium-binding agents, insulin infusion, loop diuretics, and hemodialysis. However, there is no gold standard to definitely treat acute hyperkalemia, except for hemodialysis

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[3]. Hemodialysis can definitely and immediately ameliorate acute hyperkalemia [4]. However, one of the drawbacks of hemodialysis is its requirement for blood access to the central vein. Medical expense for hospitalized management is another issue.

Sodium zirconium cyclosilicate (SZC) is a recently introduced selective potassium binder for the treatment of hyperkalemia. SZC selectively binds monovalent cations (excess potassium and ammonium) rather than divalent cations, including magnesium, due to its specific binding site geometry [5]. SZC has been shown to treat hyperkalemia immediately and to maintain serum potassium levels in the normal range for months with acceptably minimal drug-related adverse effects in patients with or without hemodialysis dependence [6].

SZC has recently been applied to treat acute hyperkalemia in real-world clinical practice [7, 8]. SZC therapy is less invasive and does not necessarily require hospitalization compared with hemodialysis. Furthermore, SZC may have an advantage in medical expenses over hemodialysis. We hypothesized that SZC-incorporated medical therapy may have advantage over hemodialysis therapy in the cost-effectiveness, even when we consider the cost of SZC itself. The medical cost is one of the great concerns in the current era, and such an advantage of SZC should be of great advantage in daily clinical practice. In this study, we compared medical expenses, as well as safety and efficacy, between SZC therapy and hemodialysis in patients with acute hyperkalemia.

Materials and methods

Patient selection

We retrospectively included patients with acute hyperkalemia who received urgent SZC therapy or hemodialysis between January 2013 and July 2022. For the SZC group, from the list of patients prescribed SZC, we included consecutive patients with serum potassium levels > 5.5 mEq/L and underwent urgent electrocardiogram who received SZC immediately or with serum potassium levels > 6.0 mEq/L who received SZC immediately. Of note, SZC became available for prescription in Japan after May 2020.

For the hemodialysis group, we included consecutive patients who underwent urgent hemodialysis to treat acute hyperkalemia on the same day of diagnosis. Patients who underwent hemodialysis to treat systemic congestion were not included because this is a definite indication of hemodialysis without any other therapeutic choices.

For both groups, patients with secondary hyperkalemia were excluded, such as acute kidney injury due to septic shock and tumor necrotic syndrome. All patients gave written informed consent. The study protocol was approved by the local Ethics Committee.

Baseline characteristics data

For both groups, baseline characteristics were obtained from the outpatient visits prior to the index occurrence of acute hyperkalemia. Baseline characteristics included demographics, comorbidities, and laboratory data. Serum potassium levels were measured by the ion-selective electrode method. Serum creatinine was measured by an enzymatic method. Estimated glomerular filtration rate (eGFR) was calculated using the GFR estimation formula for Japanese individuals [9]. CKD stage was defined as follows: stage G3a, eGFR of ≥ 45 and < 60 mL/min/1.73 m^2; stage G3b, eGFR of ≥ 30 and < 45 mL/min/1.73 m^2; stage 4, eGFR of ≥ 15 and < 30 mL/min/1.73 m^2; and stage 5, eGFR < 15 mL/min/1.73 m^2 [10].

Therapeutic intervention

This study was conducted retrospectively, and the choice between hemodialysis or SZC for the management of hyperkalemia that occurred after March 2020 was left to the discretion of the attending clinician. Although there was no formalized practice protocol in place, our clinical practice conventionally favored hemodialysis for patients presenting with complete atrioventricular block.

For the SZC group, the loading dose was 10-g three times per day for 2 days, followed by a maintenance dose of 5 g once a day, in principle. Doses were adjusted at the discretion of each attending physician. SZC was initiated at the outpatient clinic or during index hospitalization.

For the hemodialysis group, a blood access catheter was inserted into a central vein, and hemodialysis was performed for at least 3 h but less than 5 h at a time during index hospitalization. The dialysate flow rate was standardized to 500 mL/min for all dialysis sessions. The potassium concentration in the dialysate was 2.0 or 2.3 mEq/L. Treatment time, blood flow rate, types of dialyzer, and dialyzer membrane area were determined by the attending dialysis physician.

Calculation of medical expenses

Medical expenses required during outpatient clinic visits or during hospitalization were evaluated as a primary outcome.

For the clinic treatment (SZC group alone), all medical expenses at the time of SZC initiation and the next visit were summed up in addition to the drug cost of SZC taken until the next visit.

For the in-hospital treatment (SZC group or hemodialysis group), the bundled medical expense for hyperkalemia (International Statistical Classification of Diseases and Related Health Problems-10 code, E875)

based on the diagnosis procedure combination system and the piecework medical expense for any procedures were summed up.

Clinical outcome

Serum potassium and creatinine levels were followed immediately after the therapeutic intervention and 3 months later. The occurrence of arrhythmia and any interventions to the arrhythmia were counted. All-cause death or initiation of permanent hemodialysis was evaluated from day 0 (the time when therapeutic intervention for hyperkalemia was initiated).

Efficacy of SZC was considered to be the ability of treatment to quickly reduce serum potassium concentrations below 5.5 mEq/L and to have a non-inferior therapeutic effect compared to hemodialysis. Safety was defined as the absence of complications in each group. The absence of excessive reduction of serum potassium concentration below 3.5 mEq/L was also an important safety factor.

Statistical analysis

Continuous variables are expressed as median and interquartile range, and categorical variables are expressed as number and percentage. Continuous variables were compared between the two groups using the Mann–Whitney U-test. Categorical variables were compared between the two groups using Fisher's exact test.

Changes in serum potassium, creatinine, and sodium chloride gap within each group were assessed by the Friedman test, and Bonferroni's multiple comparisons were used as a post hoc test. Factors associated with the development of fatal arrhythmias were assessed by logistic regression analysis. Survival time analysis comparing the two groups was performed with the log-rank test.

In all analyses, two-tailed $p < 0.05$ was considered statistically significant. Analyses were performed using R software version 3.5.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

A total of 21 patients with acute hyperkalemia were included. Fourteen of the 79 patients for whom we prescribed SZC met the requirements for urgent treatment and were considered to be in the SZC group. In the hemodialysis group, seven patients underwent hemodialysis for hyperkalemia, all of which were treated urgently on the same day of diagnosis. Five patients in the hemodialysis group did not receive SZC and were assigned to hemodialysis therapy because SZC was not reimbursed at that time, whereas other two patients in the hemodialysis group did not receive SZC despite SZC was clinically available at that time.

The baseline characteristics of these patients, which were collected just before the onset of acute hyperkalemia, are displayed in Table 1. The median age was 81 [77, 86] years, and 14 were males. All patients had G3a stage or higher CKD.

There were no significant differences in baseline characteristics between the two groups, including serum potassium and serum creatinine levels. Serum potassium levels were 5.0 [4.8, 5.5] mEq/L in the SZC group and 5.2 [4.8, 5.5] mEq/L in the hemodialysis group ($p = 0.82$). Serum creatinine levels were 2.13 [1.60, 3.14] mg/dL in the SZC group and 1.69 [1.38, 3.10] mg/dL in the hemodialysis group ($p = 0.60$). Only 4 patients (28.6%) of the SZC group and 1 patient (14.3%) of the hemodialysis group received nutritional guidance from a dietician for hyperkalemia ($p = 0.62$).

Clinical data at the onset of acute hyperkalemia

Clinical data during the therapeutic interventions are displayed in Table 2. Two patients in the SZC group and all patients in the hemodialysis group required hospitalization ($p < 0.001$). One patient in the SZC group and five patients in the hemodialysis group had complete atrioventricular block ($p = 0.035$). Two patients in the hemodialysis group eventually required a temporary pacemaker. All these arrhythmias were ameliorated after the correction of hyperkalemia. No patients required permanent pacemakers.

Serum potassium levels were 6.8 [6.3, 7.0] mEq/L in the SZC group and 8.0 [6.6, 8.3] mEq/L in the hemodialysis group ($p = 0.13$). Serum creatinine levels were 2.40 [2.14, 3.59] mg/dL in the SZC group and 4.77 [3.06, 5.61] mg/dL in the hemodialysis group ($p = 0.044$). In all patients, elevated creatinine was considered to be due to dehydration instead of congestion. While data on bicarbonate concentration for blood gas analysis were notably absent for a substantial number of patients in the SZC group, it is worth highlighting that there was no discernible disparity in the sodium chloride gap, an indicator suggestive of metabolic acidosis, when comparing the two cohorts. Urinary potassium excretion data were mostly missing in the SZC group; fractional excretion of potassium was 16.1 [11.3, 31.9] in the hemodialysis group and tended to be lower.

Therapeutic intervention

No patients had systemic/pulmonary congestion or uremia. In the SZC group, SZC was administered for 3 [2, 7] days on median, and the serum potassium level decreased significantly to 4.7 [4.4, 5.3] mEq/L ($p < 0.001$; Fig. 1A). Serum creatinine remained unchanged ($p = 0.07$; Fig. 1B). None of the patients discontinued taking SZC

Table 1 Baseline characteristics at outpatient visit before onset of hyperkalemia

Factor	SZC group (N = 14)	HD group (N = 7)	*p* value
Demographics			
Age (years old)	81 [77, 85]	82 [75, 87]	0.63
Men (number, %)	9 (64.3)	5 (71.4)	1
Body mass index (kg/m^2)	21.7 [19.4, 23.5]	21.6 [20.5, 24]	0.68
Permanent pacemaker implantation (number, %)	1 (7.1)	0 (0.0)	1
Comorbidity			
Hypertension (number, %)	11 (78.6)	6 (85.7)	1
Diabetes mellitus (number, %)	8 (57.1)	3 (42.9)	0.66
Chronic heart failure (number, %)	8 (57.1)	2 (28.6)	0.36
History of coronary intervention	5 (35.7)	2 (28.6)	1
Dementia (number, %)	2 (14.3)	1 (14.3)	1
CKD stage			0.92
G3a (number, %)	3 (21.4)	1 (14.3)	–
G3b (number, %)	1 (7.1)	1 (14.3)	–
G4 (number, %)	6 (42.9)	2 (28.6)	–
G5 (number, %)	4 (28.6)	3 (42.9)	–
Medication			
RAS inhibitors (number, %)	10 (71.4)	4 (57.1)	0.64
Mineralocorticoid receptor antagonist (number, %)	7 (50.0)	2 (28.6)	0.64
Loop diuretics (number, %)	9 (64.3)	5 (71.4)	1
Thiazide diuretics (number, %)	0 (0.0)	0 (0.0)	NA
Tolvaptan (number, %)	3 (21.4)	3 (42.9)	0.35
Insulin (number, %)	3 (21.4)	1 (14.3)	1
Dipeptidyl peptidase 4 inhibitor (number, %)	5 (35.7)	0 (0.0)	0.12
SGLT2 inhibitor (number, %)	3 (21.4)	0 (0.0)	0.52
Laboratory data			
Serum albumin (g/dL)	3.8 [3.3, 4.0]	3.7 [3.5, 3.0]	0.55
Serum urea nitrogen (mg/dL)	43.9 [27.9, 61.7]	40.6 [3, 46.5]	0.55
Serum creatinine (mg/dL)	2.13 [1.60, 3.14]	1.69 [1.38, 3.10]	0.60
eGFR (mL/min/1.73m^2)	21.4 [15.5, 31.3]	26.3 [16.3, 36.1]	0.65
Serum uric acid (mg/dL)	6.4 [5.0, 6.9]	6.6 [5.2, 9.5]	0.40
Serum sodium (mEq/L)	139 [137, 140]	140 [138, 140]	0.73
Serum chlorine (mEq/L)	105 [103, 106]	106 [103, 109]	0.52
Serum potassium (mEq/L)	5.0 [4.8, 5.5]	5.2 [4.8, 5.5]	0.82
Serum calcium (mg/dL)	8.6 [8.4, 9.4]	8.9 [8.8, 9.4]	0.27

Continuous variables are presented as median and interquartile. Categorical variables are presented as number and percentage. Continuous variables were compared between the two groups using Mann–Whitney U-test. Categorical variables were compared between the two groups using Fisher's exact test

CKD stage was defined as follows: G3a, eGFR of ≥ 45 and < 60 ml/min/1.73 m^2; stage G3b, eGFR of ≥ 30 and < 45 ml/min/1.73 m^2; stage 4, eGFR of ≥ 15 and < 30 ml/min/1.73 m^2; and stage 5, eGFR < 15 ml/min/1.73 m^2

CKD chronic kidney disease, *eGFR* estimated glomerular filtration rate, *HD* hemodialysis, *NA* not applicable, *RAS* renin–angiotensin system, *SGLT2* Sodium–glucose cotransporter 2; and SZC, sodium zirconium cyclosilicate

until the first evaluation. No patients had hypokalemia or any other drug-related critical complications.

In the hemodialysis group, hemodialysis was performed at the day of admission to treat hyperkalemia instead of systemic/pulmonary congestion or uremia. All dialysis sessions for all patients were 3-h treatments using 0.9 square meters of cellulose triacetate membrane. The median Kt/V for urea calculated by Daugirdas method for the first hemodialysis session was 0.85 [0.69, 0.98]. Serum potassium decreased significantly down to 4.8 [4.4, 5.3] mEq/L on the next day ($p = 0.004$; Fig. 1A). Serum creatinine also decreased significantly to 2.84 [1.88, 3.55] ($p = 0.005$; Fig. 1B). Hemodialysis was performed 2 [1, 2] times during 6 [4, 6] days of hospitalization. There were no complications related to hemodialysis, such as allergic reactions, or complications related to the dialysis catheter

Table 2 Trajectory of clinical data between the two groups

Factor	SZC group (N = 14)	HD group (N = 7)	*p* value
Data at the onset of acute hyperkalemia			
Urgent hospitalization (number, %)	2 (14.3)	7 (100.0)	< 0.001*
Electrocardiogram (number, %)	10 (71.4)	7 (100.0)	0.25
Complete atrioventricular block (number, %)	1 (10.0)	5 (71.4)	0.035*
Temporary pacemaker insertion (number, %)	0 (0.0)	2 (28.6)	0.10
Serum creatinine (mg/dL)	2.60 [1.96, 3.06]	4.77 [3.06, 5.61]	0.044*
Serum potassium (mEq/L)	6.8 [6.3, 7.0]	8.0 [6.6, 8.3]	0.13
Serum sodium chloride gap (mEq/L)	31 [26, 33]	34 [30, 35]	0.29
Hyperkalemia treatment other than SZC or HD (number, %)	2 (14.3)	4 (57.1)	0.12
Therapeutic duration (days)	3 [2, 7]	1 [1]	0.0026*
Post-treatment data			
Serum creatinine (mg/dL)	2.40 [2.14, 3.59]	2.84 [1.88, 3.55]	0.94
Serum potassium (mEq/L)	4.7 [4.4, 5.3]	4.8 [4.4, 5.3]	0.85
Serum sodium chloride gap (mEq/L)	32 [31, 35]	33 [33, 34]	0.82
Data at 3-month follow-up			
SZC use (number, %)	4 (30.8)	0 (0.0)	0.25
Other potassium adsorbent use (number, %)	6 (46.2)	3 (42.9)	1.00
Use of RAS inhibitors (number, %)	9 (64.2)	3 (42.8)	0.40
Use of mineralocorticoid receptor antagonist (number, %)	4 (28.6)	1 (14.3)	0.62
Serum creatinine (mg/dL)	2.22 [1.66, 3.27]	1.21 [1.00, 3.39]	0.27
Serum potassium (mEq/L)	4.8 [4.6, 4.9]	4.7 [4.5, 5.1]	0.93
Serum sodium chloride gap (mEq/L)	34 [32, 37]	34 [33, 35]	0.83

Continuous variables are presented as median and interquartile. Categorical variables are presented as number and percentage. *$p < 0.05$ by Mann–Whitney U-test for continuous variables and Fisher's exact test for categorical variables

Hyperkalemia treatment other than SZC or HD includes furosemide infusion, calcium glucuronate infusion, and intravenous insulin therapy

Other potassium adsorbent includes calcium polystyrene sulfonate and sodium polystyrene sulfonate

Therapeutic duration is the number of days from the day after the onset of hyperkalemia until the first confirmed decrease in potassium

HD hemodialysis, *RAS* renin–angiotensin system, and *SZC* sodium zirconium cyclosilicate

insertion procedure, such as pneumothorax, bleeding, or infection.

At the initial post-treatment evaluation, all patients in both groups had serum potassium concentrations between 3.5 mEq/L and 5.4 mEq/L, and serum potassium levels were not significantly different in the two groups ($p = 0.85$, Table 2).

There was no difference in the prevalence of furosemide infusion, calcium gluconate infusion, or intravenous insulin therapy in addition to SZC therapy or hemodialysis ($p = 0.12$, Table 2). The sodium chloride gap increased significantly after treatment in the SZC group from 31 [26, 33] mEq/L to 32 [31, 35] mEq/L ($p = 0.008$), but did not change in the hemodialysis group ($p = 0.83$), resulting in no difference in the sodium chloride gap in the two groups after treatment ($p = 0.82$).

Factors associated with complete atrioventricular block

A total of six patients had complete atrioventricular block. Serum potassium concentration at onset and its change from baseline were significantly associated with the development of complete atrioventricular block in univariate analysis (odds ratio 6.54, 95% confidence interval 1.36–31.5, $p = 0.019$ and odds ratio 3.21, 95% confidence interval 1.07–9.62, $p = 0.037$, respectively, Table 3).

All complete atrioventricular block episodes improved by the first post-treatment evaluation, and the temporary pacemaker was promptly terminated.

Medical expense

We compared total medical expenses between the two groups as a primary outcome (Fig. 2). The total medical expenses of the SZC group were significantly lower than those of the hemodialysis group (55,596 [43,652, 69,761] versus 419,768 [354,270, 514,700] Japanese yen, $p = 0.004$). Similar trend was found among a subgroup without complete atrioventricular block (54,351 [42,704, 69,150] versus 675,815 [419,680, 931,950] Japanese yen, $p = 0.038$).

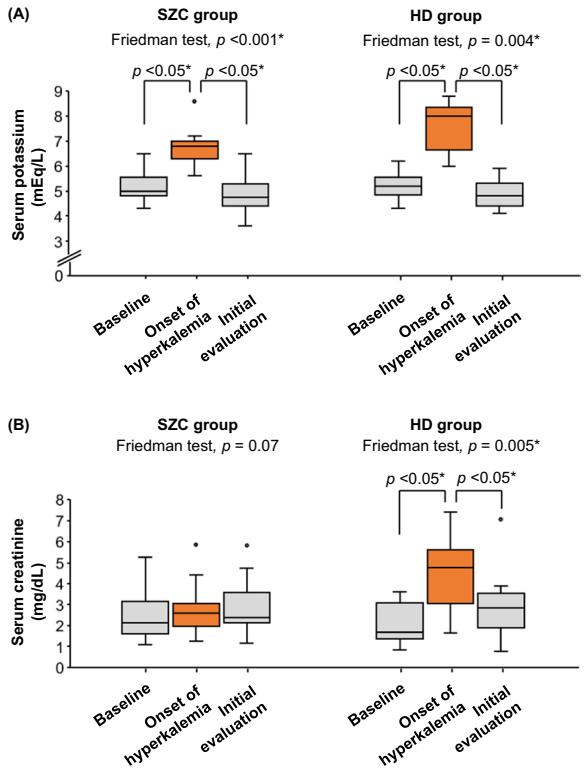

Fig. 1 Changes in serum potassium (**A**) and serum creatinine (**B**) concentrations before and after hyperkalemia treatment in the sodium zirconium cyclosilicate and hemodialysis groups. Continuous variables are presented as median and interquartile range. *$p < 0.05$ by Friedman test and by Bonferroni's multiple comparisons as a post hoc test. HD, hemodialysis and SZC, sodium zirconium cyclosilicate

Mid-term follow-up

After improvement in acute hyperkalemia in the SZC group, four patients continued SZC (Table 2). Of the other 10 patients, one patient discontinued it due to peripheral edema, and another patient switched to another potassium absorbent due to nausea, although the detailed causality between the drug and events remained uncertain. The remaining eight patients discontinued SZC due to normalization of serum potassium levels.

No patients had SZC in the hemodialysis group during and after hemodialysis. Three patients received another potassium adsorbent after hemodialysis. Eleven patients (78.6%) in the SZC group and 7 patients (100%) in the hemodialysis group received nutritional guidance after the onset of emergency hyperkalemia.

At the 3-month follow-up, serum potassium levels were 4.8 [4.6, 4.9] mEq/L and 4.7 [4.5, 5.1] mEq/L, respectively ($p = 0.93$). There was one patient in each group who had discontinued RAS inhibitors after 3 months. Patients were followed from the onset of acute hyperkalemia for 639 [377, 784] days on median. There was no significant difference in the composite survival rate for all-cause death and hemodialysis initiation between the two groups ($p = 0.56$; Fig. 3).

Discussion

In this retrospective study, we compared medical expenses, as well as safety and efficacy, between SZC therapy and hemodialysis in patients with acute hyperkalemia. All participants did not have congestion or uremia and received SZC therapy or hemodialysis to treat acute hyperkalemia. Most patients in the SZC group were managed at the outpatient clinic, whereas all hemodialysis was performed during hospitalization. Hyperkalemia improved immediately by SZC or hemodialysis in both groups, with serum potassium levels below 5.5 mEq/L and no procedure-related complications. Mid-term clinical outcomes were statistically comparable between the two interventions. Total medical expenses were significantly lower in the SZC group than in the hemodialysis group, even when we considered the cost of SZC itself in the SZC group.

Table 3 Logistic regression analysis for the development of complete atrioventricular block

Factor	Univariate analysis		Multivariate analysis	
	Odds ratio (95% confidence interval)	*p* value	Odds ratio (95% confidence interval)	*p* value
Age	1.06 (0.94–1.20)	0.34		
Men	0.36 (0.06–2.60)	0.31		
Serum creatinine at onset of hyperkalemia	0.98 (0.55–1.75)	0.94		
Change of serum creatinine	0.99 (0.53–1.85)	0.98		
Serum potassium at onset of hyperkalemia	6.54 (1.36–31.5)	0.019*	7.73 (0.46–128)	0.15
Change of potassium	3.21 (1.07–9.62)	0.037*	0.86 (0.12–6.12)	0.88

*$p < 0.05$ by logistic regression analysis

Change of serum creatinine was calculated as follows: [Serum creatinine at onset of hyperkalemia (mg/dL)]—[Serum creatinine at baseline (mg/dL)]

Change of serum potassium was calculated as follows: [Serum potassium at onset of hyperkalemia (mEq/L)]—[Serum potassium at baseline (mEq/L)]

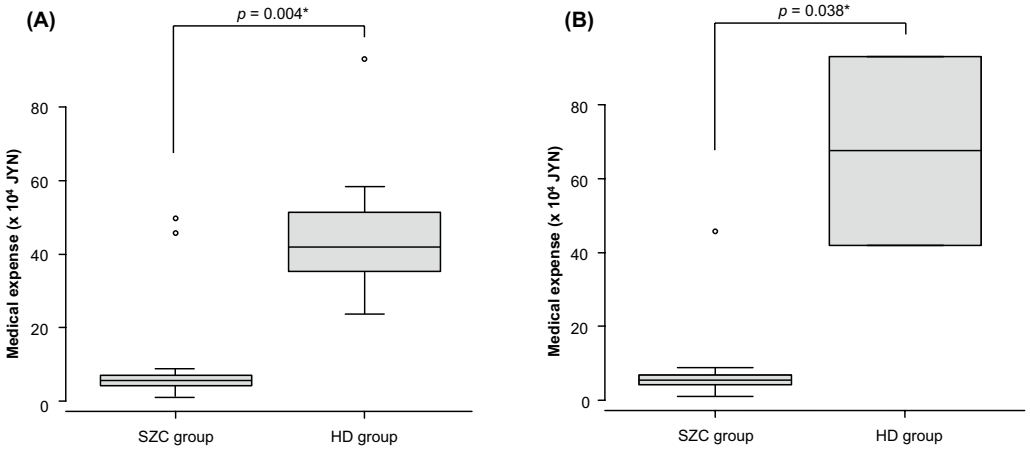

Fig. 2 Comparison of medical expenses between the sodium zirconium cyclosilicate and hemodialysis groups in all patients (**A**) and patients without complete atrioventricular block (**B**). Continuous variables are presented as median and interquartile range. *$p < 0.05$ by Mann–Whitney U-test. HD, hemodialysis; JYN, Japanese yen; and SZC, sodium zirconium cyclosilicate

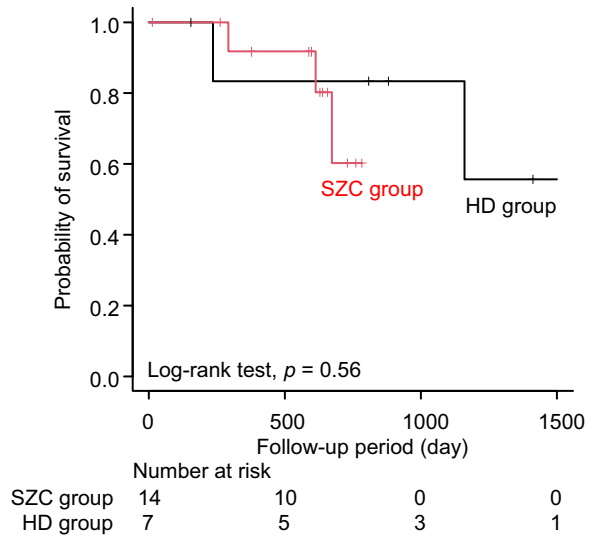

Fig. 3 Prognostic comparison between sodium zirconium cyclosilicate and hemodialysis groups. Log-rank test for survival from all-cause death and induction of hemodialysis. HD, hemodialysis and SZC, sodium zirconium cyclosilicate

Baseline characteristics and acute hyperkalemia

We included patients who required urgent intervention for acute hyperkalemia during the observation period. As expected, they were older, had advanced CKD, and had chronic hyperkalemia (serum potassium levels of approximately 5.0 mEq/L). Many patients received renin–angiotensin–aldosterone system inhibitors. These are well-known risk factors for acute hyperkalemia [3]. Despite the high risk of hyperkalemia, renin–angiotensin–aldosterone system inhibitors are recommended to be continued to protect the heart and kidney [11, 12]. Thus, urgent therapeutic intervention to immediately treat acute hyperkalemia is desired so far.

In a former survey, CKD patients rarely received adequate nutritional guidance [13]. In our cohort, patients received nutritional guidance only after experiencing severe hyperkalemia. Whether priority should be given to potassium adsorbents such as SZC or potassium-restricted diet in relation to other nutritional intake for chronic hyperkalemia is a subject for further study [14].

Several interventions have been attempted to treat acute hyperkalemia. Excretion of potassium is preferred for immediate and definite treatment of acute hyperkalemia instead of intracellular shift of potassium [3]. Thus, hemodialysis is the gold standard thus far, but it is associated with invasiveness, the requirement of specific clinical resources, the necessity of hospitalization, and high medical costs [4]. Given accumulating evidence on the safety and efficacy of SZC, a recently introduced selective potassium binder for the treatment of hyperkalemia, we compared clinical outcomes, including medical costs, between the two interventions.

Safety assessment between SZC and hemodialysis

No patients had drug-related adverse events that required drug termination during SZC therapy, including hypokalemia. In a randomized control trial, patients rarely encountered drug-related adverse events during SZC therapy, including digestive symptoms, peripheral edema, and hypokalemia [6]. Nevertheless, it is highly recommended to monitor serum potassium levels. In this study, we confirmed the normalization of serum potassium levels without hypokalemia at 3 [2, 7] days after the initiation of SZC therapy, even though most patients were managed at an outpatient clinic.

Hemodialysis patients are at risk for hypotension associated with extracorporeal circulation, allergy from exposure to drugs and dialyzers, bleeding from the use of anticoagulants, and blood loss and contamination from damage to circuit materials [15]. Central venous catheter placement also carries risks of bleeding, pneumothorax, and infection [16]. There were no such complications in our study. It is difficult to compare the risk of complications with SZC, but it is unlikely that the risk is smaller with hemodialysis.

Efficacy comparison between SZC and hemodialysis

SZC can improve hyperkalemia within 2 h with robust evidence [7]. The efficacy of SZC in improving hyperkalemia was greater than that of conventional polystyrene sulfonate [17]. Conventional potassium binders do not have any evidence to ameliorate hyperkalemia immediately [3]. Furthermore, these agents have several drug-related adverse events, including constipation and colon necrosis [18]. Another recently introduced potassium binder, patiromer, does not affect so immediately and may not be applicable to treating acute hyperkalemia [19]. The reliable serum potassium-lowering effect of SZC may be influenced not only by the potassium adsorption capacity of the drug but also by its acidosis improving effect, which promotes proton excretion into the intestinal tract [20].

Despite accumulating evidence that SZC immediately improves hyperkalemia, the indication of SZC in patients with hyperkalemia-related fatal arrhythmia is controversial. We preferred hemodialysis to SZC in patients with such arrhythmia in this study. However, the presence of complete atrioventricular block was associated with hyperkalemia instead of serum creatinine levels. SZC may be an alternative therapy in this clinical scenario, regardless of serum creatinine levels. In this clinical scenario, in-hospital monitoring of arrhythmia during SZC treatment may be preferred, as it allows for prompt initiation of hemodialysis when needed, compared to outpatient monitoring.

Another concern is concomitant systemic congestion due to the progression of CKD. All participants in our study did not have congestion, but it should be a definite indication of hemodialysis instead of SZC therapy.

Comparison in medical expense between SZC and hemodialysis

We compared medical expenses between SZC and hemodialysis for acute hyperkalemia for the first time. The medical expense of SZC therapy was approximately 10% compared with that of hemodialysis, predominantly due to the costs for in-hospital management and hemodialysis procedures. Additionally, in another study, these were dominant contributors to higher medical expenses in patients with chronic hyperkalemia [21]. Given all together, SZC therapy may be encouraged in patients with acute hyperkalemia who do not have hyperkalemia-related arrhythmia or systemic congestion/uremia.

Limitations

This study consisted of a small sample size patient cohort. Given such a small sample size, statistical non-significance between the two groups does not necessarily represent "similarity." Given the small event number, we could not construct multivariable model in the logistic analysis. This is a proof-of-concept and is not a trial to prove non-inferior between SZC therapy and hemodialysis therapy. Further studies are warranted to validate our findings. Due to the small number of cases, the hemodialysis group had to include patients prior to 2020, but the treatment of emergency hyperkalemia was deemed comparable because there have been no major changes in the past decade other than the availability of SZC. We excluded patients with systemic congestion/uremia, which is a definite indication of hemodialysis. Thus, we attempted our best to minimize selection bias. In the hemodialysis group, some patients received other potassium adsorbents after hemodialysis. We cannot compare the pure impact of both treatments on mid-term serum potassium levels.

Conclusions

Total medical expenses were significantly lower in the SZC group than in the hemodialysis group, and in our cohort, SZC therapy exhibited a comparable level of safety and effectiveness to hemodialysis in treating acute hyperkalemia. SZC therapy may be a promising alternative therapy to hemodialysis in treating acute hyperkalemia in carefully selected patients.

Acknowledgements

Not applicable.

Author contributions

HF treated patients, collected and analyzed data, and wrote the paper; TI designed the study and wrote the paper; SY, KKa, and HY treated patients; and TK and KKi were supervisors. Each author contributed important intellectual content during manuscript drafting and revision, agreed to be personally accountable for the individual's contributions, and to ensure questions about the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, is appropriately investigated and resolved. All authors read and approved the final manuscript.

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by our institutional review board (IRB approval number 27–162) and carried out following the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare that there is no conflict of interest.

Received: 28 September 2023 Accepted: 5 November 2023
Published online: 15 November 2023

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