

## Amount of Potassium Removed during Predilution Online Hemodiafiltration, with and without Glucose in Dialysate

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**Abstract:** The amount of potassium removed during a dialysis session depends on the potassium gradient between dialysate and blood, the duration of the session, the pH of the dialysate (bicarbonate content), and the presence or not of glucose in the dialysate. The last one, although theoretically known as a parameter that affects potassium removal during the dialysis session, is not known to what extent it affects. The aim of this study was to investigate how much potassium is lost with predilution online hemodiafiltration (with dialysate with or without glucose). We studied in 27 hemodialyzed patients the removal of potassium by a polyethersulfone dialyzer. Fourteen of them were males and the rest females. The median age of the patients was 73 years (range 54 - 93). They were on dialysis for  $83.2 \pm 87.6$  months (range 14 - 450). We investigate the removal of potassium by predilution online hemodiafiltration with glucose in dialysate (Group A) and without glucose (Group B). We noted significant lower amount of potassium removed in patients of group A in comparison with those in group B ( $28.3 \pm 18.6$  Vs  $38.1 \pm 22.4$  mmol,  $p < 0.02$ ). Of these patients, those who followed their diet meticulously ( $n=10$ ) and were consistent with the diet instructions had very little potassium loss/session (from 0 to 20 mEq), mainly in the first case (dialysate with glucose). It is highlighted that 9 patients of group A loss glucose during the session ( $6.4 \pm 4.7$  g/session, from 1.4 to 18.4). The amount of glucose removed during the dialysis session in group B was  $63.4 \pm 27.0$  g (from 13.3 to 133.4 g/session), along with some mild adverse events of hypoglycemia. It is concluded that the amount of potassium loss during predilution online hemodiafiltration with glucose in dialysate is significantly lower than the loss with dialysate without glucose. Also, in dialysis with glucose in dialysate, some patients lose glucose during the session, while with a glucose-free dialysate, quite significant amounts of glucose are lost (with the risk of hypoglycemia occurring).

**Keywords:** Serum Potassium, Predilution, Online Hemodiafiltration, Removed Potassium, Dialysate Glucose, Dialysate Potassium, Hypoglycemia.

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### Research Paper

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**How to cite this paper:**

Konstantinos S. Mavromatidis *et al* (2026). Amount of Potassium Removed during Predilution Online Hemodiafiltration, with and without Glucose in Dialysate. *Middle East Res J. Case Rep*, 6(1): 1-6.

**Article History:**

| Submit: 28.12.2025 |  
| Accepted: 29.01.2026 |  
| Published: 31.01.2026 |

## INTRODUCTION

Potassium is an important ion for hemodialyzed patients, which is mainly regulated through extrarenal clearance. It is present in many foods and dietary diversion, especially in our country, where it is very easy, mainly in the summer, to eat food which brings patients into life-threatening situations from hyperkalemia. Another parameter that also makes it difficult to achieve a good balance for potassium is the fact that this ion is

located intracellularly, which prevents its easy removal by dialysis.

However, because glucose in the dialysate theoretically plays a role in potassium kinetic, this randomized, prospective clinical trial was designed to investigate whether there is significant difference in the amount of potassium loss in relation to glucose in dialysate (with or without), determining the amount of potassium removed in the total ultrafiltrate during a

dialysis session of predilution online hemodiafiltration (HDF).

## PATIENTS - METHODS

### Patients

The potassium removal during predilution online HDF (with and without glucose in the dialysate) was studied in 27 chronic hemodialyzed patients. Patients >18 years of age, without diabetes mellitus, hemodynamically stable, with very good blood flow rate to the dialyzer (at least 400 ml/min), without active infections or cognitive impairment and able to provide written informed consent were included. Patients with significant liver, heart and lung dysfunction were excluded and excluded also patients who were taken of  $\beta$ -blockers or T<sub>4</sub>.

In the study included 27 patients (14M, 13F). The median age of the patients was 73 years (range 54 – 93). They were on dialysis for  $83.2 \pm 87.6$  months (range 14 - 450). The primary renal diseases were hypertensive glomerulosclerosis (7), polycystic kidney disease (4), glomerulonephritis (3), cardiorenal syndrome (3), obstructive nephropathy (1), lithium intoxication (1) and unknown cause (8). Fourteen had arteriovenous fistula, 1 had a vein graft (PTFE) and 12 had a double lumen jugular vein hemodialysis catheter. 6/25 had residual renal function (with less than 1000 ml urine/24h) with eGFR < 3 ml/min.

The study was completed at the “Dimokriton” Renal Unit of Komotini. It was approved by the Scientific Council of Komotini General Hospital (No. 6/2024, 04/08/2024) and was conducted in accordance with the Declaration of Helsinki and the Guidelines for Ethics in Medical and Health Research Involving Humans. Written consent for participation was obtained from each patient, after being informed about the study and its purpose.

### Methods

Each patient underwent one session of predilution online HDF, with glucose in dialysate (Group A) and another one a week later with dialysate without glucose (Group B) on midweek days (Wednesday or Thursday). Serum potassium, urea and glucose levels were determined in blood samples which were taken before and after the end of the dialysis session (the last one was taken after reducing the blood pump to 50 ml/min for two minutes) from the arterial fistula or arterial catheter line, to determine the differences between them, but also the serum urea levels for Kt/V and Urea Reduction Ratio (URR) determination. The amount of potassium, urea and glucose removing was determined by collecting all the ultrafiltrate during each dialysis session.

In all patients, low molecular weight heparin (vemparin) was used as an anticoagulant agent for

dialysis needs, at doses of 2,500-3,500 IU/session, depending on their dry body weight. The blood flow (pump) was 400 ml/min for all patients in each session (with negative pressure <200 mmHg) and the dialysate flow was 500 ml/min (the dialysis machines were Nikkiso DBB EXA). In all patients the dialysate bicarbonates were 33 mmol/L, sodium 140 mmol/L, potassium 3 mmol/L, chloride 110 mmol/L, magnesium 0.50 mmol/L calcium 1.5 mmol/L, acetate 3 mmol/L, while glucose was 5.6 mmol/L in group A and 0 in group B. For all patients, the duration of the session was four hours. No patient ate during the dialysis session.

Polyethersulfone-polynephron dialyzers (Elisio™ Nipro 2.1 m<sup>2</sup> high flux) were used in all patients. The substitution volume used in online HDF was 50% of the pump (i.e.  $\geq 48$  L/session). The ultrafiltrate was collected in a specially constructed, volumetric barrel, where at the end of the session it was stirred well with an electric stirrer for 10 minutes and then a sample was taken for urea, glucose and potassium determination.

For the determination of potassium in the ultrafiltrate, a modified equation of Blumberg *et al.*, was used:  $[K_{\text{Ultrafiltrate}} (\text{mmol}) = V_{\text{Ultrafiltrate}} (\text{ml}) \times K_{\text{Ultrafiltrate}} (\text{mmol}) - V_{(\text{Dialysate} + \text{Substitution volume})} (\text{ml}) \times K_{\text{Dialysate}} (\text{mmol})]$  [1]. More specifically, the potassium of the ultrafiltrate was calculated from the equation:  $168 \text{ L} [120 \text{ L of dialysate} + 48 \text{ L of substitution fluid}] \times 3 = 504 \text{ mEq/4-hour session}$ . For the laboratory exams of the parameters studied, the Abbott Alinity C analyzer was used. Urea and glucose were determined by an enzymatic method, while potassium by an ion-selective electrode.

### Statistical Analysis

Continuous variables were expressed as mean  $\pm$  standard deviation or median, according to normality of the distribution of each variable. Comparisons between the groups were performed using t-test for dependent parameters. The analysis was conducted with the Statistical software SPSS (version 30). Probability values of  $p < 0.05$  were considered statistically significant for all comparisons.

## RESULTS

The variables of serum potassium levels follow a normal distribution (Kolmogorov-Smirnov). Regarding the amount of potassium loss, a statistically significant lower was noted in Group A compared to Group B ( $28.3 \pm 18.6$  Vs  $38.1 \pm 22.4$  mmol/session,  $p < 0.02$ ). The patients' Kt/V was  $1.85 \pm 0.32$  (range 1.23 to 2.40), while the URR was  $79.5 \pm 5.8$  (range 65.4 to 88.4%) (Table 1). Nine patients in group A had glucose loss during the session  $6.4 \pm 4.7$  g (from 1.42 to 18.4 g), while glucose loss in group B during the session was  $63.4 \pm 27$  g (from 13.3 to 133.4 g). During the study in group B, the only side effect recorded was hypoglycemia symptoms (sweating, tachycardia, cold palms) in three patients,

which was confirmed in all cases by serum glucose levels, while found to be lower than 50 mg/dl and all

cases treated with intravenous administration of 35% glucose solution.

**Table 1: Contains pre and post dialysis session serum potassium levels, the amount of potassium and glucose removed during the session, as well as Kt/V and URR, in group A and B**

n	Predilution online HDF with glucose in dialysate (Group A)						Predilution online HDF glucose-free dialysate (Group B)			
	K <sup>+</sup> before session (mmol/L)	K <sup>+</sup> end of session (mmol/L)	Removed amount of K <sup>+</sup> (mmol)	Removed amount of glucose (g)	Kt/V	URR	K <sup>+</sup> before session (mmol/L)	K <sup>+</sup> end of session (mmol/L)	Removed amount of K <sup>+</sup> (mmol)	Removed amount of glucose (g)
1	5.5	4.5	39.4	5.19	1.44	72.0	4.8	4.3	37	52.4
2	6.9	4.0	57.0	7.10	1.94	80.6	7.1	4.5	75.7	54.6
3	5.6	3.1	23.0	2.10	2.48	88.4	5.8	3.8	37	49.1
4	5.0	3.5	34	18.48	2.30	86.4	5.0	3.7	40	61.2
5	4.8	4.2	23	44.90	2.02	82.6	5.1	3.9	54.4	59.2
6	4.8	3.9	6.0	-18.40	1.86	81.2	4.9	3.8	23	59.5
7	4.3	4.0	40	10.50	1.39	70.2	4.1	3.8	23	68.0
8	5.8	4.0	57	-8.20	2.05	82.2	5.0	4.3	40	56.1
9	6.4	4.0	60	-5.50	1.67	76.7	6.3	4.5	74	37.4
10	4.9	4.0	26.1	9.84	1.33	69.4	5.2	4.1	40	45.9
11	4.0	3.5	10	104.4	2.13	84.0	3.8	3.8	1.5	13.3
12	5.1	3.8	40	2.0	1.87	84.8	5.0	4.1	35.2	25.3
13	5.5	3.9	38.4	82.86	1.46	73.3	5.5	3.8	43.2	133.4
14	4.4	3.7	17	23.52	1.76	82.2	4.0	4.1	53	77.0
15	5.1	3.5	24	-3.10	1.88	79.9	4.8	3.6	19	76.0
16	6.6	4.1	58.3	4.10	1.75	77.9	6.4	4.7	91	59.5
17	5.0	4.1	6.0	7.10	1.43	71.4	4.3	3.9	6.0	61.
18	5.0	3.9	40	29.20	1.88	79.4	4.7	3.8	39.4	64.2
19	3.9	3.5	3.0	-5.76	1.95	82.0	4.0	3.3	20	55.8
20	3.9	3.6	3.0	-7.45	1.99	82.3	5.2	4.2	57	76.5
21	3.3	3.3	20	83.81	1.71	77.5	3.1	3.5	4.5	123.7
22	6.5	4.1	55	20.15	2.13	84.1	5.8	4.1	57	44.2
23	4.3	3.4	3.0	78.74	1.23	65.4	4.7	3.6	0	117.6
24	5.2	4.3	23	-5.0	1.87	80.2	6.1	4.4	58.3	93.7
25	4.3	3.6	0.6	-1.42	2.18	84.9	4.7	4.0	40	40.8
26	5.0	3.6	23	8.80	2.40	87.7	5.3	4.4	39	59.4
27	5.3	3.7	34	-3.16	1.88	80.8	4.7	3.8	20.5	45.7
p	5.05±0.86 (3.3-6.9)	3.80±0.32 (3.1-4.5)	28.3±18.6 (0.6-60) (A-B) <0.02	9 patients' loss: 6.4±4.7 g/session	1.85±0.32 (1.23-2.4)	79.5±5.8 (65.4-88.4)	5.01±0.86 (3.1-7.1)	3.99±0.33 (3.3-4.7)	38.1±22.4 (0-91)	63.4±27 (13.3-133.4)

## DISCUSSION

In the usual Western diet, the daily intake of potassium in normal people ranges from 100 - 120 mmol, where 92% and 8% are eliminated with urine and feces, respectively, to maintain homeostasis in the body. However, balance is achieved without hyperkalemia being detected, even with 10 times the potassium intake, when renal function is normal [2]. On the other hand, in

hemodialyzed patients it is recommended, a potassium diet of only 51 - 77 mmol/24 hours (2-3 g/24 hours) [3].

Conventional hemodialysis, among others, removes the potassium that accumulates in the interval between two dialysis sessions to prevent the occurrence of severe hyperkalemia before the next session, but also to prevent severe hypokalemia during and after the end of the dialysis session [1-4]. The guidelines do not

currently provide recommendations regarding the prescription of dialysate potassium, however some nephrologists apply the "rule of 7", in which the sum of the patient's serum and dialysate potassium concentrations should be approximately 7 mmol/L [5], although there are limited data to support this rule.

From studies with hemodialyzed patients, it has been found that the potassium removed in one dialysis session of conventional hemodialysis is just lower of 100 mmol [6], or slightly more than this amount as noted by investigators who used dialysate potassium of 1 mmol/L (which is not currently used or is used very rarely as it is dangerous) [1], i.e., much more than that of the extracellular space which constitutes the 1/3 of body fluids, and which contains approximately 4-5 mmol/L (i.e. for a man weighing 70 kg with 14 liters extracellular fluids is  $14 \times 4 = 56$  or  $14 \times 5 = 70$  mmol). Also, in this study it is worth noting that the investigators studied 14 hemodialyzed patients with hyperkalemia (serum potassium  $>5.5$  mmol/L). Of their patients, who were not diabetic, 6 received atenolol at a dose of 25-50 mg/24 hours ( $\beta$ -adrenergic blockers inhibit the entry of potassium intracellular and, in cases of renal failure, can contribute to the development of hyperkalemia) and their patients ate during the session (which may affect their serum insulin and potassium distribution). This means that this study cannot be compared with ours, as regards the amount of potassium removed in one dialysis session, where in addition to these differences, we studied our patients and the differences in the removed potassium in a predilution HDF session and not in conventional hemodialysis, which is likely to remove a higher amount of potassium than conventional hemodialysis [7].

The available literature data on the amount of potassium removed in a conventional hemodialysis session is limited. Ward *et al.*, were the first to study 12 hemodialyzed patients (4 were diabetic, 2 of whom were receiving insulin, which, as is known, is responsible for hyperkalemia when they have uncontrolled diabetes). The duration of the sessions was 4.0 - 4.5 hours; the filter surface area was  $1 \text{ m}^2$  and the blood flow was 200 ml/min. The potassium of the dialysate was 2 or 3 mmol/L depending on the patient's needs. The study was carried out, among other things, with glucose (11 mmol/L) or without glucose (0 mmol/L) in the dialysate. In those without glucose in the dialysate, they found a glucose loss of  $30.0 \pm 92$  g. Finally, they found a greater loss of potassium with the dialysate without glucose in comparison with dialysate with glucose ( $72.0 \pm 26.4$  Vs  $54.5 \pm 24.1$  mmol,  $p=0.0358$ ), a quantity that was a little smaller than what we found in this study [8]. On the other hand, Zehnder *et al.*, in 12 stabilized hemodialyzed patients, found that with a dialysate potassium of 2 mmol/L and without glucose,  $63.3 \pm 5.2$  mmol of potassium were lost in 4 hours (the filter used has surface of  $1.8 \text{ m}^2$ , the blood pump was 300 ml/min, the dialysate pump 500 ml/min and the bicarbonates of dialysate 40 mmol/L) [9]. Although these data agree to some extent

with ours, there are significant differences, such as in the study by Ward *et al.*, the use of insulin (which affects the distribution of potassium), the potassium of the dialysate during the sessions (which was not the same for everyone), in the dialysis conditions (they had  $1 \text{ m}^2$  filters and a blood flow of 200 ml/min, compared to those used today and which we also applied), so it is impossible to transfer the data from that time to today [8]. Accordingly, in the study by Zehnder *et al.*, they used a dialysate potassium of 2 mmol/L, i.e. lower than ours, which obviously affects the removal of potassium by the dialyzer [9].

The exchange mechanisms of potassium between the intra- and extra-cellular space plays a central role in its removal during the dialysis session. The movement of potassium through the cell membrane takes place by passive diffusion from the intracellular to extracellular compartment and in the opposite direction with the action of the  $\text{Na}^+\text{-K}^+\text{-ATPase}$  (active transport). The activity of this pump depends mainly on the extracellular concentration of potassium, which changes significantly during the dialysis session.

Other metabolic variables that may affect the movement of potassium between intracellular and extracellular space are the rapid correction of acid-base balance (change of acidemia to alkalemia) [10, 11], entering potassium intracellularly. Dialysate bicarbonates when elevated is known to enhance  $\text{Na}^+\text{-K}^+\text{-ATPase}$  activity, resulting in the movement of higher amounts of extracellular potassium into the intracellular space, although this process was found not to affect significantly the total amount of potassium removed during the dialysis session (despite total removal was  $116.4 \pm 21.6$  mmol/session for low bicarbonate dialysate and  $73.2 \pm 12.8$  mmol/session for standard dialysate bicarbonates) [12]. This parameter, of course, did not affect the results of our study, since the dialysate bicarbonates were the same in both cases (with and without glucose in dialysate). In normal, healthy adults, increased serum bicarbonate levels have been associated with markers that reflect higher insulin sensitivity [13]. On the other hand, it should also not be forgotten that the increase of intracellular bicarbonates (as occurs during the hemodialysis session) favors the entry of glucose into the cells and its consumption [14], which may explain the hypoglycemia experienced by some patients in group B during the session, but not in all of them.

It is known that dialysis with glucose-free dialysate is associated with a decrease in insulin levels [8], by approximately 50% when the dialysate glucose is reduced from 11 to 0 mmol/L [15], and such a decrease in insulin is associated with an increase in serum potassium by 0.6 mmol/L [16]. As far as it concerns Sherman *et al.*, found in 8 hemodialyzed patients (who dialyzed with blood flow 200 ml/min, dialysate potassium 2.0 mmol/L, and dialysate glucose 0) increase of potassium removal by a mean of 28%, difference

which wasn't statistically significant ( $p=0.16$ ), in comparison to those with glucose 11 mmol/L in dialysate, who measured potassium in the total ultrafiltrate collected in a barrel [17]. Fischbach *et al.*, studied 5 non-diabetic children undergoing conventional hemodialysis with bicarbonate in dialysate (35 mmol/L), with 0 mmol/L potassium and with glucose 9.17 mmol/L or without glucose, in 3-hour sessions. They found in ultrafiltrate collection that the potassium loss did not differ between the session with glucose and without glucose (70 vs. 73 mmol/session) [18]. In our study, using predilution online HDF, we noted that the glucose in dialysate is associated with lower potassium removal compared to the glucose free dialysate. Also, in group A (with glucose in dialysate), some patients ( $n=9$ ) lose glucose during the session, and some ( $n=18$ ) gain, while with a glucose-free dialysate, quite significant amount of glucose was lost from all the patients (with the risk of hypoglycemia occurring) (Table 1). Probably this loss in group B justifies the greater loss of potassium, since those who lost glucose would obviously have lower levels of insulin (which normally moves potassium intracellularly and prevents its removal).

It is concluded that the potassium loss with predilution online HDF with glucose-free dialysate, is higher than that removed during dialysis session with glucose in dialysate. From the amount of glucose lost in patients without glucose in dialysate, it is obvious that the lower levels of insulin play an important role in the amount of potassium removed during dialysis. The adverse events of patients who underwent dialysis with a glucose-free dialysate were mild hypoglycemia in only three of them.

### Limitations

The study has been a relatively small number of patients, although the statistical significance of the differences were quite large. Also, C-peptide levels were also not measured to show the contribution of insulin to potassium removal during the dialysis session.

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