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" Impact of Dialysate Temperature on Interdialytic and Intradialytic Hypotension, Serum Potassium, and Dialysis Adequacy Among Hemodialysis Patients "

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ABSTRACT:

Background: Intradialytic hypotension (IDH) is a significant complication of hemodialysis, affecting patient outcomes and quality of life. Dialysate cooling has been proposed to mitigate IDH by stabilizing blood pressure and improving dialysis adequacy. This study aimed to evaluate the effects of cooling dialysate to 36°C and 35°C on dialysis adequacy, potassium levels, and intradialytic blood pressure stability.

Methods: This prospective single-center crossover study included 60 hemodialysis patients treated at Ezbet Al-Borg Dialysis Center, Damietta, Egypt, from January to June 2024. Participants underwent three study phases: a standard phase with a dialysate temperature of 37°C, followed by two cooling phases at 36°C and 35°C. Data collected included blood pressure measurements, dialysis adequacy parameters (Kt/V), and serum potassium levels. Statistical analyses utilized repeated measures ANOVA and Pearson correlation.

Results: Cooling dialysate to 35°C significantly improved Kt/V values (1.22 ± 0.2) compared to 37°C (1.14 ± 0.2, $p = 0.004$). In contrast, cooling to 36°C showed no significant effect. Serum potassium levels remained stable across phases. Intradialytic systolic and diastolic blood pressures were significantly higher during cooling phases, particularly at 35°C ($p < 0.001$). Positive correlations were observed between Kt/V and intradialytic and interdialytic blood pressures ($p < 0.001$).

Conclusion: Cooling dialysate to 35°C significantly improves dialysis adequacy and stabilizes intradialytic blood pressure without adverse effects on potassium levels. Personalized cooling protocols may optimize dialysis outcomes.

Keywords: Intradialytic hypotension, Dialysate cooling, Hemodialysis, Blood pressure, Dialysis adequacy.

Background:

Hemodialysis is a cornerstone therapy for patients with end-stage renal disease (ESRD), offering life-sustaining benefits through the removal of uremic toxins, excess fluid, and electrolytes. Despite its efficacy, the treatment is frequently accompanied by complications, most notably intradialytic hypotension (IDH). IDH, characterized by a symptomatic drop in systolic blood pressure during dialysis sessions, compromises tissue perfusion and increases the risk of ischemic injury to vital organs such as the heart and brain (Arghide et al., 2023; Elemshaty et al., 2023).

IDH arises from a complex interplay of factors, including ultrafiltration-induced hypovolemia, impaired vascular and autonomic responses, and reduced cardiac output. This hemodynamic instability is a barrier to achieving optimal dialysis efficiency and contributes to adverse patient outcomes (Khamis et al., 2024).

Dialysate cooling, involving the reduction of dialysate temperature below the standard 37°C, has emerged as a promising intervention to mitigate IDH. By reducing thermal energy transfer and preventing vasodilation, cooled dialysate supports vascular tone, myocardial contractility, and systemic vascular resistance (Rootjes et al., 2022; Sivasankari et al., 2019). Improved hemodynamic stability during dialysis may also enhance solute clearance and facilitate better treatment outcomes. Intradialytic hypotension (IDH) is a frequent and serious complication of hemodialysis, affecting a significant proportion of patients and posing challenges for achieving optimal therapeutic outcomes. Characterized by a drop in blood pressure during dialysis, IDH can lead to symptoms like dizziness, nausea, and muscle cramps. In severe cases, IDH can compromise vital organ perfusion, increasing the risk of myocardial or cerebral ischemia. Beyond its impact on patient well-being and quality of life, IDH also limits the effectiveness of ultrafiltration and dialysis adequacy, hindering the achievement of optimal therapeutic goals.

Dialysate cooling, involving the reduction of dialysate temperature below the standard 37°C, has emerged as a potential intervention to mitigate IDH. This technique aims to minimize thermal energy transfer to the patient, thereby preventing vasodilation and the associated decrease in systemic vascular resistance commonly observed during normothermic dialysis. By stabilizing vascular tone and supporting myocardial contractility, cooled dialysate can help maintain intradialytic blood pressure and enhance cardiovascular stability. This improved hemodynamic stability may contribute to increased patient tolerance to dialysis, potentially facilitating more effective fluid removal and better overall dialysis adequacy (Sivasankari et al., 2019; Sarbaz et al., 2019).

This study investigates the impact of cooling dialysate to 36°C and 35°C on dialysis adequacy, potassium levels, and blood pressure stability. Through a prospective crossover design, we aim to elucidate the optimal cooling protocol to improve patient outcomes.

Methods

Study Design and Population

This prospective, single-center crossover study was conducted at the Ezbet Al-Borg Dialysis Center in Damietta, Egypt, between January and June 2024. The study included 60 adult hemodialysis patients undergoing thrice-weekly treatment for at least six months.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Patients aged ≥18 years.
- Regular hemodialysis for at least six months.
- Stable interdialytic weight changes.

Exclusion Criteria:

- Acute intercurrent illness or hospital admission during the study.
- End-organ failure (e.g., heart or liver failure).
- Malignancies or significant noncompliance with dialysis schedules.
- Use of potassium-rich diets or medications affecting serum potassium.
- Fever or other systemic conditions**.**

Data Collection

Participants underwent three study phases:

1. **Standard Phase:** Dialysate temperature was set at 37°C for three months.
2. **Cooling Phase 1:** Dialysate temperature was reduced to 36°C for six weeks.
3. **Cooling Phase 2:** Dialysate temperature was further reduced to 35°C for six weeks.

During each phase, data collected included:

- **Dialysis adequacy parameters:** Kt/V, pre- and post-dialysis urea, and serum creatinine levels.
- **Blood pressure monitoring:** Hourly intradialytic measurements and interdialytic averages.
- **Laboratory tests:** Serum potassium, calcium, phosphate, and intact parathyroid **hormone levels.**

Statistical Analysis

Data were analyzed using SPSS software (version 27). Continuous variables were expressed as mean ± standard deviation or median (range), while categorical data were presented as percentages. Repeated measures ANOVA assessed within-group differences across study phases. Pearson correlation evaluated relationships between Kt/V and blood pressure parameters. A p-value <0.05 was considered statistically significant.

Results

A total of 60 patients with a mean age of 52.2 ± 11.9 years were included in the study. Males constituted 60% of the cohort (Table 1). The most common comorbidities were hypertension (75%), diabetes (20%), and hepatitis C infection (11.7%). Patients had been on hemodialysis for an average duration of 4.65 ± 0.6 years, with 75% of the patients using a left-sided arteriovenous fistula (AVF) (Table 2). Hypertensive nephropathy was the most prevalent cause of end-stage renal disease (ESRD) (46.7%), followed by cystic kidney disease (18.3%) and diabetic nephropathy (16.7%) (Table 2).

Laboratory findings revealed a mean pre-dialysis serum creatinine of 8.2 ± 2.1 mg/dL and a mean urea reduction ratio of 68.4 ± 9.7%. Intact parathyroid hormone (iPTH) levels varied widely, with a median value of 287 pg/mL. The mean hemoglobin level was 10.8 ± 1.2 g/dL, while the median ferritin level was 220 ng/dL. The mean albumin level was 3.6 ± 0.6 g/dL, and mean alanine aminotransferase (ALT) was 17.2 ± 6.9 IU/L (Table 3).

Cooling dialysate temperatures to 35°C (cooling phase 2) significantly improved Kt/v values compared to the standard phase (1.22 ± 0.2 vs. 1.14 ± 0.2, $p = 0.004$) (Table 5). Cooling phases did not result in significant differences in serum potassium levels between standard and cooling conditions ($p = 0.23$) (Table 4).

Blood pressure responses varied significantly between the phases. During the standard phase, systolic blood pressure (SBP) decreased progressively from pre-dialysis to the end of the session ($p < 0.001$). In contrast, SBP during cooling phases remained stable in phase 1 and increased significantly during phase 2 ($p < 0.001$) (Table 7). Diastolic blood pressure (DBP) during the standard phase also progressively decreased ($p < 0.001$), while it remained stable during cooling phase 1 and increased during cooling phase 2 (Table 5).

Mean intradialytic SBP and DBP were significantly higher during both cooling phases compared to the standard phase ($p < 0.001$), as were interdialytic pressures (Table 9). A strong positive correlation was observed between Kt/v and intradialytic SBP ($r = 0.9$, $p < 0.001$), as well as with interdialytic SBP ($r = 0.93$, $p < 0.001$) (Table 6).

Table (1): Demographics and associated medical disorders:

	Total cohort (n= 60 patients)
Age (years) Mean ±SD	52.2 ± 11.9
Sex No. (%) - Male - Female	 36 (60%) 24 (40%)
Diabetes No. (%)	12 (20%)
Hypertension No. (%)	45 (75%)
Ischemic heart disease No. (%)	2 (3.3%)
Hepatitis C infection	7 (11.7%)

Table (2): Dialysis related data among the included patients:

	Total cohort (n= 60 patients)
Dialysis duration (years) Mean ± SD	4.65 ± 0.6
Side of A- v fistula No. (%) - Left - Right	 45 (75%) 15 (25%)
Ultrafiltration rate (L/session) Mean ± SD	2.5 ± 0.9
Causes of end- stage kidney disease No. (%) - Hypertensive nephropathy - Diabetic nephropathy - Autoimmune disease - Pre- eclampsia - Analgesic nephropathy - Cystic kidney disease - Congenital solitary kidney	 28 (46.7%) 10 (16.7%) 3 (5%) 4 (6.7%) 2 (3.3%) 11 (18.3%) 2 (3.3%)

Table (3): Laboratory findings of the included patients:

	Total cohort (n= 60 patients) Mean ± SD
Dialysis adequacy	
Pre- dialysis s. creatinine (mg/dL)	8.2 ± 2.1
Pre- dialysis urea (mg/dL)	125 ± 23.8
Post- dialysis urea(mg/dL)	52.4 ± 12.5
Urea reduction ratio (%)	68.4 ± 9.7
Kt/ v	1.1 ± 0.18
Mineral bone disease parameters	
Intact PTH (pg/mL) Median (min, max)	287 (4.5, 1862)
Total calcium (mg/dL)	8.8 ± 1.2
Ionized Calcium (mg/dL)	4.2 ± 0.6
Phosphate (mg/dL)	5.6 ± 1.9
Anemia parameters	
Hemoglobin (g/dL)	10.8 ± 1.2
Ferritin (ng/dL) Median (min, max)	220 (6.4, 1482)
Others	
Albumin (g/dL)	3.6 ± 0.3
Alanine aminotransferase (IU/L)	17.2 ± 6.9

iPTH: intact Parathormone hormone.

Table (4): Effect of cooling on potassium:

	Serum potassium (mEq/L) Mean ± SD
Standard phase	3.9 ± 0.08
Cooling phase 1	3.88 ± 0.14
Cooling phase 2	3.86 ± 0.12
F	1.5
Effect size	0.013
P value	0.23

(F) Repeated measures analysis of variance (ANOVA) test. Level of significance < 0.05

Table (5): Fluctuation of diastolic blood pressure differences during standard phase, cooling 1 and cooling 2 phases:

	Pre- dialysis	After 1 hour	After 2 hours	After 3 hours	At the end of the session	F/ effect size	P value
Standard phase	79.3 ± 3.6	77.9 ± 2.9 a	76.9 ± 4.8 a	74.6 ± 4.4 a, b, c	73 ± 5.2 a, b, c, d	60.8/0.2	***<0.001***
Cooling phase 1	78 ± 6.2	79 ± 2.3	79.4 ± 2.3	79.8 ± 2.4	79.7 ± 2.3	2.1/0.03	0.06
Cooling phase 2	77.7 ± 6.1	79.7 ± 6.7 a	79.6 ± 3.4 a	79.7 ± 3.7 a	80 ± 3.7 a, c, d	3.7/0.03	***0.006***

(F) Repeated measures analysis of variance (ANOVA) test. (a) Significance against pre- dialysis < 0.05; (b) Significance after 1 hour < 0.05; (c) Significance against after 2 hours < 0.05; (d) Significance against after 3 hours < 0.05; Level of significance < 0.05

Table (6): Correlation analysis between Kt/ v, average intradialytic blood pressure and inter- dialytic blood pressure including all phases:

	(r)	P value
Systolic intradialytic pressure	0.9	***<0.001***
Diastolic intradialytic pressure	0.89	***<0.001***
Systolic inter- dialytic pressure	0.93	***<0.001***
Systolic inter- dialytic Pressure	0.88	***<0.001***

(r) Pearson correlation; Level of significance < 0.001

Discussion

Intradialytic hypotension (IDH) is a frequent and serious complication of hemodialysis, affecting a significant proportion of patients and posing challenges for achieving optimal therapeutic outcomes. Characterized by a drop in blood pressure during dialysis, IDH can lead to symptoms like dizziness, nausea, and muscle cramps. In severe cases, IDH can compromise vital organ perfusion, increasing the risk of myocardial or cerebral ischemia. Beyond its impact on patient well-being and quality of life, IDH also limits the effectiveness of ultrafiltration and dialysis adequacy, hindering the achievement of optimal therapeutic goals.

Dialysate cooling, involving the reduction of dialysate temperature below the standard 37°C, has emerged as a potential intervention to mitigate IDH. This technique aims to minimize thermal energy transfer to the patient, thereby preventing vasodilation and the associated decrease in systemic vascular resistance commonly observed during normothermic dialysis. By stabilizing vascular tone and supporting myocardial contractility, cooled dialysate can help maintain intradialytic blood pressure and enhance cardiovascular stability. This improved hemodynamic stability may contribute to increased patient tolerance to dialysis, potentially facilitating more effective fluid removal and better overall dialysis adequacy.

he present study investigated the effects of dialysate cooling on dialysis adequacy, potassium levels, and intra-dialytic blood pressure fluctuations in 60 hemodialysis patients receiving treatment three times a week at the Ezbet Al-borg Dialysis Center in Damietta, Egypt. The patients, with a mean age of 52.2 ± 11.9 years, underwent three distinct phases: a standard phase with a dialysate temperature of 37°C for three months, followed by two cooling phases with dialysate temperatures of 36°C and 35°C, each lasting for six weeks. During each phase, blood pressure monitoring, dialysis adequacy assessment using Kt/v, and post-dialysis potassium measurements were performed.

The study's findings revealed that cooling the dialysate to 35°C for six weeks significantly improved dialysis adequacy as reflected by Kt/v (standard vs. 35°C cooling: 1.14 ± 0.2 vs. 1.22 ± 0.2; $p= 0.004$). This observation aligns with previous research demonstrating the positive impact of dialysate cooling on dialysis adequacy. For instance, Sivasankari et al. (2019) reported significant improvements in both urea reduction ratio (URR) and Kt/v with dialysate cooling to 35°C. Similarly, Sarbaz et al. (2019) and Borzou et al. (2015) found significant enhancements in Kt/v with cooled dialysate compared to standard dialysis.

However, it is essential to acknowledge that the literature presents conflicting findings regarding the impact of dialysate cooling on dialysis adequacy. Some studies, including those by Mathew et al. (2024), Ahmadi et al. (2023), and Khamis et al. (2021), did not observe a significant effect of dialysate cooling on dialysis adequacy measures such as Kt/v and URR. These discrepancies might be attributed to variations in study methodologies, patient populations, and the duration of the cooling phases. Notably, Khamis et al. (2021) highlighted that the sequence of cooling and standard phases could influence Kt/v measurements, as they did not assess Kt/v before initiating the cooling phase.

Furthermore, several studies, including two systematic reviews, have concluded that cold dialysis does not significantly alter blood volume, urea rebound, or the effective Kt/V index, suggesting that dialysis efficiency remains unchanged. This perspective stems from the vasoconstriction induced by cold dialysis, which was initially hypothesized to reduce dialysis efficiency indices due to increased urea compartmentalization and a heightened post-dialysis rebound effect (Mustafa et al., 2016; Selby & McIntyre, 2006).

In the present study, both cooling temperatures (36°C and 35°C) led to significant improvements in intradialytic blood pressure compared to the standard dialysate temperature ($p< 0.001$). Cooling to 36°C effectively maintained stable blood pressure throughout the dialysis session, with no significant changes in mean systolic and diastolic blood pressures. However, cooling to 35°C resulted in a significant elevation of both systolic and diastolic blood pressure at the end of the session. In contrast, during the standard phase, systolic and diastolic blood pressure measurements showed a significant decline over the course of the dialysis session. These findings align with previous research supporting the beneficial effects of dialysate cooling on intradialytic blood pressure (Mathew et al., 2024; Ahmadi et al., 2023; Elemshaty et al., 2023).

Numerous studies have reported similar improvements in intradialytic blood pressure with cooled dialysate. Mathew et al. (2024) observed significantly higher intradialytic systolic and diastolic blood pressure at the third hour of dialysis with cooled dialysate. Ahmadi et al. (2023) demonstrated a significant positive effect of cooled dialysate on hourly measurements of intradialytic systolic and diastolic blood pressures. Similarly, Elemshaty et al. (2023), Elpasiony et al. (2022), and Elsayyad et al. (2021) reported significant reductions in intradialytic hypotension after dialysate cooling. Moreover, a meta-analysis conducted by Mustafa et al. (2016), which included 17 clinical trials, revealed a substantial 70% reduction (95% confidence interval [95% CI], 49% to 89%) in the rate of intradialytic hypotension with cool dialysis compared to standard dialysis ($p < 0.001$).

These findings underscore the potential of dialysate cooling as an effective strategy to mitigate IDH and improve hemodynamic stability during dialysis. However, similar to the findings on dialysis adequacy, the literature also presents conflicting results regarding the impact of dialysate cooling on intradialytic blood pressure. Some studies, such as those by Arghide et al. (2023), Khamis et al. (2021), and Cha et al. (2017), did not find significant differences in intradialytic blood pressure between cooled and standard dialysate.

These inconsistencies further highlight the need for more comprehensive and robust research to definitively establish the effects of dialysate cooling on blood pressure control during dialysis. The present study also investigated the impact of dialysate cooling on blood pressure at the end of the dialysis session. The results demonstrated that cooling dialysate to 35°C had a significant positive impact on systolic blood pressure at the session's end ($p < 0.001$), effectively countering the significant decrease in both systolic and diastolic blood pressure observed during the standard phase. This finding aligns with previous studies that have reported higher post-dialysis blood pressure with dialysate cooling. Mathew et al. (2024), Ahmadi et al. (2023), and Elsayyad et al. (2021) all observed significantly higher blood pressure at the end of the dialysis session with cooled dialysate compared to the standard phase.

Furthermore, the present study revealed a significant positive effect of dialysate cooling on average inter-dialytic blood pressure, which was significantly higher during both cooling phases compared to the standard phase ($p < 0.001$). This observation is consistent with previous research demonstrating the positive impact of dialysate cooling on interdialytic blood pressure. Elsayyad et al. (2021), Azar (2009), and Ayoub et al. (2004) all reported significantly higher inter-dialytic blood pressure in patients receiving cooled dialysate compared

Finally, this study found a significant positive correlation between average intra- and inter-dialytic blood pressure and average Kt/v, suggesting that maintaining stable blood pressure during dialysis can contribute to improved dialysis adequacy. This finding is supported by Uduagbamen et al. (2021) , who reported that intradialytic hypotension was associated with significantly lower Kt/v. However, conflicting evidence exists, as Khamis et al. (2021) and Tayyebi et al. (2012) did not find significant correlations between blood pressure and Kt/v during dialysis.

In conclusion, the present study provides further evidence supporting the potential benefits of dialysate cooling in hemodialysis patients. Cooling the dialysate to 35°C was associated with significant improvements in dialysis adequacy, intradialytic blood pressure stability, and interdialytic blood pressure control. However, it is crucial to acknowledge the presence of conflicting findings in the literature regarding the effects of dialysate cooling on both dialysis adequacy and blood pressure control. These inconsistencies may stem from variations in study design, patient characteristics, and the duration of cooling interventions. Future research should focus on addressing these discrepancies and establishing clear guidelines for the optimal implementation of dialysate cooling in clinical practice.

Moreover, further investigation is needed to comprehensively evaluate the long-term effects of dialysate cooling on cardiovascular outcomes, patient quality of life, and survival. While the present study did not assess adverse events related to dialysate cooling or explore its long-term impacts, these aspects are crucial for determining the overall safety and efficacy of this intervention. By conducting more robust and comprehensive research, the potential of dialysate cooling as a valuable tool to enhance the safety, efficacy, and patient experience of hemodialysis can be fully realized.

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