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Original article

# Short-term Individualized Dialysate Cooling in Chronic Hemodialysis: Therapeutic benefits for Patients and A favorite choice for Nephrologists

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## ABSTRACT

**Background:** Intra-dialytic hypotension (IDH) and pruritus are frequent and distressing complications during hemodialysis; moreover, they are associated with adverse outcomes.

**The aim of the work**: The current work aimed to investigate the effect of applying individualized cool dialysate (ICD) on IDH, dialysis adequacy, pruritus and its acceptance by both patient and nephrologists.

**Patients and Methods**: This is a non-randomized single center study that was conducted at Al-Azher nephrology and dialysis unit. The study was carried out over a period of fvie weeks. Core body temperature (CBT) and dialysis adequacy (by Kt/v) were measured. Patients who fulfilled the inclusion and exclusion criteria underwent hemodialysis for six consecutive sessions at dialysate temperature of 37°C, followed by another six consecutive sessions at ICD temperature (0.5 °C below CBT). Blood pressure (BP) measurements, episodes of hypotension, pruritus score, patients and nephrologist questionnaire were collected during both standard and cool phases.

**Results:** The study included 50 patients, the mean age 51.10±11.57 years, and males constituted 64% . The implementation of ICD has been associated with a significant reduction in IDH episodes ($p<0.001$). The lowest intra-dialytic and post-dialytic BP measurements were statistically higher during cool phase. There was a significant reduction in pruritus VAS score during cool phase ($p<0.001$), whereas Kt/v and ultrafiltration rate did not statistically differ between both phases. ICD was well tolerated by patients; although 60% of them experienced cold sensation that warranted no intervention. Nephrologists (n=20) trusted in cool dialysate as an effective intervention for IDH management. However, a proportion of them (60%) had a concern about patient tolerability.

**Conclusion**: ICD is a well-tolerated intervention that is universally applied without additional cost. It improves hemodynamic instability and pruritus during hemodialysis treatment without negative impact on dialysis adequacy. It is accepted by nephrologists as an effective tool in stabilizing hemodynamic instability during dialysis treatment.

**Keywords:** Cool; Hemodialysis; Hypotension; Pruritus; Adequacy.



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* Main subject and any subcategories have been classified according to the research topic.

## INTRODUCTION

End stage renal disease (ESRD) is an irreversible decline of the kidney function that may be fatal in the absence of renal replacement therapy [1].

One of the fundamental challenges in hemodialysis care is to minimize the risk of complications, and adverse events during and after dialysis sessions. This can be achieved through providing sufficient dialysis, maintaining vascular access, encouraging adequate nutrition, achieving optimal volume status, avoiding intra-dialytic hypotension or hypertension, minimizing hospitalization and, improving the quality of life [2].

Intra-dialytic hypotension is one of the common complications during hemodialysis, and is associated with a series of cumulative multisystem ischemic insults, which ultimately lead to end-organ dysfunction; such as arrhythmias, congestive heart failure, cognitive impairment, and loss of residual kidney function [3].

Pruritus is another major complication of end-stage renal disease, affecting more than one-third of those patients. Pruritus has a strong negative impact on patients' quality of life, often inducing sleeplessness and mood disorders [4, 5].

Another important target in hemodialysis service is to achieve dialysis adequacy to improve quality of life, and prolong life expectancy. Inadequate hemodialysis has been associated with multiple comorbidities and mortality [6,7].

It is well known that the core body temperature (CBT) is lower in hemodialysis patients than in healthy people, and it increases during hemodialysis [8].

Cooling of dialysate below 36.5°C or 0.5 below patient's core body temperature has been described before as one of the important interventions that may improve clinical and hemodynamic performance during hemodialysis.[9]

Interestingly, this intervention can be delivered without any additional cost and it can be universally applied. Although some advantages of cooled dialysis were observed; safety, tolerability, short and long term outcomes are still a matter of controversy. Up till now, dialysate cooling has not been introduced as a standard of care recommendation in the current hemodialysis guidelines.

## AIM OF THE WORK

We aimed in this short-term study to investigate the effect of applying ICD on intradialytic hypotension, pruritus, dialysis adequacy, patients' acceptance, and nephrologists' preferability.

## PATIENTS AND METHODS

*Study design and patient criteria:*

This is a non-randomized single-center study that was conducted at Al-Azher nephrology and dialysis unit, AL- Azher University, New Damietta, Egypt. The study was carried out over a period of five weeks starting from July 2019 to August 2019. This study included patients who fulfilled the following criteria: whose age of more than 18 years old, who were on regular hemodialysis for six months or more, who received thrice, regular, four-hour hemodialysis sessions weekly, and those who agreed to participate in the study and applying cool dialysate after and informed consent has been taken. We excluded from the study patients who had fluctuating changes in their dry body weight, patients with acute intercurrent illness or who needed hospital admission during study period, patients with other end-organ failure such as advanced heart failure NYHA III, and IV, liver cell failure, advanced chronic lung diseases as COPD & emphysema, and those who had any advanced malignancies, patients who were not compliant with regular dialysis treatments, or had missed any of their HD session during study period.

*Methods:*

Hemodialysis was delivered through bicarbonate-based volumetric machines and dialysate sodium was kept at 140 meq/L through all study periods. Sodium profiling was not used at any time during the study.

The study passed through three phases:

Phase 1 (Preparatory phase): This is the stage of data collection and patients' assessments, it lasted for one week. During this week the followings were done: Demographic date including age, sex, duration of dialysis, associated comorbidities (hypertension, diabetes, cardiac problems, chronic HCV infection) and etiology of end-stage renal disease (ESRD), were collected. Blood samples have been collected from each patient and routine lab (such as; serum creatinine, CBC, albumin, bilirubin, sGOT, sGPT,

random blood glucose) were done. Core body temperature (CBT) was determined by obtaining oral temperature measurements before every dialysis session in this week (the mean of three measurements was calculated and used as CBT). Oral temperature was measured by a Glass and mercury thermometer, a single thermometer was separately designated for each patient.

Phase 2 (Standard temperature phase): it lasted two weeks (6 dialysis sessions). During this phase, the dialysate temperature was kept universally at 37°C for all patients.

Phase 3 (Cooled dialysate phase): It lasted for another two weeks (6 dialysis sessions). During this phase, the dialysate temperature was changed to be 0.5°C below CBT, which was applied separately for each patient.

During the preceding two phases, patients were evaluated for the following items:

1. Blood pressure Monitoring:

Similar to routine practice in blood pressure monitoring during dialysis, both systolic and diastolic blood pressure measurements were taken immediately before starting HD sessions from the access-free arm, then at 30 minutes intervals during the HD treatment, and finally at the end of HD treatment (total of 10 readings per each hemodialysis treatment).

Both measurements that were taken before starting and at the end of HD treatment were taken in the sitting position. All blood pressure measurements were taken by the auscultatory method using mercury sphygmo-manometer.

We recorded episodes of IDH to determine the frequency of this complication for each participant during standard and cool phases and patients were diagnosed with IDH if their SBP measurements were reduced by ≥20 mmHg at any point of time during hemodialysis treatment with or without symptoms of hypotension [10].

2. Dialysis adequacy:

Dialysis adequacy was assessed using Kt/V according to a single–pool variable volume Kt/V equation; In which $Kt/V = -\ln(R - 0.008 \times t) + (4 - 3.5 \times R) \times UF/W$ [11]. (- ln = the negative natural logarithm, R = predialysis to postdialysis urea ratio, *t* = dialysis duration in hours, UF = ultrafiltration volume in liters, W= post dialysis weight in kg)

We used online calculator (© 2020 QxMD Software) to calculate kt/v where the following variables were measured then introduced:

- Pre-dialysis urea (mmol/L)
- Post-dialysis urea (mmol/L)
- Dialysis duration (hours)
- Ultrafiltration volume (L): We determined the average ultrafiltration in the six hemodialysis sessions of each phase of the study (standard and cool)
- Post-dialysis weight (Kg)

3. Assessment of pruritus:

All patients were asked about their itching problem regarding the following:

a. The distribution of pruritus (leg, arm, back, chest or all the body)

b. Time that patient suffering more pruritus (diurnal, nocturnal, or on dialysis)

c. If there are other dermatological diseases ( those who had a non-uremic causes of pruritus were excluded from this assessment)

We assessed the severity of pruritus using a visual analogue scale (VAS) [12], during dialysis sessions in both standard and cool phases. The patients were asked to mark the severity of their itching on a scale ranged from zero to 10, with the starting point denoting "no itching" (0 points) and the finish point denoting "the worst itching imaginable" (10 points) (Figure 1).

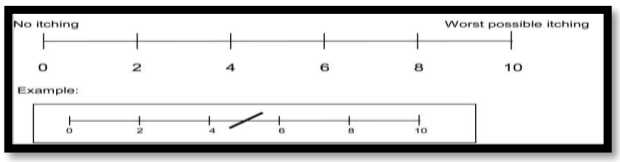


Figure [1]: Visual Analogue scale for the assessment of pruritus [12]

4. Assessment of patients' and nephrologist' acceptance of cool dialysate:

We assessed patients' as well as nephrologist' satisfaction during standard phase and at the end of cool phase using a questionnaires generated by Bullen et al. [13]

Patient questionnaire included five items that assess fatigability immediately after as well as day after hemodialysis treatment, the frequency of cramps, dizziness, and cold sensation during dialysis sessions were also assessed. This questionnaire was translated into an Arabic language, then conducted universally to all patients by a nephrologist. Nephrologists asked the questions and recorded patients' answers manually in separate sheets. We evaluated the nephrologists' opinion about cool dialysate via a self-reported questionnaire that contains three questions including: the efficacy of ICD in reducing IDH, their preferability to use it in such situations, and their experience about patients cold tolerability.

**Statistical Analysis**

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of data was first tested with one-sample Kolmogorov-Smirnov test. Qualitative data were described using number and percent. The association between categorical variables was tested using Chi-square test while Fischer exact test was used when expected cell count was less than 5. Continuous variables were presented as mean± SD (standard deviation) for parametric data and median (min-max) for non-parametric data. The two groups were compared by paired t-test (parametric data) and Wilcoxon signed rank test for paired non parametric data. For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value). The results were considered non-significant when the probability of error is more than 5% ($p > 0.05$) while significant when the probability of error is less than 5% ($p \leq 0.05$).

## RESULTS

In the current study, we evaluated fifty-nine ESRD patients on regular hemodialysis, and nine of them were excluded for the following reasons (5 patients with congested heart failure, two patients with liver cell failure, two patients with missed dialysis sessions and one patient was admitted to hospital with pneumonia).

The baseline demographic clinical, and laboratory data are listed in table (1).

The mean age of the included sample was 51.10±11.57, and males constituted 64% (n=32) of them. Sixty-four percent of patients had hypertension, 36% were positive for HCV antibody, and 18% of them with known cardiac diseases.

Forty three patients (86%) had episodes of intra-dialytic hypotension. Further comparison between patients with and without IDH (n=43, n=7) respectively regarding demographic, clinical, and laboratory data was done, and raveled a non-significant differences between both groups (data were not shown).

Table (2) shows the changes in blood pressure measurements during both study' phases.

There was a significant reduction in the median of intra-dialytic hypotensive episodes during cool phase in comparison to the standard phase [3.00 (0-6) vs 1.00 (0-3), $p < 0.001$].

Although, there were non-significant differences in pre-dialysis SBP, DBP and MAP during both standard and cool phases with p value (0.379, 0.174 & 0.248) respectively, the lowest intra-dialytic SBP, DBP and MAP were significantly higher during the cool phase in comparison to the standard phase (p value; 0.002, 0.003 & 0.001) respectively.

On the other hand, the end-dialysis SBP, DBP and MAP were significantly higher in the cool phase in comparison to the standard phase with p value (0.001, 0.001 & 0.0001) respectively.

The current results showed neither significant difference in Kt/v nor net ultrafiltration rate during both standard and cool phases (p value; 0.068 & 0.149) respectively (Table 3).

Regarding pruritus, we found that all patients (n=50) had pruritus at different degrees of severity and distribution. Thirty-eight% of patients suffered from diurnal pruritus and 36% suffered from pruritus at night while 26% of patients suffered from itching during hemodialysis. According to pruritus distribution, forty-two % of patients suffered from pruritus all through the body, followed by legs (24%). None of them suffered from overlapping dermatological disorders (table 4).

The severity of pruritus was assessed in the current study using (VAS score), there was a significant reduction in the mean values of pruritus VAS score during cool phase ($p<0.001$) [Figure 2). There were non-significant differences in almost all parameters of the patients questionnaire However, there was a significant difference in feeling cold between the two

phases (P = 0.04), with more participants reporting feeling cold during the cool phase as shown in table (5).

Regarding the nephrologist's questionnaire, it was conducted on 20 nephrologists. One hundred percent of them reported that the use of a cool dialysate is an effective technique to decrease IDH, however 60% (n=12) of nephrologists reported that they are frequently using it, while 40% of them (n=8) always use it. On the other hand, 60% (n=12) of nephrologists thought that, cool dialysate is associated with patient discomfort.

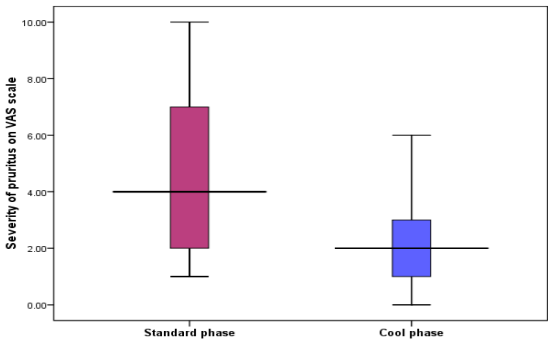


Figure 2: Box plot for median Severity of pruritus on VAS score between Standard phase and Cool phase

**Table [1]:** Basal demographic, clinical and laboratory data of the studied group

| Vairables | | Values |
|---|---|---|
| **Age/ years (Mean ± SD)** | | 51.10±11.57 |
| **Sex (n,%)** | **Male** | 32 (64%) |
| | **Female** | 18 (36%) |
| **Dry weight (kg) (Mean ± SD)** | | 80.14±16.85 |
| **BMI (kg/m$^2$) (Mean ± SD)** | | 26.77±4.67 |
| **Core temperature (°C) (Mean ± SD)** | | 36.96±0.22 |
| **HCV (n, %)** | | 18 (36%) |
| **Diabetic (n, %)** | | 4 (8%) |
| **Hypertensive (n, %)** | | 32 (64%) |
| **Cardiac (n, %)** | | 9 (18%) |
| **Intradialytic hypotension (n, %)** | | 43 (86%) |
| **Hb (g/dl) (Mean ± SD)** | | 9.37±1.53 |
| **WBC (Mean ± SD) x10$^3$ cell/dl** | | 5.85±2.63 |
| **PLT (Mean ± SD) x10$^3$ cell/dl** | | 196.78±67.34 |
| **Pre-dialysis serum creatinine (mg/dl) (Mean ± SD)** | | 9.81±2.21 |
| **Serum albumin (gm/dl) (Mean ± SD)** | | 3.70±0.46 |
| **Bilirubin (mg/dl) (Mean ± SD)** | | 0.59±0.38 |
| **sGOT (IU/L) (Mean ± SD)** | | 23.51±12.29 |
| **sGPT (IU/L) (Mean ± SD)** | | 25.06±11.54 |
| **Random blood glucose (mg/dl) (Mean ± SD)** | | 116.89±30.30 |

BMI: body mass index, HCV: hepatitis c virus, °C: degree centigrade, Hb: hemoglobin, WBC: white blood cell, PLT: platelet, sGOT: serum glutamic oxaloacetic transaminase, sGPT: serum glutamic pyruvic transaminase, SD: standard deviation

**Table [2]:** Blood pressure changes during standard and cool phases

| Parameters | | Standard phase | Cool phase | p Value |
|---|---|---|---|---|
| Episodes of IDH; median (min-max) | | 3.00 (0-6) | 1.00 (0.0-3) | <0.001 |
| Pre-HD BP(mmHg) | SBP | 134.68±20.81 | 131.30±17.29 | 0.379 |
| Mean ± SD | DBP | 82.81±9.78 | 80.33±8.30 | 0.174 |
| | MAP | 100.11±12.99 | 97.32±10.84 | 0.248 |
| Lowest BP(mmHg) | SBP | 105.80±19.28 | 110.60±19.73 | 0.002 |
| Mean ± SD | DBP | 61.80±11.00 | 66.80±10.77 | 0.003 |
| | MAP | 76.47±13.22 | 81.40±13.35 | 0.001 |
| Post-HD BP(mmHg) Mean ± SD | SBP | 122.60±23.08 | 127.43±18.97 | 0.001 |
| | DBP | 73.70±11.23 | 77.68±9.67 | 0.001 |
| | MAP | 90.00±14.90 | 94.26±12.47 | <0.001 |
| Change in BP(mmHg) | SBP | -12.08±9.26 | -3.87±5.26 | <0.001 |
| Mean ± SD | DBP | -9.12±6.92 | -2.65±5.14 | <0.001 |
| | MAP | -10.11±7.26 | -3.06±4.99 | <0.001 |

BP: blood pressure, IDH: intra-dialytic hypotension, SD: standard deviation, SBP: systolic blood pressure, DBP: diastolic blood pressure, MAP: mean arterial blood pressure.

**Table [3]:** Changes in ultrafiltration rate, Kt/V, and pruritus score in standard and cool phases

| Parameters | Standard phase | Cool phase | p Value |
|---|---|---|---|
| UF (kg) Mean ± SD | 1.89±0.87 | 1.79±0.72 | 0.149 |
| Kt/V Mean ± SD | 1.27±0.16 | 1.23±0.12 | 0.068 |
| Severity of pruritus on VAS scale median(min-max) | 4 (1-10) | 2 (0.0-6) | <0.001 |

UF: ultrafiltration, SD : standard deviation, VAS: visual analogue scale, min: minimum, mix: maximum

**Table [4]:** Pruritus questionnaire among the study group (n=50)

| | **Variables** | |
|---|---|---|
| Time of maximum itching | 1.Diurnal | 19 (38%) |
| | 2.Noctornal | 18 (36%) |
| | 3.on Dialysis | 13 (26%) |
| Distribution | 1.Leg | 12 (24%) |
| | 2.Arm | 5 (10%) |
| | 3.Back | 9 (18%) |
| | 4.Chest | 3 (6%) |
| | 5.All The Body | 21 (42%) |
| Other skin/ dermatological diseases | Yes | 0 (0.0%) |
| | No | 50 (100%) |

**Table [5]:** Patient' questionnaire among the study group (n=50)

| Parameters | | Standard phase | Cool phase | p Value |
|---|---|---|---|---|
| Energy Level n(%) | 1.Weak<br>2.Adequate<br>3. Energetic | 12 (24%)<br>23 (46%)<br>15 (30%) | 14 (28%)<br>27 (54%)<br>9 (18%) | 0.373 |
| Cramps During Dialysis n(%) | 1. Often<br>2.Some of The Time<br>3.Rare | 8 (16%)<br>15 (30%)<br>27 (54%) | 10 (20%)<br>10 (20%)<br>30 (60%) | 0.502 |
| Light Headed After Dialysis n(%) | 1.Often<br>2.Some of The Time<br>3. Rare | 5 (10%)<br>18 (36%)<br>27 (54%) | 8 (16%)<br>12 (24%)<br>30 (60%) | 0.359 |
| Energy Next Day n(%) | 1.Unable to Do Usual Activities<br>2.Some Problems<br>3.No Problems | 5 (10%)<br>16 (32%)<br>29 (58%) | 5 (10%)<br>16 (32%)<br>29 (58%) | 0.976 |
| Temperature Sensation N(%) | 1.Cold<br>2.Normal<br>3. Warm | 21 (42%)<br>25 (50%)<br>4 (8%) | 33 (66%)<br>16 (32%)<br>1 (2%) | 0.04 |

## DISCUSSION

Hemodialysis represents the most commonly used renal replacement therapy in the current era, however, it has some complications and undesirable side effects including hypotension, itching, muscle cramps..etc [14].

The occurrence of such side effects during hemodialysis may be intolerable by the patient and can lead to patient' noncompliance and therefore premature dialysis session termination and insufficient dialysis treatment [15].

One of the most effective strategies to improve the hemodynamic efficiency during HD is the reduction of dialysate temperature, which was initially described by Maggiore and his colleagues in the 1980s, [16] and it takes into consideration the fact that, the body temperature rises during standard dialysis [17].

The reasons for increased body temperature during hemodialysis are not fully understood however, different hypothesis have been postulated including; heat transfer from warm dialysate, reduced heat loss from the skin due to vasoconstriction, and increased thermogenesis as a result of an inflammatory response generated by interaction between blood constituents and the hemodialysis membrane [18].

Cooling of dialysate is non-expensive technique and can be universally applied, however it is relatively underused due to the fears of causing intolerable cold and shivering symptoms, Furthermore, there was a concern about the reduction of dialysis adequacy due to peripheral solute sequestration owing to greater

vasoconstriction. In the current study we aimed to investigate the impact of introducing a short-term dialysate cooling protocol on IDH, pruritus, and dialysis adequacy. Moreover, to assess patients' and nephrologists' satisfaction with this intervention as well.

In the current study, we found a relatively higher number of patients who had IDH (86% of the included sample), as we select patients with IDH based on the reduction of SBP by ≥ 20 mmHg at any time during dialysis even without symptoms of hypotension or nursing intervention. In the available literature, there are multiple definitions of IDH, and hence the prevalence of IDH is varying between different studies. There are a variety of studies that used a similar IDH concept [19,20].

In a study conducted by Kuipers et al , 2016 on 3818 HD session, they observed a prevalence of IHD in 77.7% of dialysis session (based on reduction in SBP, and MAP), while clinical symptoms was developed, and nursing intervention was needed in 21.4%, and 8.5% respectively [21].

The selection of IDH patients based on more liberal definition as used in the current study could have important clinical relevance, as asymptomatic IDH could have a deleterious effect in the vascular bed of different body organs, and subsequently carries adverse outcomes [22,23].

In the current study, it was found that cooling dialysate significantly increased the lowest blood pressure values during observed hemodialysis session, and the number of hypotensive episodes decreased as well. Furthermore, at the end of the dialysis session, SBP, DBP, and MAP measurements were higher in cool than in standard phase. Our results are in consistence with previous publications which illustrated that dialysate cooling can decrease the rate of IDH episodes, increase intradialytic MAP, and improve hemodynamic instability during dialysis [13,24].

The mechanism by which cooled dialysis does such a beneficial effect is not fully understood, it was postulated that cooled dialysate avoids heat accumulation and its related counterproductive vasodilatation and improves systemic vascular resistance. Furthermore, it enhances catecholamine release and hence increases peripheral vasoconstriction and cardiac contractility [25].

The potential sequences and side effects of implementing this intervention are not clear. One of these concerns is dialysis adequacy and whether it becomes substandard with cooled dialysis or not. It was hypothesized that peripheral vasoconstriction induced by dialysate cooling might enhance urea sequestration or compartmentalization and subsequently the urea rebound will increase post-dialysis leading to reduction in dialysis adequacy [26].

In the current work, we investigated this issue, and we found that ICD did not have impact of dialysis adequacy (measured by Kt/v), or ultrafiltration goal. Our results are in agreement with Pérgola, et al 2004 & Selby, et al 2006 who found that ICD can improve hemodynamics during dialysis without alteration in urea reduction or dialysis adequacy [18,19].

On the other hand, Ayoub and Finlanson have demonstrated an increment in ultrafiltration rate during cooled dialysis than in standard dialysis, which might add additional benefits of using cold dialysis [26].

The effect of ICD on pruritus severity especially during hemodialysis treatment was another aim of the current study. We found that pruritus severity (as assessed by VAS score) was significantly reduced during the phase of cooled dialysis than in the standard phase, these findings are compatible with those described by Rad, and his associates 2017 [15].

Ramezanpour, and Falah have found that, the use of cold fomentations, ice pieces or cooling factors might help vasoconstriction and thus they can alleviate itching [27]. The cool effect on skin blood vessels decreases the release of stimulants for pruritus, moreover, it affects nerve membranes and makes them less irritable [28].

In addition to improved pruritus severity, cool dialysate lacks the side effects of other antipruritic measures. It was stated that cold dialysis is a fast, affordable, and non-medicinal intervention for pruritus that does not have adverse or unwanted effects like other pharmacological alternates [15].

Considering the length of time consumed by our patients in dialysis facilities, patient satisfaction with ICD was another concern of the current work. We found that cold feeling during cooled hemodialysis was significantly higher than in standard hemodialysis, however the use of ICD was well tolerated and none of

included samples rejected completing the study' intervention owing to cold feeling.

It was theorized that improved hemodynamic performance by cold dialysis could increase levels of energy in HD patients both during and after dialysis sessions. [13] Conversely, in the current work we found that patients' energy levels were not significantly differ in both phases of the study. These findings are in agreement with Bullen et al. [13], while contradict that were described by Ayoub, and Finlanson who found a very positive results regarding energy and activity levels during cold dialysis, however their study was limited by the small sample size and short intervention time that might give inconsistent results [26]

Among nephrologists, we noticed a universal agreement that cold dialysis is an effective intervention to improve hemodynamic instability during dialysis, and the majority of them use it to manage IDH; however a considerable proportion of them concerned about patients tolerability and discomfort. This is might reflect the importance of shared decision-making, and patient preferability during conduction of hemodialysis service.

***Strength and limitation of the study:***

In the current study we conducted the cold dialysis through individualization of dialysate temperature rather using a universal cold dialysate; which was applied before by decreasing the dialysate temperature at least 1 $^0$C below standard dialysis (most of studies applied it at 35-36$^0$C). This could alleviate the extreme cold sensation complicating this intervention, however applying personalized isothermal hemodialysis via watchful observation of CBT throughout the session seems to be better but quiet difficult to be applied. We applied a liberal definition of IDH based on isolated reduction of SBP even without symptoms of hypotension; which might have important clinical relevance. However this study is limited by lacking randomization and blinding, patient blinding might lessen bias toward ICD intervention and gives more consistent results, but it was quite difficult to apply a blind protocol with our group of patients. To the best of our knowledge, this is one of the few studies that investigate the effect of cold dialysate on dialysis related complications (including IDH, pruritus, dialysis inefficiency, cramps, peri-dialysis patients' energy and fatigability) which are considered important aspects of hemodialysis service. We encourage conducting randomized controlled trails (RCT) on larger sample size to investigate the valuable results of applying cool dialysate in hemodialysis patients and to elucidate its long term effect on different target organs.

**Conclusion**: Individualized cool dialysate (ICD) has a positive impact on improving hemodynamic instability and IDH. It could alleviate pruritic symptoms in hemodialysis patients without affection for dialysis adequacy. It is generally well tolerated and well accepted by both patients and nephrologists.

**Financial and Non-financial Relationships and Activities of Interest**

None

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