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Comparison of the Effect of Cold Dialysate versus Stretching Exercises on Severity of Restless Legs Syndrome in Patients Undergoing Hemodialysis: A Randomized Controlled Trial

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Abstract

Background: Restless legs syndrome (RLS) is prevalent among patients undergoing hemodialysis. This research suggests that cold dialysis solution and stretching exercises are effective approaches reducing RLS; however, they should be adopted according to the patient's condition.

Aim: This study aimed to compare cold dialysate with stretching exercises on RLS severity in patients undergoing hemodialysis.

Method: This two-group randomized clinical trial was conducted on 44 hemodialysis patients with RLS. One group received cold dialysis (35.5°C) and the other group performed stretching exercises in two hemodialysis centers in Sabzevar, Razavi Khorasan Province, Iran, in 2019. The severity of RLS was measured in both groups using the IRLS scale at the baseline and end of each week for 6 weeks. The data were analyzed in SPSS (version 21) using repeated measures ANOVA and Friedman's test.

Results: The mean age of participants in cold dialysis and stretching exercise groups were 54.5±13.6 and 54.5±10.8 years, respectively. The Friedman test results showed a significant reduction in the severity of RLS in both groups (P=0.001). Moreover, the repeated measures ANOVA results revealed that the time effect was significant (P=0.001). However, group effect (P=0.09) and interaction between time and group (P=0.25) were not significantly different.

Implications for Practice: Both methods of cold dialysate and stretching exercises decreased RLS severity; therefore, they can be suggested to nurses as effective strategies. Due to the limited sample size, studies with larger sample sizes are recommended.

Keywords: Cold temperature, Dialysis solutions, Kidney failure, Restless legs syndrome, Stretching exercises

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Introduction

Patients undergoing hemodialysis often deal with several complications, some of which are related to end-stage renal disease, while some are related to the type of treatment (1). One of the complications is related to neuromuscular issues, such as restless legs syndrome (RLS), which is accompanied by sensory symptoms and movement disorders of the extremities, especially in the legs (2, 4). Specific criteria have been introduced by the International Restless Legs Syndrome Study Group to diagnose this syndrome, including continuous urge for moving the legs, temporary relief of unpleasant symptoms by moving, the onset or intensification of symptoms by resting or lack of mobility, and onset or intensification of symptoms in the evening and at night (5).

According to the reports, the RLS is prevalent among 36.5% of patients undergoing hemodialysis (6). Considering the existing hypotheses of RLS, factors related to the onset or worsening of this condition include peripheral neuropathy, dopaminergic system dysfunction, and iron deficiency in specific cerebral regions (7). Patients with RLS experience chronic insomnia, daytime sleepiness, stress, and depression which can be related to the functional roles of patients, social activities, family life, and occupation (8, 9).

The basic treatments for RLS are kidney transplants and receiving specific care and drugs (10). The prescribed drugs in this area include dopamine agonists (e.g., L-DOPA), which reduce the severity of RLS and are the treatment chosen for these patients (11, 12). Since drug treatments are associated with specific complications in addition to the financial burden on governments, the adoption of non-pharmaceutical approaches is preferred by the healthcare system (13). Regarding this, two of the more common non-pharmaceutical methods are cold dialysis solution and stretching exercises.

Cold dialysis solution is the dialysis performed at a temperature range of 34-36°C. No adverse effects have been reported for dialysis at 35.5°C, except experiencing tolerable shivering while using cold dialysis solution in hemodialysis (14, 15). In fact, cold dialysis solution can increase the dialysis quality by removing more toxic compounds (e.g., urea and creatinine) and decreasing their effect on the peripheral nervous system (16). In addition, cold dialysis alleviates the RLS symptoms by decreasing fatigue, increasing energy, and improving the mental-physical status of an individual, which in turn, increases sleep quality. Moreover, the results of studies have shown that cold dialysis improves energy and a sense of well-being in patients by decreasing their anxiety and secondary depression, thereby reducing their neuropathy level (17).

Since RLS symptoms emerge or aggravate in absence of mobility (18), mild exercises, such as walking, massaging, stretching, and swimming, can alleviate RLS symptoms. Stretching exercises can be also beneficial, including hip rotation and quadriceps, gluteal muscles, and hamstring stretch (19). Moreover, tensile forces stimulate the endothelial cells, increase blood flow, and activate nitric oxide synthases. The nitric oxide, being synthesized, diffuses across the endothelial cell membrane and enters the vascular smooth muscle cells. This process is followed by the rapid spread of the substance through the vascular smooth muscle. Notably, nitric oxide activates the guanylate cyclase, thereby, activating the second messenger (i.e., guanosine monophosphate). This pathway leads to vasodilation and consequently increases localized blood flow (20).

In contrast to cold dialysis, which causes shivering and needs hospitalization, specialized dialysis equipment, and experienced personnel, stretching exercises can be performed by patients themselves. Furthermore, such activities can be included in patients' daily schedule, whether during, before, or after the dialysis. Among the non-pharmaceutical treatments of RLS (e.g., reflexology, acupuncture, or transcutaneous electrical nerve stimulation), the researchers of this study selected cold dialysis and stretching exercises due to their availability and lack of necessity for another trained person to perform the treatment process.

To the best of our knowledge, no specific research has been performed to investigate the effect of cold dialysis and stretching exercises on RLS. In fact, there is just one study conducted in this domain, which is not sufficient for confirming the impact of the mentioned approaches. Studies in this field mostly focused on either the effect of exercise on RLS in the general population or the impact of aerobic exercises (e.g., stationary bicycle or treadmill) on RLS (12).

Dialysis nurses should control the complications of hemodialysis and use effective non-pharmacological methods to manage dialysis complications. As mentioned, RLS influences the patient's physical and mental status negatively and disrupts their life process. Moreover, a large number of drugs, used to cure these patients, are mostly excreted by the kidneys causing additional

problems for patients. These issues highlight the necessity of using non-pharmacological methods for the treatment of treat restless legs syndrome.
The effect of stretching exercises and cold dialysis on RLS has been identified in some studies (10-12). Nurses are required to choose the best effective evidence-based interventions for the treatment of RLS. With this background in mind, this study aimed to evaluate and compare the effect of two non-pharmaceutical methods of cold dialysis solution and stretching exercises on the severity of RLS in patients undergoing hemodialysis.

Methods

This randomized controlled clinical trial, double-blind with a parallel-group design, was conducted on 40 hemodialysis patients with RLS for 2 months from March to April in 2019 in Sabzevar, Razavi Khorasan Province, Iran. The research population included all patients diagnosed with end-stage renal disease undergoing three sessions of dialysis per week (four h per session). The research setting was the hemodialysis wards in Vasei Hospital and Kashefi Dialysis Center, where dialysis patients were admitted in three shifts. Vasee Hospital admits 87 hemodialysis patients and has 18 hemodialysis beds. Kashefi Dialysis Center accepts 43 hemodialysis patients and has 10 hemodialysis beds.
The sample size was estimated at 20 participants in each group using the formula of "comparison of two independent population means" with 95% confidence level, 80% power, and standard deviation of 5.2, considering the 14.3-unit difference in the severity of RLS based on a study performed by Shahgholian et al. (21). Out of 130 patients referring to these two places, 44 cases were selected through convenience sampling (considering 10% sample attrition) based on International Restless Legs Scale (IRLS) after applying the inclusion and exclusion criteria. Finally, using the permuted block randomization technique, 22 patients were assigned in each group (i.e., cold dialysate group marked with the letter 'A' and stretching exercise group identified with the letter 'B'). Each block consisted of 4 patients, the number of blocks was 11, and the number of possible permutations was 4.
For instance, if the first block was BABA, the first, second, third, and fourth participants were assigned in group B, group A, group B, and group A, respectively. Four cases were lost during the research process, two cases of which belonged to the stretching exercise group (immigration [n=1] and unwillingness [n=1]), and the two others were in the cold dialysis group (feeling chill [n=1] and unwillingness [n=1]). Eventually, the analysis was performed on 40 participants (Figure 1).
The patients were entered into the study based on the following inclusion criteria: 1) age above 18 years (maximum age of 71 years), 2) minimum hemoglobin level of 10 mg/dl (RLS prevalence in patients with iron deficiency anemia is four to five times higher than in the general population) (22), 3) diagnosis of chronic renal failure (at least 3 months of hemodialysis), 4) arteriovenous fistula for hemodialysis, 5) undergoing dialysis three times a week (four h per session), 6) experiencing RLS during hemodialysis in the past 2 months, 7) KT/V $\geq$ 1 (if hemodialysis adequacy is not appropriate, the patient's blood toxins levels will not be controlled and related complications will increase) (23), 8) vision and hearing health, 9) lack of pregnancy and liver problems, 10) lack of receiving any kind of management for RLS during dialysis (e.g. oral drugs, complementary medicine, acupuncture, and local moisturizers), 11) lack of any feet infection or wound, 12) lack of orthopedic problems, 13) lack of having lower extremity arterial disease, 14) lack of having a mental disorder and severe mood-affective disorder preventing effective communication, and 14) lack of hypercalcemia.
On the other hand, the subjects with the following criteria were excluded from the study: 1) showing acute complications, convulsion, air embolism, dysrhythmia, cardiac and respiratory arrest, and coma during dialysis, 2) lacking continued dialysis, 3) receiving transplants during the research, 4) changing in the number and time of dialysis sessions, 5) lacking tolerance of cold dialysis, 6) unwilling to cooperate with the researcher, and 7) not performing stretching exercises for three consecutive sessions and six non-consecutive sessions.
Two questionnaires were used as the tools of this study to collect the data, namely the demographic form and the IRLS. This scale consists of 10 items scored on a five-point Likert scale (no RLS=0 to very severe RLS=4) with a minimum and maximum score of 0 and 40, respectively. Therefore, based on the obtained points, the severity of RLS is classified into five categories, including without difficulty (0), mild (1-10), moderate (11-20), severe (21-30), and very severe (31-40) (24). Since the construct validity of the IRLS was not examined in Iran, the content validity index (CVI) was assessed based on ten experts' opinions. The mean score of CVI was obtained at 0.81 being

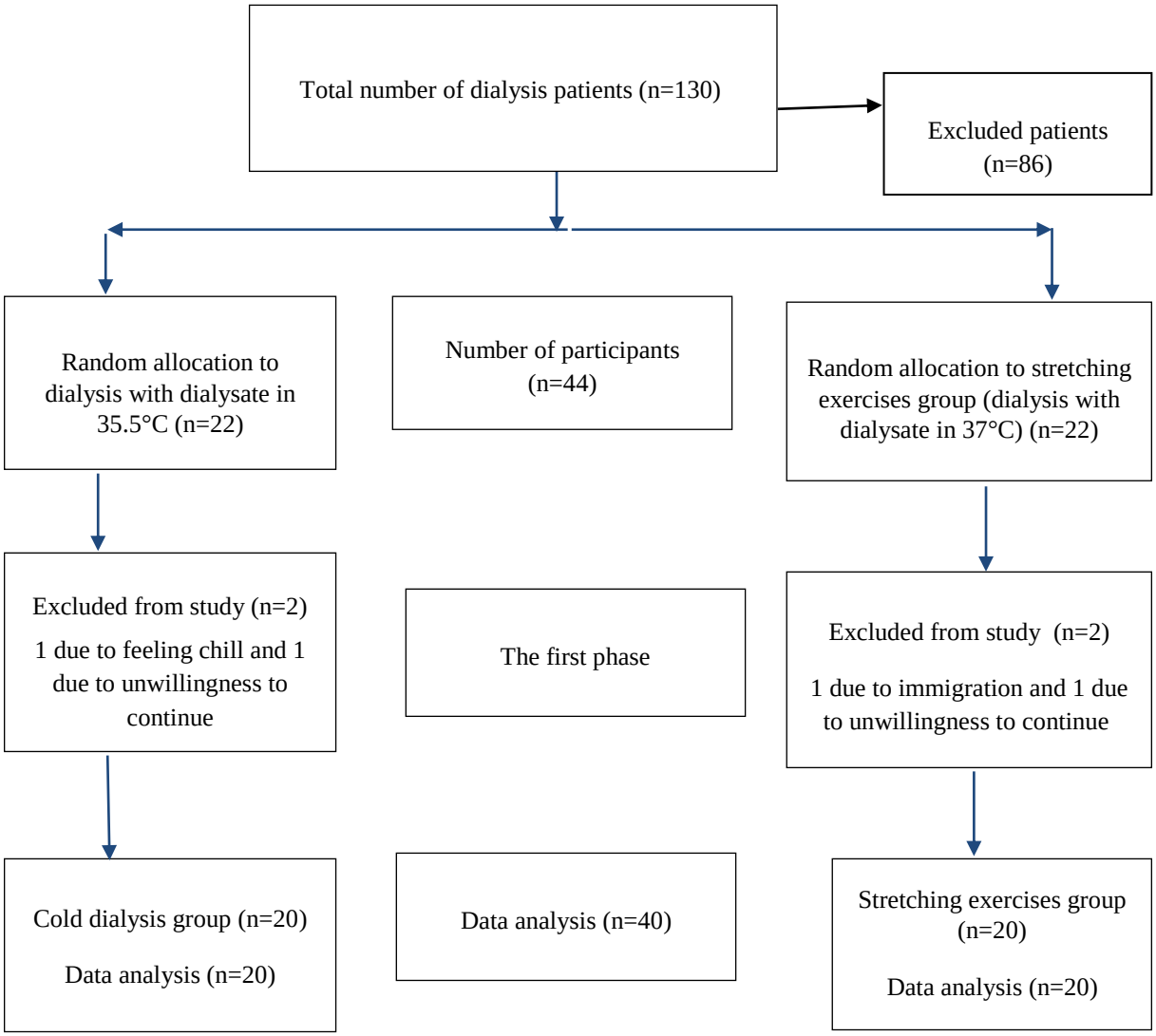

Figure 1. Flowchart of the design, groups, and participants in the study

considered appropriate. The reliability of the questionnaire was calculated as 0.94 using Cronbach's alpha coefficient method.

After filling out the IRLS, the subjects were examined by a neurologist for the differential diagnosis of RLS from neuropathies, such as diabetic neuropathies. A neuropathy examination was performed using the Michigan Neuropathy Screening Instrument. In order to maintain the quality of dialysis, the filters used for hemodialysis were constant for each patient during the study and the hemodialysis solution flow rate in all patients was 500 ml/min. Moreover, before the intervention, dialysis devices were calibrated in terms of temperature settings. In this study, the researcher's assistance completed the questionnaires, and the researcher was blinded. The statistician was also unaware of the group allocation in the study.

To perform the study, the research objectives were first explained to all subjects. However, stretching exercises were only explained to the participants in the stretching exercises group. Subsequently, the IRLS was filled with the researcher's assistant at the baseline and at the end of each week for 6 weeks. Patients in the cold dialysis group (dialysis with 35.5°C which was selected based on the previous studies) (10, 16) received hemodialysis with cold solution 4 h a day, 3 times a week, for a period of 6 weeks. During the same period, patients in the stretching exercise group received dialysis with the usual temperature of dialysis solution (i.e., 37°C) and performed stretching exercises for half an hour at the beginning of dialysis. Stretching exercises included 5 min warm-up, 20 min isotonic stretching exercises, and 5 min cool down. Isotonic stretching exercises included pelvic rotation, knees-to-chest pose, and quadriceps, gluteal, and

hamstrings muscles stretching. The type, sequence, and number of movements were designed and trained under the supervision of a master in sports physiology.

The study protocol was approved by the Ethics Committee of Sabzevar University of Medical Sciences, Sabzevar, Iran (IR.MEDSAB.REC.1397056), and was recorded in the clinical trial center with the code of IRCT20181108041594N1.

Data analysis was performed in SPSS (version 21) using Chi-square, Fisher's exact test, t-test (to assess demographic characteristics), repeated measures ANOVA, Friedman's test (to evaluate the effect of cold dialysis solution and stretching exercises variables), and Shapiro-Wilk test (to evaluate the normality). Based on the results, a p-value of 0.05 was considered significant.

Results

Shapiro-Wilk test was used to evaluate the normality of the distribution of quantitative variables. The mean ages of the participants in cold dialysis and stretching exercise groups were 54.5±13.6 and 54.5±10.8 years, respectively. No significant difference was observed between the two groups in terms of demographic characteristics (Table 1; P>0.05). According to the Friedman test results, the mean RLS score before and after the intervention had a significant difference in the cold dialysis solution and stretching exercises groups (Table 2; P=0.001). Table 2 summarizes the comparison of the mean severity score of RLS before and after intervention in cold dialysis and stretching exercise groups.

Since the assumption for the univariate tests does not hold using Mauchly's test (P-value=0.00), the Huynh-Feldt correction was applied to adjust the degrees of freedom. The results of repeated measures analysis of variance showed that time had a significant effect on the severity of RLS (P=0.001). Furthermore, the interaction effect between the time (trend) and the intervention groups was not significant (P=0.25). Additionally, the mean severity of RLS revealed no significance between the cold dialysis and stretching exercises groups (Table 2; P=0.09).

Table 1. Demographic information of patients in the intervention 1 (cold dialysis) and intervention 2 (stretching exercise) groups

Group Variable		Intervention 1 n (%) or Mean±SD*	Intervention 2 n (%) or Mean±SD	P-value
Age (year)		54.5±13.6	54.5±10.8	0.87**
Duration of hemodialysis treatment (month)	2-6 7-12 >13	2 (10.0) 4 (20.0) 14 (70.0)	1 (5.0) 7 (35.0) 12 (60.0)	0.52***
Gender	Male Female	9 (45.0) 11 (55.0)	15 (75.0) 5 (25.0)	0.75***
Duration of RLS during dialysis	Less than 8 weeks 9 weeks to 6 months 7 months to 12 months More than a year	0 (0.0) 2 (10.0) 4 (20.0) 14 (70.0)	0 (0.0) 1 (5.0) 7 (35.0) 12 (60.0)	0.52****
History of taking medication to relieve RLS symptoms	Oral and medication Supplementary Supplementary medication No medication	12 (60.0) 8 (40.0) 0 (0.0)	12 (60.0) 8 (40.0) 0 (0.0)	0.99****
Factors exacerbating RLS during dialysis	Rest Stress and rest Heat and rest Stress, heat, and rest	15 (75.0 2 (10.0) 2 (10.0) 1 (5.0)	18 (90.0) 0 (0.0) 2 (10.0) 0 (0.0)	0.35****

*Standard Deviation, ** Independent t-test, ***Chi‑square test, **** Fisher's exact test

Table 2. Comparison of severity score of restless legs syndrome pre- and post-intervention in cold dialysis and stretching exercise groups

	Cold dialysis group Mean±SD*	Stretching exercise group Mean±SD
Pre-intervention	27.0±6.7	23.4±7.1
End of first week	26.5±6.8	22.5±6.2
End of second week	25.2±6.8	21.1±6.4
End of third week	22.5±6.2	19.2±6.8
End of fourth week	19.5±5.6	16.2±6.2
End of fifth week	18.6±5.7	15.8±6.3
End of sixth week	16.7±6.1	14.1±6.2
Friedman test result	P=0.001	P=0.001
Repeated measures ANOVA	Time effect P=0.001 Group effect P=0.09 Interaction between time and group P=0.25	

*Standard Deviation

Discussion

According to the results of this study, cold dialysis and stretching exercises reduced the severity of RLS and can be applied as safe non-pharmaceutical methods to control the syndrome. However, no significant difference was detected between the two methods. In a double-blind study performed by Sakkas et al., it was reported that although a one-degree reduction in body temperature had no impact on the blood pressure of the participants, it improved motor and sensory symptoms by 50-60% and 10%, respectively (18). These results are in line with those of the present study indicating a decrease in body temperature leading to a reduction in RLS severity.

Our findings are in agreement with the results obtained by Kashani et al. regarding the effect of cold dialysis on the decrease of RLS severity (10). The improvement of RLS symptoms by lowering body temperature may be due to a decrease in sensory receptors function leading to widespread numbness caused by reduced neuronal activity (25). Moreover, coldness can cause smaller oscillations and lower frequencies of impulse inputs to the nerve terminals, reducing pain perception and a palliative response as a result (26).

In the present study, it was also found out that stretching exercises decreased the severity of RLS. This result is consistent with those obtained by Shahgholian et al., who confirmed a decrease in RLS severity by stretching exercises and reflexology (21). Giannaki et al., comparing dopamine agonists (ropinirole) with exercising as two treatment methods, reported an equal impact for both techniques (12). These results were indicative of the considerable effect of stretching exercises on RLS. Accordingly, exercising improves motions related to RLS in patients with idiopathic RLS, as well as alleviating RLS symptoms by releasing β-Endorphin (27).

In another study, an increase in the β-Endorphin level was reported in patients without RLS symptoms four h after performing dialysis at 34.5°C (28). In addition, exercising might increase local blood flow by vasodilation, thereby affecting the RLS symptoms (20). Various studies have shown the positive effects of cold dialysis solution on complications during dialysis, compared to the use of dialysis solution at 37°C. Regarding, the positive effects were reported as a decrease in hypotension, hemodynamic disorder, brain ischemic, cardiac dysfunction, fatigue, and consequently the number of nursing interventions. Therefore, this method can be adopted as a non-pharmaceutical approach to improving RLS symptoms.

This study was also conducted to compare the effect of stretching exercise with cold hemodialysis in reducing RLS. The results of the study were indicative of the comparability of the effects of the two methods under investigation. Due to the different mechanisms of these two non-pharmacological methods in reducing RLS, they can be applied in different situations. The adoption of the stretching exercise method is recommended in patients unable to tolerate cold dialysis and suffer from the chill. The reason is related to the fact that performing exercises increase blood flow to the muscles and facilitate food transfer. On the other hand, cold dialysis can reduce the severity of RLS by increasing the adequacy of dialysis and decreasing the central body temperature. Therefore, this method can be employed in patients who cannot tolerate exercise or when hemodialysis catheters may detach during movement.

One of the major limitations of this study was the small sample size, decreasing the generalizability of the results. In addition, since RLS was a subjective phenomenon reported by participants, researchers' uncertainty about the correctness of participants' responses could be another limitation of this study. The other limitation was related to the lack of a control group due to the limited number of samples.

Implications for Practice

Based on the results of the present study, the two methods of cold dialysis solution and stretching exercises can reduce the severity of RLS at a similar scope. Therefore, nurses and other healthcare providers should adopt the appropriate method to reduce RLS according to the condition of patients. In this regard, they are recommended to employ stretching exercises in cases feeling chill, while conducting cold dialysis in patients unable to perform stretching exercises due to physical limitations. Since this study was performed with a limited number of participants, it is recommended that further studies be performed with a larger sample.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

References

1. Kakhki Jaghargh H, Bagheri M, Aghebati N, Esmaily H. Effect of increased blood flow velocity on fatigue in hemodialysis patients. Evid Based Care. 2020;10(2):48-57.
2. Kallenbach JZ. Review of hemodialysis for nurses and dialysis personnel-e-book. Amsterdam, Netherlands: Elsevier Health Sciences; 2020.
3. Khojandi S, Shahgholian N, Karimian J, Valiani M. Comparison the effect of two methods of reflexology massage and stretching exercises on the severity of restless leg syndrome among patients undergoing hemodialysis. Iran J Nurs Res. 2015;10(1):86-94.
4. Lin XW, Zhang JF, Qiu MY, Ni LY, Yu HL, Kuo SH, et al. Restless legs syndrome in end stage renal disease patients undergoing hemodialysis. BMC Neurol. 2019;19(1):47.
5. Kushida C, Martin M, Nikam P, Blaisdell B, Wallenstein G, Ferini-Strambi L, et al. Burden of restless legs syndrome on health-related quality of life. Qual Life Res. 2007;16(4):617-24.
6. Rafie S, Jafari M, Azizi M, Bahadoram M, Jafari S. Restless legs syndrome in hemodialysis patients. Saudi J Kidney Dis Transpl. 2016;27(2):326-30.
7. Massey T, Robertson N. Restless legs syndrome: causes and consequences. J Neurol. 2020;267(2):575-7.
8. Scherer JS, Combs SA, Brennan F. Sleep disorders ,restless legs syndrome, and uremic pruritus: diagnosis and treatment of common symptoms in dialysis patients. Am J Kidney Dis. 2017;69(1):117-28.
9. Tayebi A, Kasra Dehkordi A, Ebadi A, Sahraei H, Einollahi B. The effect of aromatherapy with lavender essential oil on depression, anxiety and stress in hemodialysis patients: a clinical trial. Evid Based Care. 2015;5(2):65-74.
10. Kashani E, Mirhosseini Z, Rastaghi S, Rad M. The effect of the cool dialysate on the restless leg syndrome in hemodialysis patients: Randomized triple-blind clinical trial. Iran J Nurs Midwifery Res. 2019;24(3):200-5.
11. Mortazavi M, Vahdatpour B, Ghasempour A, Taheri D, Shahidi S, Moeinzadeh F, et al. Aerobic exercise improves signs of restless leg syndrome in end stage renal disease patients suffering chronic hemodialysis. Sci World J. 2013;2013:628142.
12. Giannaki CD, Sakkas GK, Karatzaferi C, Hadjigeorgiou GM, Lavdas E, Kyriakides T, et al. Effect

of exercise training and dopamine agonists in patients with uremic restless legs syndrome: a six-month randomized, partially double-blind, placebo-controlled comparative study. BMC Nephrol. 2013;14(1):194.
13. Toth-Manikowski SM, Sozio SM. Cooling dialysate during in-center hemodialysis: Beneficial and deleterious effects. World J Nephrol. 2016;5(2):166-71.
14. Moujerloo M, Molaie E, Montazer Z, Behnampour N, Shariati A, Khari M. Effect of cool dialysate on hypotention and some interventions during dialysis. J Res Dev Nurs Midwifery. 2015;12(1):56-63.
15. Rad M, Jaghouri E, Sharifipour F, Rakhshani MH. The effects of cool dialysate on pruritus status during hemodialysis of patients with chronic renal failure: a controlled randomized clinical trial. Iran Red Crescent Med J. 2017;19(1):e34759.
16. Sajadi M, Gholami Z, Hekmatpour D, Soltani P, Haghverdi F. Cold dialysis solution for hemodialysis patients with fatigue: a cross-over study. Iran J Kidney Dis. 2016;10(5):319-24.
17. Rad M, Shomoossi N, Mirhosseini Z, Kashani E. Can cool dialysate alleviate restless leg syndrome in hemodialysis patients. J Res Med Sci. 2017;22:124.
18. Sakkas GK, Tsaknaki E, Rosa CS, Giannaki CD, Krase AA, Lavdas E, et al. The effect of cold dialysis in motor and sensory symptoms of RLS/WED occurring during hemodialysis: a double-blind study. ASAIO J. 2018;64(1):110-4.
19. Aliasgharpour M, Rafii F, Abbasi Z. The effect of stretching exercises on the quality of life of hemodialysis patients with restless legs syndrome. Iran J Nurs. 2014;27(90):94-101.
20. Mitchell UH. Nondrug-related aspect of treating Ekbom disease, formerly known as restless legs syndrome. Neuropsychiatr Dis Treat. 2011;7:251-7.
21. Shahgholian N, Jazi SK, Karimian J, Valiani M. The effects of two methods of reflexology and stretching exercises on the severity of restless leg syndrome among hemodialysis patients. Iran J Nurs Midwifery Res. 2016;21(3):219-24.
22. Allen RP, Auerbach S, Bahrain H, Auerbach M, Earley CJ. The prevalence and impact of restless legs syndrome on patients with iron deficiency anemia. Am J Hematol. 2013;88(4):261-4.
23. Jones CB, Bargman JM. Should we look beyond Kt/V urea in assessing dialysis adequacy? Semin Dial. 2018;31(4):420-9.
24. Walters AS, LeBrocq C, Dhar A, Hening W, Rosen R, Allen RP, et al. Validation of the international restless legs syndrome study group rating scale for restless legs syndrome. Sleep Med. 2003;4(2):121-32.
25. Downie G, Krimsky W. Response to spray cryotherapy in a patient with adenocarcinoma in the parietal pleura. Respiration. 2010;80(1):73-7.
26. Palmieri-Smith RM, Leonard-Frye JL, Garrison CJ, Weltman A, Ingersoll CD. Peripheral joint cooling increases spinal reflex excitability and serum norepinephrine. Int J Neurosci. 2007;117(2):229-42.
27. Liu GJ, Wu L, Wang SL, Ding L, Xu LL, Wang YF, et al. Incidence of augmentation in primary restless legs syndrome patients may not be that high: evidence from a systematic review and meta-analysis. Medicine. 2016;95(2):e2504.
28. Mustafa RA, Bdair F, Akl EA, Garg AX, Thiessen-Philbrook H, Salameh H, et al. Effect of lowering the dialysate temperature in chronic hemodialysis: a systematic review and meta-analysis. Clin J Am Soc Nephrol. 2016;11(3):442-57.