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The Effect of Increasing Blood Flow Rate on Severity of Uremic Pruritus in Hemodialysis Patients: A Single Clinical Trial

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Conflicts of interest: There are no conflicts of interest for the present study.

Funding: There is no funding for the present study to declare.

Acknowledgment: This article is the extracted from master's thesis that approved in Tehran University of Medical Sciences with the contract number of 132/1393, IRCT code 201110292226N6 and code of ethics 12809 in 2011. In this regard, the researchers would like to give their gratitude to the deputy of Nursing and Midwifery School of Tehran University of Medical Sciences, personnel of hemodialysis wards of hospitals affiliated to Tehran University of Medical Sciences, and all patients who have had the necessary cooperation to carry out this research.

Abstract: Background: Although the prevalence of uremic pruritus has decreased compared to the past, the problem still remains as a matter of health and a major challenge of research in medical field, and has no effective treatment at present. This study aimed to investigate the effect of increasing blood flow rate on severity of uremic pruritus in hemodialysis patients in Iran.

Methods: This clinical trial was performed on 60 hemodialysis patients that referred to hospitals affiliated to Tehran University of Medical Sciences and these patients were selected through the convenience method and were treated for four weeks. They were divided into two groups of experimental and control as random allocation block, and studied for 4 weeks. Information on pruritus severity was collected using a researcher-made questionnaire in three steps of before intervention and two and four weeks after start of intervention. The rate of blood flow was increased in the first two weeks and the second two weeks by 25 and 50 rounds per minute (rpm) compared to the mean rate of blood flow of hemodialysis device in the last two sessions before intervention. Data were analyzed using the tests Mann–Whitney, Fisher, and *t*-test.

Results: Analysis of data from 50 persons in both groups who completed the study revealed a significant difference between the groups in the severity of pruritus between the two sessions of hemodialysis (pruritus at home) at the end of the first two weeks of the intervention (<0.05) and the number of cases of pruritus (<0.05) at the end of the study.

Conclusions: Increasing blood flow for hemodialysis machine can induce significant statistical and clinical reduction in the severity and the frequency of pruritus in hemodialysis patients and can be help to be improve the quality of life of these persons by increased the blood flow rate.

Keywords: Blood flow rate ■ Uremic pruritus ■ Hemodialysis machine pump

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<http://dx.doi.org/10.1016/j.jnma.2017.04.008>

INTRODUCTION

Pruritus is an unpleasant sensation that stimulates the desire to scratch. It is an important symptom of skin diseases and a frequent manifestation of systemic diseases. Uremia is the leading cause of pruritus among all systemic diseases.¹ The complication affects 50-90% of peritoneal dialysis and hemodialysis patients and its symptoms range from mild, local to severe, generalized.² The rate of pruritus in hemodialysis patients was 52% in 2011³ and 45.2% in 2015.⁴ Uremic pruritus is often uncontrollable and leads to many problems in hemodialysis patients,¹ so that the quality of life is drastically reduced and less attention has been paid at the bedside to the psychosocial impact of skin dryness and uremic pruritus.⁵ Increased severity of pruritus is associated with frequency of scratching and sleep disturbance,² with negative effect on sleep and mood,⁶ resulting in decreased quality of life of these patients² and since pruritus occurs mostly at night⁶ it causes sleep disruption is 70% in patients. Prognosis of patients with severe pruritus is significantly worse than other patients,⁷ so that it can increase the risk of mortality and morbidity by 17% and this relationship between mortality and pruritus can also be attributed to poor quality of sleep.⁸

Pathophysiological mechanism of pruritus associated with chronic renal failure still remains unknown.⁹ Some references have been attributed the intensity of uremic pruritus to the level of calcium, phosphorus, and urea nitrogen before dialysis.⁷ Many pharmacological and non-pharmacological therapies have been used for the treatment of uremic pruritus including antihistamines, mild soaps, local anesthesia, cholestyramine, ultraviolet light, acupuncture, parathyroidectomy, gamma rays, oral activated charcoal, and increased dialysis adequacy.^{10,11} Some studies such as Heliotherapy that after treatment of patients with severe pruritus (grade 4), the intensity of pruritus has decreased from grade 4 to grade 3 in 41.66% and it has decreased from grade 4 to grade 2 in 8.33%¹² and capsaicin 3% ointment that reduced average of pruritus score

from 15.9 to 2.5 during the 4 weeks, it has been used in the treatment of uremic pruritus.¹³ Although the prevalence of uremic pruritus has decreased compared to the past, the problem still remains as a matter of health⁹ and a major challenge of research in medical field,¹⁴ and has no effective treatment at present.²

One indicator in study of therapeutic effects of hemodialysis can be dialysis adequacy that cause of increased or decreased of symptoms¹⁵ and to increase dialysis adequacy can be used to increase blood flow rate.^{16,17} Damage kidney function leads to accumulation of different materials of pruritus-causing and accumulation of waste products such as urea and phosphorus is one of the reasons of pruritus in hemodialysis patients¹¹; also according to studies increase blood flow rate is effective in removing phosphorus¹⁸ and increasing adequacy of dialysis,^{16,17} now the question is whether increased blood flow rate will change the severity of pruritus or not. According to literature review no study was performed in this regard therefore this study aimed to investigate the effect of increasing blood flow rate on severity of uremic pruritus in hemodialysis patients in Iran.

METHODS

This study is a single-blind clinical trial (the interviewer did not know the patients grouping into intervention and control) performed after approval in 2011 by Tehran University of Medical Sciences. In this study due to lack of sufficient sample in a center and sampling is performed by Sampling Access Method. In this way, patients at one center were selected as the intervention group and those in two other centers as controls group. The selected hospitals were similar in terms of treatment type and equipment. Initially the number of samples was 30 subjects in each group which declined to 25 due to sample drop. It is noteworthy that the subjects were matched in terms of age and gender. The type of filter and type of anti-pruritus medications (Renagel and Hydroxyzine) were the same during the study. The data were collected in this study through self-report during interviews, observation of the files and recording the information in questionnaire and the mean changes in body weight were measured with a digital scale (Seca marking) and blood pressure with a sphygmomanometer (Welch allyn marking). The data were collected in this study through self-report during interviews which contains four parts of testimonial, inclusion and exclusion criteria, demographic data, and recording the information about machine (round of pump) and questions related to disease. Questions about the disease were included hemodialysis history, cause of

kidney failure, infusion times of eprex in a week, use of anti-pruritus drug, pruritus immediately before, during, immediately after and between two sessions of hemodialysis (at home), the number of cases of pruritus in a day pruritus without scratching, mild (1-3), moderate (4-6), and severe (7 and more), and the site of pruritus (pruritus in a local member and more than one member of general). It is noteworthy that the positive pruritus in the each mentioned times, the patient responds to questions related to the severity of pruritus that was divided into three parts of mild (pruritus without scratching), moderate (scratching without scrape), and severe (scratching with scrape). Inclusion criteria were included hemodialysis for at least six months, hemodialysis duration three times a week for 4 h, pruritus (mild, moderate, and severe), absence of severe heart disease, and exclusion criteria were blood pressure less than 100/60 mmHg, hospitalization due to acute problem, death, skin disease that cause pruritus, active hepatobiliary disease. Bicarbonate dialysate, hemodialysis machine (Fresenius 4008B), heparin, sets, and filter used for all patients in the study were the same. At first average of pump velocity was considered two sessions before the intervention and then 25 rpm in the first two weeks (6 session) and 50 rpm in the second two weeks (the second six session) compared to the mean pump velocity in two sessions. The intervention was performed as twelve 4-h sessions for four weeks. In the first 15 min of each session, the pump velocity was low and then was gradually increased to the desired velocity. Drugs were recorded that patients used for pruritus and were asked to patients that are not change these drugs. During the study, Patients' blood pressure and weight (for the 4-h hemodialysis) were measured and recorded by the investigator before initiation of dialysis. It is noteworthy that in all sessions, the researcher and two research assistants attended in the hospitals and the conditions of patients' hemodialysis were stable. Information questionnaire was collected verbally in three stages, before the intervention, at the end of the second week and at the end of the fourth week. The tool's validity was determined using experts' comments (10 persons) and content validity and reliability through the Pearson correlation coefficient (90%). To analyze the data based on normal Kolmogorov-smirnov of nonparametric tests was used Exact fisher's test (age, education, marital status, and cause of kidney failure), independent *t*-test (duration of hemodialysis, duration of pruritus, the frequency of pruritus), Chi-square (gender, site of pruritus, and use of anti-pruritus drug and Eprex), Mann-Whitney (severity pruritus), and ANOVA with repeated measures (frequency of pruritus before and after in each group) and software of SPSS-18. Values are significant at $P < 0.05$.

The study is approved by the ethical committee of Yasuj University of Medical Sciences. The study was performed according to Helsinki principals in ethics. All of the participants signed a written constant.

RESULTS

During the study 72% and 52% of patients in the experimental and control group consumed medications such as antihistamines, renagel, hydroxyzine, Erythropoietin and Gabapentin respectively ($P > 0.05$).

The results related to demographic and clinical characteristic have been illustrated in Table 1.

As shown in Table 2, the two groups had no statistically significant difference regarding the severity in all four stages before intervention, while the severity of pruritus between the two sessions of hemodialysis became significant after two weeks and four weeks using the Mann–Whitney test ($P \leq 0.05$).

The two groups had no statistically significant differences in terms of pruritus frequency per day before and two weeks after the intervention, while the difference became significant after four weeks ($P \leq 0.05$, independent t -test) (Table 3).

Analysis of variance with repeated measures showed a significant difference between before and after the intervention in the experimental group in terms of pruritus frequency ($P \leq 0.05$). No significant difference in improvement the number of cases of pruritus during treatment between two groups and the number of cases of pruritus significantly decreased each time. There was significant effect between type of group and pruritus improvement during the time and the implication is that achieved improvement at any point of time compared to

the other time points. The results related to site of pruritus have been illustrated in Table 4.

DISCUSSION

The results of this study showed that increased blood flow rate causes a change of pruritus terms from generalized to locally, reduced the severity of pruritus between the two sessions of hemodialysis (pruritus at home) and the number of cases of pruritus in hemodialysis patients but it is not effect of pruritus immediately before, during, immediately after hemodialysis. Two weeks after the intervention, the severity of pruritus reduced immediately before, during, immediately after in all three steps and between two sessions of hemodialysis after four weeks of intervention in the experimental group, but in the control group, pruritus decreased in the first and last steps and remained unchanged in the second steps and increased in third steps.

The study of Borzoo et al showed that increasing blood flow rate is effective in removal of phosphorus and increasing of hemodialysis adequacy.^{16,18} Another study titled the impact of increased blood flow rate on dialysis adequacy in hemodialysis patients with low Kt/v by Kim et al. This study showed that blood flow rate increased by 15–20% can increase dialysis adequacy compared to before.¹⁹ In addition, a study by Shahdadi et al showed that an appropriate increase in blood flow rate can improved dialysis adequacy.²⁰ Also a study by Gotzwiller approved the impact of increased round of pump from 200 to 250 on removal of phosphorous.¹⁷ In another study by Aliasgharpou et al increasing blood flow rate improves sleep disturbance Induced By Uremic Pruritus in hemodialysis patients.²¹ Therefore, since some references have

Table 1. Table of demographic and clinical characteristic.

	Experimental	Control	P-value	Statistic
Age (40-59) ^{***}	52	44	>0.05	0.00
Male [*]	68	86	>0.05	$\chi^2 = 0.00$, df = 1
Under high school diploma ^{**}	58	52	>0.05	0.55
Married ^{**}	100	92	>0.05	0.49
History of hemodialysis (1-5 years) ^{***}	44	44	>0.05	-0.34
Cause of disease (hypertension) ^{**}	48	52	>0.05	0.77
History of pruritus less than one year ^{***}	52	72	>0.05	1.36

Two groups was not significant demographic and clinical characteristic ($P \geq 0.05$).

^{*}Chi-square test.

^{**}Exact fisher's test.

^{***}Independent T-test.

Table 2. Table of severity of uremic pruritus difference between the two groups.

Pruritus severity		Immediately before hemodialysis				During hemodialysis				Immediately after hemodialysis				Between 2 session hemodialysis			
		Low	Medium	Severe	Without pruritus	Low	Medium	Severe	Without pruritus	Low	Medium	Severe	Without pruritus	Low	Medium	Severe	Without pruritus
Before intervention	Control	0	8	4	88	4	40	0	56	0	12	0	88	0	72	28	0
	Experimental	0	12	20	68	8	36	4	52	0	16	16	68	0	52	44	4
P-value		>./05				>./05				>./05				>./05			
Mann–Whitney																	
Statistic		-1/54				-./27				-1/51				-1/51			
2 weeks after	Control	0	16	4	76	4	44	0	52	0	12	0	88	1	76	4	8
	Experimental	0	8	8	84	12	28	0	60	8	20	0	72	0	88	12	0
P-value		>./05				>./05				>./05				<./05			
Mann–Whitney																	
Statistic		-./83				-./26				-1/47				-1/97			
4 weeks after	Control	4	16	4	76	4	44	0	52	0	20	0	80	0	80	16	4
	Experimental	8	4	0	88	24	0	0	76	16	0	0	84	52	24	0	24
P-value		>./05				>./05				>./05				<./05			
Mann–Whitney																	
Statistic		-./94				-./97				-./7				-2/23			

The two groups showed no statistically significant difference in terms of pruritus severity in all four stages before intervention, but after two and four weeks after start of intervention, pruritus severity between two hemodialysis sessions became significant (Mann–Whitney. P = 0.04 and P = 0.02).

Table 3. Table of differences between the two groups in the number of cases of pruritus per day.

	Experimental group			Control group			P-value	Statistic
	Mild	Medium	Severe	Mild	Medium	Severe		
Before intervention	24	28	48	24	44	32	>0.05	1/88
2 weeks after	40	24	32	12	76	12	>0.05	.42
4 weeks after	56	16	12	8	72	20	<0.05	-3/74

The two groups had no statistically significant difference in the number of cases of pruritus before intervention. Two weeks after the intervention the difference was not significant either. However, after four weeks it became significant ($P \leq 0.05$, independent T-test).

mentioned that cause of pruritus in hemodialysis patients is increased of waste resources include phosphor, calcium, and urea nitrogen.^{7,11} The results of the mentioned studies support the findings of this study. It is noteworthy that results of these studies are the result of increased blood flow rate in a session but the present study was conducted in 12 dialysis sessions.

Zuker et al stated that resting of patients worsens pruritus⁶ and insignificance of pruritus during and immediately after hemodialysis can be justified to this fact, because patients are at rest during hemodialysis. Insignificance of pruritus immediately before hemodialysis may also be due to accumulation of waste products generated between two hemodialysis sessions. In this study, the frequency of pruritus at the end of intervention was reduced in the experimental group (the result could be due

to the long duration of the intervention compared with other studies and the reasons of reducing the severity of pruritus that are mentioned in the previous paragraph). The mentioned studies have measured the impact of increased blood flow rate on some electrolytes and dialysis adequacy. However, the present study assessed the effect of intervention on pruritus as one of the complications of renal failure and hence the accumulation of waste products. Therefore, it seems that increased blood flow rate improves pruritus of patients through removal of electrolytes and waste materials and increases hemodialysis adequacy.

The results of this study show that increasing blood flow rate of hemodialysis machine is causing reduce the severity and number of cases of pruritus and limiting it from general to locally.

Table 4. Table of Local Pruritus (the site of itching).

Time	Local of pruritus	Group		P-value	Statistic
		Experimental	Control		
Before intervention	Local	32	20	>0.05	$\chi^2 = 4.50$, df = 1
	General	68	80		
	Without pruritus	0	0		
2 weeks after	Local	52	8	<0.05	1.91
	General	44	92		
	Without pruritus	4	0		
4 weeks after	Local	56	8	<0.05	$\chi^2 = 18/87$, df = 2
	General	28	92		
	Without pruritus	0	0		

Two groups was not significant in site of pruritus before intervention ($P \geq 0.05$) but it was significant two and four weeks after the intervention (<0.05 Chi-square test).

Limitations and suggestions

Pruritus is a mental phenomenon making difficult its measurement and it may be influenced by many variables such as air temperature, skin moisture, and nutrition and results of this study is resulting thesis and there was a time limitation. Therefore, it is suggested that a study can be done with the same title and with simultaneous control of nutrition and environmental factors or with more time.

Implication fore practice

This result can be help to be improve the quality of life of these persons by increased the blood flow rate in the patient's tolerance and reduced the severity of pruritus, and this intervention can be used to help patients due to the fact that it can be done without additional spending time and manpower.

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