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Research Article

The Effect of Acupressure on the Severity of Pruritus and Laboratory Parameters in Patients Undergoing Hemodialysis: A Randomized Clinical Trial

Fatemeh Karjalian [1], Marzieh Momennasab [2,*], Amin K. Yoosefinejad [3], Shahrokh E. Jahromi [4]

[1] Student Research Committee, School of Nursing and Midwifery, Shiraz University of Medical Sciences, Shiraz, Iran
[2] Department of Nursing, School of Nursing and Midwifery, Shiraz University of Medical Sciences, Shiraz, Iran
[3] Physical Therapy Department, School of Rehabilitation Sciences, Shiraz University of Medical Sciences, Shiraz, Iran
[4] Nephrology-urology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

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ABSTRACT

Background: Uremic pruritus is a common boring complaint in patients suffering from chronic renal failure. Owing to cost and the side-effects of medications, complementary therapies are more attractive for pruritus treatment.
Objectives: The aim of this study is to determine the effect of acupressure on the severity of pruritus and some laboratory parameters in patients undergoing hemodialysis.
Materials and methods: The present clinical trial was conducted on 90 patients undergoing hemodialysis who were allocated in intervention, sham control, and negative control groups (30 in each group). Pressure was applied on SP6, SP10, ST36, and LI11 points in the intervention group and on ineffective points for the sham control group. The negative control group received routine care. The severity of pruritus was measured using the numeric rating scale before, two weeks, and five weeks after intervention. The laboratory parameters were measured before and after the intervention.
Results: There was a significant reduction in the severity of pruritus over the course of the study in the intervention and sham control groups ($p = 0.001$). In addition, significant differences were observed at the end of the intervention in terms of serum phosphorus ($p = 0.045$) and parathyroid hormone ($p = 0.004$) levels between groups.
Conclusion: Acupressure can improve the severity of pruritus dramatically in hemodialysis patients. It can also reduce serum phosphorus and parathyroid hormone levels, which affect pruritus, significantly. Therefore, this simple and inexpensive intervention may be recommended for reducing uremic pruritus among patients undergoing hemodialysis.

1. Introduction

Chronic kidney failure is one of the main causes of pruritus caused by systemic diseases. Although not fatal, this complication is very annoying and affects the patients' quality of life. Uremic pruritus is an unpleasant and distressing subjective complaint that arouses the desire to scratch and renders the skin function as a major protective barrier ineffective [1, 2]. Uremic pruritus usually appears before hemodialysis treatment and begins to progress. Uremic pruritus affects 15% to 49% of patients with chronic kidney failure before dialysis and 50% to 90% of patients undergoing hemodialysis [3]. The prevalence of uremic pruritus has increased in recent decades and ranges from 10% to 77% [4]. Uremic pruritus can extend to the entire body or be localized in a particular area; it can also be continuous or intermittent. Various treatments have been proposed to abate pruritus, including medicinal therapies such as oral antihistamines, gabapentin, naltrexone, Nalfurafine, active

* Corresponding author. Department of Nursing, School of Nursing and Midwifery, Shiraz University of Medical Sciences, Zand St., Namazee Sq, 7193613119, Shiraz, Iran
E-mail addresses: karjalian1990@gmail.com (F. Karjalian), momennasab@sums.ac.ir (M. Momennasab), yoosefinejad@sums.ac.ir (A.K. Yoosefinejad), shahrokhjahromi@gmail.com (S.E. Jahromi).

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charcoal, and so on [5]. Because of the cost and the side-effects of these medications such as drowsiness, fatigue, weakness, dizziness, headache, dystonia or blurred vision, anxiety, memory problems, nausea, vomiting, joint pain, and seizures [6, 7], there has been greater emphasis on complementary therapies for reducing pruritus, including aromatherapy [8], yoga [9], acupressure [10], and acupuncture [11].

Acupressure is one such complementary method in which points located in different energy-carrying meridians are stimulated by pressure, using fingertips, palms, small beads, or especial devices [12]. Acupressure enhances well-being by restoring body energy and promoting blood circulation and neurotransmitters secretion. Acupressure as a nonaggressive, simple, and cost-effective method recommended for many symptoms and problems in different diseases [13].

Some studies have demonstrated the beneficial effects of acupressure on the various problems experienced by hemodialysis patients, including fatigue [14], xerostomia [15], musculoskeletal pains [16], sleep quality [17], and anxiety [18]. Very few studies have been conducted on the effect of acupressure on the severity of pruritus in patients undergoing hemodialysis [19-22]. One of these studies showed that acupressure reduces uremic pruritus through the electrical stimulation of the skin [22]. Another study also found auricular acupressure effective [20]. Yet, there have been very few studies on the effect of this intervention on the severity of pruritus and serum biochemical parameters in these patients. The aim of this study is to determine the effect of acupressure (points SP6, SP10, ST36, and LI11) on the severity of pruritus and some laboratory parameters in patients undergoing hemodialysis.

2. Materials and methods

2.1. Design and settings

The present randomized, double-blind, before-after clinical trial was conducted from May 2017 to February 2018 in the hemodialysis wards of two hospitals affiliated to Shiraz University of Medical Sciences in the south of Iran.

2.2. Sampling and randomization

Based on the results obtained by Kılıç Akça et al. [19] in 2013 and taking into account a test power of 0.9, $\alpha = 0.05$ and a potential attrition of 10%, the sample size was determined as 90 (30 per group). The samples were randomly divided into the intervention, sham control, and negative control groups by block randomization in blocks of three.

The inclusion criteria consisted of age 18 to 65 years, at least a six-month dialysis history, complaints of pruritus for at least three months, undergoing 3-4 hours of hemodialysis three times per week and healthy pressure point in terms of integrity and sense and no hepatic disorders or immunodeficiency. The patients who had received new medications or a change in their dosage of antipruritus medications over the last month or had experienced severe physical or mental stress or a change in their state, such as the incidence of active infection, surgery, and kidney transplant, were excluded from the study.

Of the total of 115 patients treated in the two noted centers, 18 were not included in the study for failing to meet the eligibility criteria, and 90 patients were then randomly selected and allocated to the three groups. There were no cases of sample withdrawal over the course of the study (Fig. 1).

2.3. Measurement

The severity of pruritus was measured using the numeric rating scale (NRS), which is a 10-point scale from zero (no pruritus) to ten (intolerable pruritus), and the patients were required to identify the severity of their pruritus on this scale. The NRS is a standard and popular scale for determining the severity of pruritus, and its validity and reliability have been confirmed for this purpose. The test–retest correlation coefficient of this tool was 0.83 in a previous study [23].

To assess the laboratory parameters, 5-CC intravenous blood samples (2 CC oxalate and 3 CC clot) were taken from each patient immediately before their hemodialysis and were sent to laboratory. All the tests were carried out in the central laboratory of each hospital by the same technician and the same technique. Sodium (Na) and Potassium (K) were measured by electrolyte analyzer (Medica EasyLyte® – USA), and blood urea nitrogen (Bun), creatinine (Cr), calcium (Ca), and phosphorus (P) were measured by chemical autoanalyzer (Birui- China).

An automated hematology analyzer (Sysmex XWTM-100- Kobe, Japan) was used to measure hematological indices including hemoglobin (Hb) and hematocrit (Hct). Parathyroide hormone (PTH) was measured by chemiluminescence immunoassay (ARCHITECT i2000sr - USA).

2.4. Intervention and data collection

In the intervention group, pressure was applied on SP6, SP10, ST36, and LI11. Some studies have previously demonstrated the effects of the stimulation of these points (individually and in combination) on pruritus [19, 21]. The location of these points is listed below:

- LI11: on the outside end of the crease on the elbow
- SP10: with knee flexed, 2 cun above the superior medial border of the patella on the bulge of the medial portion of vastus medialis
- SP6: 3 cun directly superior to the tip of the medial malleolus on the posterior border of tibia
- ST36: 3 cun inferior to ST35, one finger width lateral to the anterior crest of the tibia, in the tibialis anterior muscle

Symmetrical pressure was applied continuously for one minute, followed by three intermittent pressures on each point. The researcher applied a 4-kg pressure with the thumb. The amount of pressure was adjusted and practiced on a pressure gauge. The researcher and her assistant trained in six 2-hour sessions working with acupressure specialist using Saehan Hydraulic Pinch Gauge sh 5005, Sahean Com, South Korea device, and the accuracy of the points and the right technique with a 100% precision was ensured on 20 patients undergoing hemodialysis under the supervision of an expert.

For the sham control group, pressure was applied at 2-cun distances of the main points with the same technique and duration. Both groups received the intervention three times per week right before their hemodialysis for four weeks. The negative control group received routine care.

All the participants completed informed consent forms, a demographic questionnaire, and pruritus NRS before the intervention. Blood samples were then taken from all the three groups. By the end of the second week of the intervention, all the patients completed the NRS again. One week after the intervention, blood samples were retaken from the patients, and they completed the NRS once again. Blood sample collection, laboratory testing, and

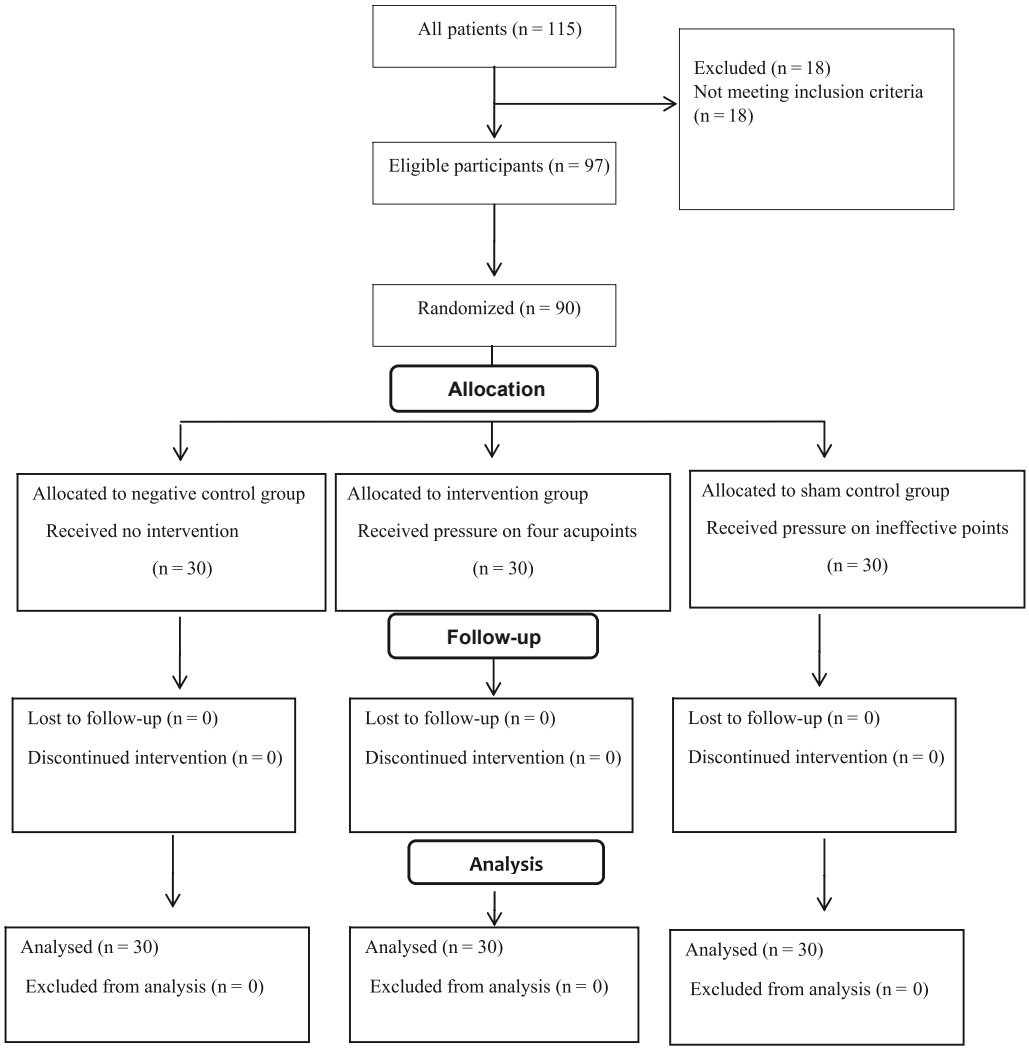

Figure 1. Flow of participants.

statistical analysis were carried out by people with no knowledge of the samples' allocation in the three groups.

2.5. Ethical considerations

At the beginning of the study, researchers provided verbal explanations about the objective and methods and then all participants signed written informed consents form. The confidentiality and anonymity were guaranteed, and gender compatibility was observed between the patients and the interventioners. The present study was approved by the Research Ethics Committee of Shiraz University of Medical Sciences (No: IR. SUMS.REC.1396.2.9) and registered at the Iranian Registry of Clinical Trial's website (reference number: IRCT201704197546N8).

2.6. Data analysis

Data were analyzed with SPSS 18. Owing to normal distribution of data, repeated measure ANOVA was used for comparing mean of pruritus scores between three groups in three time points, and independent and paired t-tests were used for comparing laboratory parameters between and within groups. Besides, $p < 0.05$ was considered as statistically significant. Data analysis were performed by someone who was unaware of the intervention.

3. Results

In accordance with the results obtained, participants' mean ± SD of age was 54.4 ± 10.31 years, and the dialysis duration was 7.04 ± 3.01 years, and the history of pruritus was 22.83 ± 9.71 months. The majority of the participants were men (55.1%), married (83.3%), and had below high school education (42.2%). No significant differences were observed between the three groups in terms of demographic and clinical details such as age, gender, marital status, employment status, education, dialysis duration, and history of pruritus ($p > 0.05$; Table 1).

No significant differences were observed between the intervention, sham control, and negative control groups in terms of the severity of pruritus before the intervention ($p = 0.055$). The results of the repeated measures test showed that the effect of time, the effect of group, and the effect of time and group were significant ($p = 0.001$). The severity of pruritus reduced over the course of the study in the intervention and sham control groups, but this reduction was greater in the intervention group than in the sham controls. The scores of the severity of pruritus remained constant in the negative control group, and no change was observed. Nonetheless, two weeks after beginning the intervention, no significant differences were observed between the three groups in the severity of pruritus ($p = 0.66$), but five weeks after the starting intervention,

Table 1
Demographic and clinical characteristics of patients in the intervention, sham control, and control groups.

Characteristic	Groups				
	All patients (n = 90)	Intervention (n = 30)	Sham control (n = 30)	Control (n = 30)	*p*-value
Age (year)					
Mean (SD)	54.4(10.31)	55.31(8.88)	52.67(10.89)	55(11.14)	0.54[a]
Sex, n (%)					
Female	44(48.9)	15(50)	14(46.7)	17(57)	0.14[b]
Male	46(51.1)	15(50)	16(53.3)	13(43)	
Marital status, n (%)					
Single	15(16.7)	4(13.3)	5(16.7)	6(20)	0.78[b]
Married	75(83.3)	26(86.7)	25(83.3)	24(80)	
Education, n (%)					
Illiterate	19(21.1)	6(20)	8(26.6)	5(16.7)	
Under diploma	38(42.20)	14(46.7)	11(36.7)	13(43.3)	0.86[b]
Diploma or higher	33(36.7)	10(33.3)	11(36.7)	12(40)	
Job status n (%)					
Unemployed	43(47.8)	13(43.3)	13(43.3)	17(56.7)	
Housewife	35(38.9)	13(43.3)	12(40)	10(33.3)	0.82[b]
Employed	12(13.3)	4(13.4)	5(16.7)	3(10)	
Use of pruritus drugs n (%)					
Yes	10(11.1)	2(6.7)	4(13.3)	4(13.3)	
No	80(88.9)	28(93.3)	26(86.7)	26(86.7)	0.64[b]
Hemodialysis treatment duration (year)					
Mean (SD)	7.04(3.01)	6.93(2.97)	6.17(2.72)	8.03(3.14)	0.05[a]
Pruritus duration (month)					
Mean (SD)	21.61(9.18)	22.69(9.5)	19.28(8.10)	22.83(9.71)	0.25[a]

[a] ANOVA.
[b] Chi square test.

the severity of pruritus decreased significantly in the intervention group, and the mean ± SD of the severity of pruritus declined from 8.37 ± 1.22 at the start of the study to 2.87 ± 0.90 five weeks after the starting intervention ($p < 0.001$; Fig. 2).

Regarding the effect of acupressure on the laboratory parameters, the ANOVA showed significant differences between the three groups in serum levels of phosphorus ($p = 0.045$) and PTH ($p = 0.004$). The paired t-test showed a significant reduction in serum levels of these two parameters in the intervention group after performing acupressure ($p = 0.02$ for phosphorus and $p = 0.029$ for PTH). Although serum sodium levels reduced significantly in all three groups over the three stages, the ANOVA did not show a significant difference between the three groups ($p > 0.05$). No significant differences were observed between the three groups

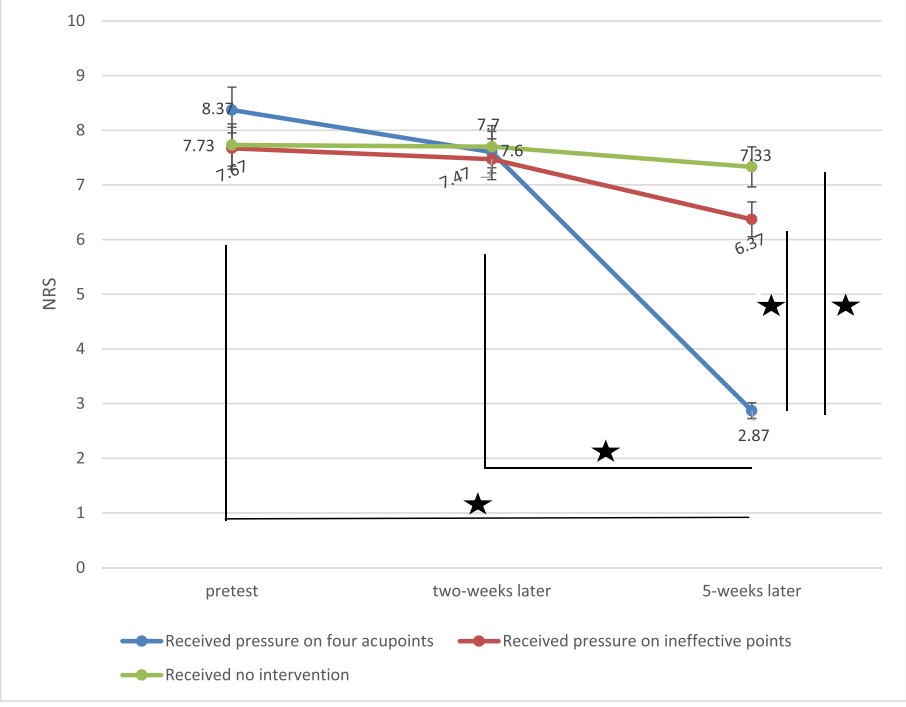

Figure 2. Comparison of the severity of the pruritus among the intervention, sham control, and control groups in three phases (before, two weeks, and five weeks after the starting intervention).

before and after the intervention in terms of the other parameters including sodium, Bun, Hb, Hct, Ca, Cr, and potassium ($p > 0.05$) [Table 2). No side-effects were reported by the patients during the study.

4. Discussion

Dialysis is associated with several complications but using complementary and alternative therapies can help reduce these complications. The present findings showed a significant reduction in the severity of pruritus in the patients undergoing hemodialysis in the intervention group as a result of acupressure. This finding agrees with the results reported by Yan et al. [20] in their study of the effect of ear acupressure on the severity of pruritus in patients undergoing hemodialysis in China and also the study by Kılıç Akça et al. [19] conducted in four hemodialysis centers in Turkey to determine the effect of acupressure using the Transcutaneous Electrical Nerve Stimulation method on the severity of pruritus in patients undergoing hemodialysis. The results of another study conducted to compare the effect of acupressure using two different methods, i.e. using pressure applied by the fingers and by electrical stimulation, on the severity of pruritus in patients undergoing hemodialysis showed that both methods can reduce the severity of pruritus dramatically [22]. This study concurs with the present study in terms of the duration of the intervention and the pressure points used. In a study conducted in the US, Lee et al. [24] assessed the effect of acupressure on pruritus and atopic dermatitis in skin patients and showed a reduction in the severity of pruritus in the intervention group. Overall, acupressure can be said to reduce uremic pruritus in patients undergoing hemodialysis. Nonetheless, the present findings showed no significant reductions in the severity of pruritus by the end of the second week of the intervention, but a reduction was observed in pruritus after five weeks of acupressure, which shows that acupressure is unable to reduce pruritus in the short-term but can be effective in periods longer than one month.

Many etiologies have been proposed for uremic pruritus, including a rise in the number of mast cells [25]. These cells release large numbers of inflammatory markers such as histamine, tumor necrosis factors, and IL6. One study showed that the activation of acupressure points, especially LI11, can destroy mast cells in the connective tissue and can reduce visceral inflammation and prevent the destruction of the 'friendly' cells that can cause pruritus in patients undergoing hemodialysis [26, 27].

Moreover, in accordance with Chinese medicine, pruritus is caused by a disharmony between the Mu and Kappa receptors. Accordingly, the activation of Mu receptors and the obstruction of Kappa receptors cause pruritus, and acupressure activates Kappa receptors by applying pressure on specific points [5].

The anticoagulative effects of acupressure can also activate the alpha receptors of opioids, which have positive effects on uremic pruritus. The anticoagulative effect of acupressure can be due to the effects exerted on the hypothalamus–pituitary–adrenal axis, the nervous system, and the cerebral neurotrophic factor [28, 29].

The present findings showed a significant reduction in the phosphorus and parathyroid factors in the blood compared with the base values. These biochemical parameters have a role in the development of uremic pruritus. Renal dysfunction impairs metabolism and serum Ca–P levels and leads to an increased phosphorus level and the further release of parathormone. Hyperphosphatemia and hyperparathyroidism cause pruritus in uremic patients [30-32]. No significant differences were observed in the other laboratory factors, including Hb, Hct, Cr, Ca, and potassium; however, serum sodium levels reduced in all the three groups after the intervention, which could be associated with other variables, such as the quality of hemodialysis. Unlike the present study, the study by Che-Yi et al. [21] showed no significant differences in these biochemical parameters following acupressure at LI11 in patients with hemodialysis. This disparity of findings could be due to the differences in the points used because they only used one point, whereas four points were used in the present study.

The results of another study showed that ear acupressure reduces the severity of pruritus in patients with hemodialysis, but biochemical parameters such as P-tryptase, Ca, phosphorus, and PTH did not change, despite the significant difference in the serum histamine level [20]. In a study conducted by Kılıç Akça [19] on the effect of acupressure using the TENS method on the severity of

Table 2
Comparison of the laboratory parameters among the intervention, sham control, and control groups in two phases (before and after the intervention).

Parameter[c]	Groups						*p*-value Post-test[b]
	Intervention		Sham control		Control		
	Before	After	Before	After	Before	After	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Hb	11.5(1.42)	11.32(1.37)	11.47(1.42)	11.48(1.37)	11.34(1.37)	11.34(1.37)	0.877
p-value[a]	0.2		0.1		0.24		
Hct	34.68(5.4)	35.01(4.56)	33.66(5.82)	35.67(4.64)	36.4(5.37)	36.02(4.32)	0.135
p-value[a]	0.27		0.983		0.158		
Ph	8.78(0.93)	7.4(0.72)	8.54(0.79)	8.69(0.64)	8.61(0.56)	8.7(0.7)	**0.045**
p-value[a]	**0.02**		0.748		0.224		
Cr	8.28(2)	8.94(1.4)	8.44(1.7)	8.86(1.8)	8.8(2)	9.1(1.8)	0.32
p-value[a]	0.1		0.1		0.5		
Na	138.63(3.7)	140.13(3.5)	138.1(3.54)	139.77(4.34)	137(4.03)	138.6(3.92)	0.277
p-value[a]	0.001		0.002		0.0001>		
K	6.1(0.81)	6.56(1.38)	6.16(1.1)	6.65(1.27)	5.95(0.8)	6.65(1.79)	0.811
p-value[a]	0.1		0.1		0.2		
PTH	1114.9(200.2)	981.9(119)	1056.1(168.4)	1091.5(134)	1002.6(126)	1111.5(206.6)	**0.004**
p-value[a]	**0.029**		0.4		0.1		
BUN	54.97(12.74)	55.25(12)	55.23(19.28)	56.43(17.7)	59.13(14)	60.83(12.5)	0.48
p-value[a]	**0.1**		0.084		0.717		
Ca	7.33(1.27)	6.94(1.18)	7.30(0/78)	7.62(1.35)	7.6(0.76)	7.19(1.1)	0.087
p-value[a]	0.053		0.237		0.1		

[a] Paired T-Test
[b] ANOVA.
[c] Hb = hemoglobin, Hct = hematocrit, Ph = phosphorus, Cr = creatinine, Na = sodium, K= potassium, PTH = parathyroide hormone, Bun = blood urea nitrogen, Ca = calcium.

pruritus in patients with hemodialysis, no significant differences were observed in terms of the biochemical parameters.

The present findings showed an improvement in pruritus in the sham control group, even though it was less than that reported in the intervention group. This change in the sham controls' condition can be attributed to psychological inducements. Other studies have also reported significant positive results after acupressure and acupuncture on false points [33-36].

The strengths of the present study include the use of several acupressure points, a three-stage data collection and having two control groups. The study limitations include the fact that pruritus can be affected by various physical, psychological, and environmental factors, which could not be entirely controlled by the researcher, although attempts were made to control these factors by having both a sham and a control group and establishing certain inclusion and exclusion criteria. The short intervention period is another limitation of this study, and future studies are recommended to increase the duration of their interventions.

5. Conclusion and implications for nursing

Overall, acupressure applied manually on SP6, SP10, ST36, and LI11 can reduce the severity of uremic pruritus dramatically in patients with hemodialysis; however, this intervention should last at least one month, as it has no significant short-term effects. It can also reduce serum phosphorus and parathyroid hormone levels, which affect pruritus, significantly. Given its simplicity of application, inexpensiveness and safety, acupressure can be used as a complementary therapy for reducing uremic pruritus in patients with hemodialysis. Nurses can benefit from the present findings for reducing their patients' annoying pruritus and improving their well-being.

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Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

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