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Efficacy of Topical Application of Sweet Almond Oil on Reducing Uremic Pruritus in Hemodialysis Patients: A Randomized Clinical Trial Study

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Abstract

Background: While the application of anti-pruritus medications may be useful for hemodialysis (HD) patients, they are at risk of drug toxicity because of their renal inability to eliminate drug metabolites.
Objectives: To examine the effect of the topical application of sweet almond oil on reducing uremic pruritus in HD patients.
Methods: This study is a randomized clinical trial research. The study population consisted of patients referred in 2013 to the HD ward of Shahid Beheshti hospital, which is affiliated with Yasuj University of Medical Sciences, Iran. From a total of 60 patients, 42 that met the inclusion criteria were selected using a nonrandom sampling method; they were allocated to two groups through a random-allocation method. Sweet almond oil (with a traditional medicine certification and a registration number for the production license) was topically applied on the pruritus location(s) in the intervention group once daily over two weeks. The data were collected using a pruritic score questionnaire at one week and two weeks post-intervention. The data were analyzed using descriptive statistics, such as central tendency and dispersion indices, as well as statistical tests, including repeated measures ANOVA with a P-value significantly less than 0.05 and a confidence interval of 95%.
Results: Pre-intervention, there was no significant difference in the mean scores for the severity of pruritus between the test and control groups, but significant differences were observed between the two groups ($P < 0.05$) at one week and two weeks post-intervention. The result of repeated measures ANOVA for within group comparison shows a significant difference in the mean of pruritus severity pre-intervention (19.63 ± 11.67), one week post-intervention (12.22 ± 11.33), and two weeks post-intervention (7.27 ± 5.74) ($P < 0.05$) in the test group.
Conclusions: In this study, topical application of sweet almond oil, which was not followed by any specific complications, was able to significantly reduce the uremic pruritus in hemodialysis patients; however, these findings require further studies.

Keywords: Almond oil, End Stage Renal Disease, Hemodialysis, Pruritus

1. Background

Uremic pruritus is a common dermatologic symptom for end-stage renal disease (ESRD) patients. The rates of uremic pruritus were reported as 42% - 72.9% in some studies (1-3). In a systematic review study, the rate of uremic pruritus was reported as 10% - 77% (4). For about 70% the patients, pruritus was experienced in the back of the trunk (5). Pruritus in HD patients was observed at rates 2.8 times higher than in the same patients without HD therapy; this problem was reported at rates 7.4 times higher in female HD patients than in the same patients without HD therapy (6).

Although the main cause of pruritus is unknown, uremia is the most important factor in these patients (7). Other factors, such as xerosis, increases in skin mast cells, hyperparathyroidism, high serum magnesium, and increased vitamin A, may lead to onset or may aggravate uremic pruritus (7-11). Not only is the treatment of uremic pruritus complex (12), but dialysis also has a mild effect on it (13), as the severity of pruritus can increase on the day of dialysis therapy or on the following day (14).

Essential fatty acids and their derivatives may be useful because they decrease lymphocytes and lymphokines (15) and increase prostaglandins and leukotrienes, which results in decreased itching and inflammation of the skin (16), and they can have a protective effect on skin structure (17). For instance, linolenic acid and arachidonic acid play roles in protecting skin, and their deficiency could lead to pruritus and other cutaneous disorders (18). In addition to the reduction of acids, such as linolenic, linoleic, and arachidonic, that exacerbate uremic pruritus (19), the effect of linolenic and linoleic acid on alleviating pruritus in HD patients has also been reported in the literature (15, 18).

The effects of many pharmacological therapies on re-

ducing uremic pruritus, including tacrolimus (20), hydroxyzine (21), naltrexone (22), and ondansetron (23), have been studied, but so far none of these have been accepted as a definitive treatment. Sweet almond products, either as a grain or an oil, have been considered by researchers because they contain essential fatty acids, such as oleic, linoleic, palmitic, and stearic acid (24). Shahgholian et al. (2010) and Kang and Kim (2008) reported a reduction in uremic pruritus following massage therapy with aromatherapy, using a combination of three oils diluted in sweet almond oil (25, 26).

In comparison with bitter almond, sweet almond is a component of people's diet. Sweet almond contains essential fatty acids, such as oleic, linoleic, palmitic, and stearic acids (24), that have no adverse effects on the ESRD patients, particularly if it is applied topically. However, its therapeutic effects on reducing uremic pruritus require further study. Given the facts above, and that research had studied the effect of sweet almond oil on uremic pruritus in combination with other oils or the aromatherapy method, its isolated effects have not yet been studied. Therefore, the application of this natural substance, which has no unfavorable effects and is inexpensive, acceptable, and accessible for patients, could be effective in reducing uremic pruritus.

2. Objectives

This study was carried out to examine the effect of the topical application of sweet almond oil on reducing uremic pruritus in HD patients.

3. Methods

3.1. Design

This randomized clinical trial research was conducted among HD patients that had been referred to the HD ward of Shahid Beheshti hospital at Yasuj University of Medical Sciences, Iran, in 2013, and 42 HD patients were allocated to two groups: intervention and control. This article was extracted from the proposal of the deputy of research and technology at Yasuj University of Medical Sciences and was written by the first and corresponding authors (Reference no. 1345). The research has been registered at the Iranian registry clinical trials (IRCT) with the number IRCT2014121520313N1 and was confirmed by the research ethics committee at the Yasuj University of Medical Sciences (reference no. 93.12.25.06), dated 03/16/2015. Written informed consent was obtained before starting the intervention and after a full explanation of the objectives of the research was provided. Also, emphasis was placed on the confidentiality of information, the voluntary nature of participation in the research and the option to exit at any stage of the study. The participants were assured that the information collected would be used solely for study purposes and would remain confidential. In this study, no financial costs were imposed on the patients, their families, the institution, or the hospital. No side effects were reported following the topical application of sweet almond oil, and the participants were observed for complications.

3.2. Sampling

The population of this research consisted of 60 HD patients that had been referred to the HD ward of Shahid Beheshti hospital at Yasuj University of Medical Sciences, Iran, in 2013. The sampling and interventions were completed in the HD ward of the mentioned hospital. Random sampling was not possible because of the limited population of the study. Therefore, of the initial 60 patients, 44 patients who met the eligibility criteria to participate in the study were selected via a nonrandom sampling method. However, the selected patients were allocated to two groups test (22 cases) and control (22 cases) (Figure 1) using block randomization. From the total of 24 blocks, with four samples in each, 11 blocks were randomly selected. The date of recruitment was 08/23/2013, and the study lasted for 40 days. Two patients in the control group were excluded from the study because of kidney transplantation; therefore, the data of 42 HD patients was analyzed.

3.3. Inclusion and Exclusion Criteria

The inclusion criteria were as follows:

1) An age of more than 18 years

2) At least 6 months of HD treatment (27)

3) A history of at least two weeks of uremic pruritus (27)

4) The lack of a known cause

5) No psychological, cognitive, or audio-visual disorders

6) A willingness to participate in the study.

The exclusion criteria were as follows:

1) Unwillingness to continue participation in the study

2) Kidney transplant

3) Failure to apply the sweet almond oil

4) Long-term treatment with anti-histamines of other itch-relieving medicines

3.4. Interventions

Sweet almond oil (certified as traditional medicine and with a registration number for the production license: "S - 90 - 050") was used by the intervention group. This oil contains a compound of 77% oleic acid and 17% - 20% linoleic acid (24); HD patients topically applied a dosage of 5 - 10

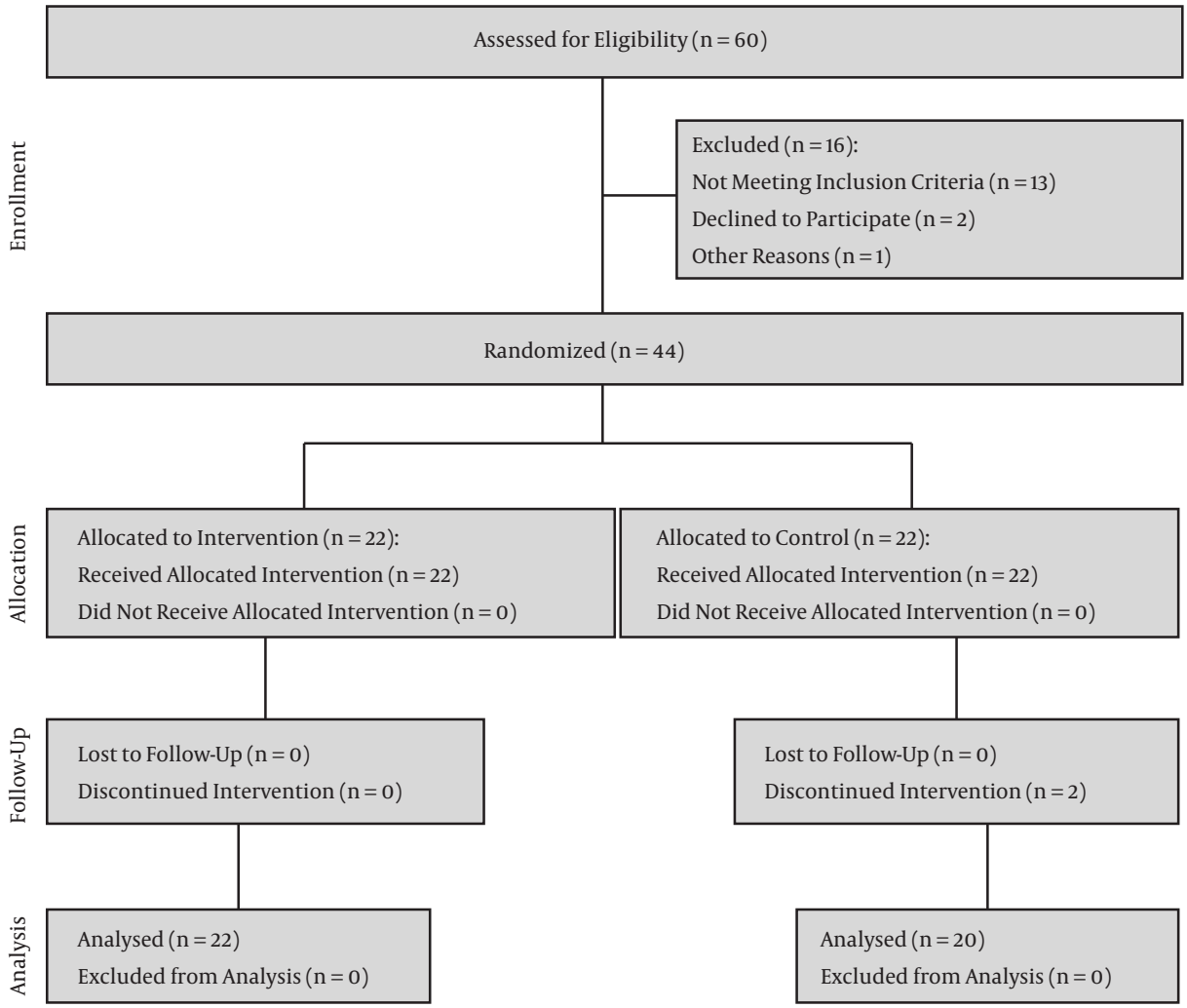

Figure 1. CONSORT Flow Diagram

cc of sweet almond on the pruritus location (either a part of the body or the whole body) once daily over two weeks. Guidance for the topical application was provided to the patients based on the leaflet guidelines inserted in the drug package. The use or non-use of the sweet almond oil by the sample was monitored using a checklist following the referral of the patients to the HD ward. No intervention was performed in the control group.

3.5. Measures

The data were collected in three stages: one week pre-intervention, one week post-intervention, and two weeks post-intervention with sweet almond oil.

3.5.1. Demographic Information Questionnaire

The questionnaire included demographic and associated data about renal disease and dialysis therapy.

3.5.2. Questionnaire of Pruritic Score

The scale has 48 questions to assess the severity, distribution, and frequency of pruritus (28). The questionnaire was designed by Duo (29) and modeled on the Yosipovitch questionnaire (30). The validity and reliability of this questionnaire was confirmed in foreign research (29). This questionnaire has been applied previously in Iranian studies to assess uremic pruritus (31, 32).

3.6. Statistical Analysis

The collected data were analyzed using IBM SPSS Statistics 22.0. Descriptive statistics, such as central tendency and dispersion indices (mean, standard deviation, frequency, percentage, and graphs), were used to summarize demographic variables, the mean difference of uremic pruritus severity, and sampling. All the data were used for analysis, and no participants were removed from the analysis due to missing data. The independent samples t-test was used to compare the mean of age, the duration of suffering from ESRD, the duration of HD therapy, and the mean difference of uremic pruritus severity between the two groups. The Fisher's exact test was used to compare sex, marital status, place of residence, and the number of HD therapies per week. The chi-square test was used to measure the level of education and occupations. Repeated measures ANOVA was used to compare the mean difference of uremic pruritus severity between the two groups in terms of the times of intervention and a pairwise comparison of the means difference of the scores for uremic pruritus severity in the two groups. All tests were two-sided and had a confidence interval of 95%, and a $P < 0.05$ indicated statistically significant differences. Parametrical tests were used in the analysis of the data because the distribution was normal.

4. Results

In the present study, 52.40% (22 cases) of the patients were in the intervention group and 47.60% (20 cases) were in the control group. Overall, 52.40% (22 patients) were male and 47.60% (20 patients) were female. In this research, 7.20% (3 patients) were single, 23.80% (10 patients) were widowed or divorced, and 69% (29 patients) were married. During the timeframe of the study, 61.90% (26 patients) were inhabitants of cities, while 38.10% (16 patients) lived in villages. In addition, 57.10% (24 patients) were illiterate, 16.70% (7 patients) had completed primary school, 9.50% (4 patients) had completed guidance school, 14.30% (6 patients) had a diploma, and 2.40% (1 patient) had an associate degree. In terms of occupations, 52.40% (22 patients) were unemployed, 2.40% (1 patient) were employed, and 45.20% (19 patients) were housewives. Furthermore, 28.60% (12 patients) were undergoing hemodialysis twice per week, while 71.40% (30 patients) were undergoing hemodialysis three times per week. A comparison of the demographic data of the two groups is shown in Table 1. Based on the results of the statistical tests, no significant statistical difference was observed between the two groups in terms of demographic variables ($P > 0.05$).

The severity of the uremic pruritus between the two groups was measured three times. Based on the findings of repeated measures ANOVA, a significant statistical difference was reported in the mean for the severity of uremic pruritus between the two groups ($P < 0.05$). Comparing the mean of the pruritus severity with the time of intervention in the two groups showed that there was no significant statistical difference in the mean of the severity of pru-

Table 1. Demographic Variables in the Intervention and Control Groups (N = 42)[a]

Variable	Group		P Value
	Intervention (22 Patients)	Control (20 Patients)	
Age	58.35 ± 17.38	50.75 ± 16.46	0.10[b]
Duration of suffering from ESRD	38.13 ± 28.55	34.35 ± 31.78	0.68[b]
Duration of HD therapy	38 ± 28.63	34 ± 32.02	0.67[b]
Number of HD therapies			0.40[c]
Twice per week	5 (58.30)	7 (41.70)	
Three times per week	15 (50)	15 (50)	
Sex			0.40[c]
Male	12 (54.50)	10 (45.50)	
Female	10 (50)	10 (50)	
Marital status			0.40[c]
Single, widowed or divorced	6 (46.20)	7 (53.80)	
Married	16 (55.20)	13 (44.80)	
Place of residence			0.40[c]
City	(50) 13	13 (50)	
Village	9 (56.30)	7 (43.70)	
Level of education			0.12[d]
Illiterate	14 (58.30)	10 (41.70)	
Primary-Guidance	3 (27.30)	8 (72.70)	
High school or higher	5 (71.40)	2 (28.60)	
Occupation			0.50[d]
Unemployed	12 (54.50)	10 (45.50)	
Employed	1 (100)	0	
Housewife	9 (47.40)	10 (52.60)	

[a] Values are expressed as mean ± standard deviation or No. (%).
[b] Independent samples t-test.
[c] Fisher's exact test.
[d] Chi-square test.

ritus between the two groups pre-intervention (P > 0.05), but one week and two weeks post-intervention showed a significant difference in the mean of pruritus severity between the groups (P < 0.05) (Figure 2).

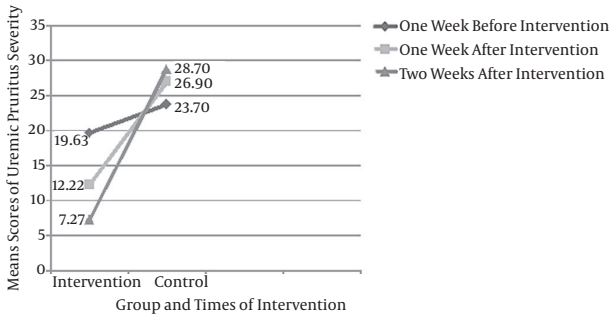

Figure 2. Plot of Mean Scores for Uremic Pruritus Severity for Each Group and Each Time

Pruritus severity in both groups was analyzed separately as a within-group comparison. The results of repeated measures ANOVA showed a significant statistical difference in the mean of uremic pruritus severity in the intervention group in the three measurements (P < 0.05). A significant difference was also observed in the direction of an increased mean of pruritus severity in the three different times for the control group (P< 0.05). In addition, pairwise comparison of the difference of means in the intervention group indicated that there was a significant difference in the mean of the severity of pruritus for all three measurements (P < 0.05) (Table 2).

5. Discussion

The present study, which aimed to investigate the effect of the topical application of sweet almond oil on uremic pruritus in HD patients, showed that the sweet almond oil was able to significantly reduce uremic pruritus in the patients in the intervention group. A wide literature review was performed on the effect of sweet almond oil on uremic pruritus, but only two other studies were found. In a study by Shahgholian et al. (2010), which aimed to investigate the effect of aromatherapy on pruritus in HD patients, the first group was exposed to six sessions of massage (7 minute duration) and aromatherapy, which used aromatic oils lavender, peppermint, and tea tree diluted in sweet almond oil. After one week of washing-out, they were exposed to six sessions of massage (7 minutes) without the aromatherapy and sweet almond oil. The second group received a treatment contrary to the first group (25). The other study was carried out by Kang and Kim (2008) on the effect of aroma hand massage on HD patients with pruritus. The patients were exposed to twelve sessions of aroma hand massage (5 minute duration) using a compound of three aromatic oils lavender, chamomile, and geranium diluted in sweet almond oil (26). The findings of the two mentioned studies are inconsistent with the results of the present study. However, it is necessary to note that the two studies differed in terms of methodology, scale, and times of pruritus measurement. In addition, it is not clear whether the relief of uremic pruritus was due to the effect of sweet almond oil or to the combination of this oil with other oils.

Also, the fatigue, stress, and quality of life of these patients was reported following the aroma hand massage with a compound of three aromatic oils lavender, chamomile, and geranium diluted in sweet almond oil (26). In addition, studies have shown the relief of uremic pruritus following the use of granisetron (33), gabapentin (21), cromolyn sodium, and pimecrolimus cream (32).

Xerosis is one of the factors that can cause or intensify uremic pruritus (8). In justifying the effectiveness of sweet almond oil on the relief of uremic pruritus, it can be said that sweet almond contains essential fatty acids, such as linoleic acid (24), that have been shown to be effective in relieving pruritus (18). The essential fatty acids reduce pruritus and dermal inflammations by increasing prostaglandins (16). Indeed, the reduction of prostaglandins can cause symptoms such as xerosis and flaking of the skin (34). Thus, the essential fatty acids, such as linoleic acid, that exist in sweet almond oil can act as precursors for prostaglandins as well as moisturizing and softening the skin, and they play an important role in eliminating xerosis and pruritus.

Although the results of this study show a reduction of pruritus, some restrictions should be taken into consideration when generalizing the findings. The sample of HD patients is limited, which necessitates research on a larger population. The participants in the study were receiving HD treatment. It is recommended that a study be carried out on the effect of this oil with patients undergoing peritoneal dialysis in order to compare the effectiveness of sweet almond oil in the two groups. Another limitations is the shortage of articles in the field on the effect of sweet almond oil on uremic pruritus in HD patients, which made it difficult to compare results. However, one of the strengths of the present study was its new approach to a treatment method, which involved no complications, for controlling uremic pruritus in HD patients.

Topical application of sweet almond oil, which was not followed by any specific complications, has been shown to reduce uremic pruritus in HD patients. Sweet almond oil could be useful as a simple, cheap, and safe method for

Table 2. Pairwise Comparison of the Means of Differences for the Scores of Uremic Pruritus Severity in the Two Groups

Pairwise Difference of Means	T1[a] - T2[b]		T1[a] - T3[c]		T2[b] - T3[c]		Statistical Test[d]
	Mean Difference	P Value	Mean Difference	P Value	Mean Difference	P Value	
Group							
Intervention	7.40	0.001	12.36	0.001	4.96	0.002	0.001[a]
Control	-3.20	0.008	-5	0.002	1.80	0.004	0.05

[a] One week pre-intervention.
[b] One week post-intervention.
[c] Two weeks post-intervention.
[d] Repeated measures ANOVA.

the relief of uremic pruritus. Applying this oil as a natural method without complications could be a non-invasive, accessible, easy, affordable, and acceptable method for helping patients to reduce uremic pruritus. It is proposed that sweet almond oil be prescribed by physicians, nephrologists, and dermatologists for the relief of uremic pruritus.

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Footnotes

Authors' Contribution: Ardashir Afrasiabifar: surveillance of the intervention, analysis of data, and compiling the article; Zahra Mehri: designing the research, sampling, allocating the samples to the study groups, implementing the intervention, collecting data, and compiling the article; Nazafarin Hosseini: surveillance of the intervention and compiling the article.

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