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The effect of the omega-3 supplement on uremic pruritus in hemodialysis patients; a double-blind randomized controlled clinical trial

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ABSTRACT

Background: Chronic kidney disease (CKD) and uremic syndrome cause malfunction in most of organs including skin.
Objectives: This study was designed to investigate the effects of omega-3 supplement on uremic pruritus in chronic hemodialysis patients.
Patients and Methods: In this double-blind randomized controlled clinical trial study (#IRCT cod; 29363; http://irct.ir/trial/29363), the effect of the omega-3 supplement on uremic pruritus was assessed in 64 chronic hemodialysis patients (using standard 5-D itch scale questionnaire). Patients were surveyed at the hemodialysis department of Imam Khomeini and Razi hospitals in Ahvaz city, Iran.
Results: We found that the mean score of itching degree in the intervention and the placebo groups decreased from 3.56 to 1.72 ($P<0.001$) and 3.63 to 3.09 ($P<0.05$) respectively.
Conclusions: In our study, the omega-3 supplement could reduce uremic pruritus in chronic hemodialysis patients.

Implication for health policy/practice/research/medical education:
In a double-blind randomized controlled clinical trial, we found omega-3 supplement could reduce uremic pruritus in chronic hemodialysis patients.

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1. Background

Chronic kidney disease (CKD) and uremic syndrome cause malfunction in most of organs including skin. In most cases, uremic pruritus is resistant to treatment with ordinary anti-itch agents such as moisturizing, antihistamines, glucocorticoids and ultraviolet radiation (1).

Based on pathologies proposed for uremic pruritus such as increasing oxidants and inflammatory processes and loss of serum anti-oxidants that increase in CKD patients during hemodialysis through membranes, and imbalance of ions and electrolytes and nitrogen products and other waste materials, using antioxidant agents to reduce pruritus was taken into consideration. Although the definite mechanisms for uremic pruritus have not been determined (2,3).

CKD patients have abnormal lipid, especially profiles of fatty acids and most of the symptoms are associated with this abnormality like pruritus, delayed wound healing, cardiovascular diseases, anemia and coagulopathy (4).

Therefore, the administration of derivatives of essential fatty acids seems to help CKD patients. Omega-3 fatty acids in addition to anti-inflammatory effects have been used to decrease the pruritus (3,5).

While pruritus is a qualitative variable, it is assessed by a standard scale to compare the values obtained from patients.

2. Objectives

In this study, we attempted to assess the effect of omega-3 in reducing the intensity of itching in hemodialysis patients

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by the standard 5-D itch scale (1,3).

3. Patients and Methods

3.1. Study population

This study is a randomized, double-blind, controlled clinical trial that evaluates the effect of the omega-3 supplement in 64 hemodialysis patients with uremic pruritus in the hemodialysis department of the Imam Khomeini hospital and Razi hospital, Ahvaz, Iran.

All patients were over 18 years old and their hemodialysis duration was more than three months. Exclusion criteria were liver diseases, skin diseases, malignancy and allergy to omega-3 supplements or kidney transplantation. Patients were divided into the control and intervention groups randomly using blocks of six for allocation concealment.

Using blocking for allocation concealment, someone who was unaware of the study, prescribed omega-3 and placebo to patients. Before prescribing omega-3 and placebo, itch degree was evaluated by the questionnaire.

Patients in the intervention group received an orally single-dose of 2 g omega-3 daily before lunch. To evaluate the correct consumption of medications, patients were visited weekly and checked in terms of health status and drug side effects. Patients in the control group received an orally single- dose of placebo daily before lunch as well.

Placebo capsules were similar to omega-3 capsules in color, shape, size, and taste. Placebo capsules consisted of an appropriate ratio of microcrystalline cellulose (Avicel. PH 101), and, lactose (2-8) produced by the direct compression method. Treatment with placebo and omega-3 was done three weeks in the same way in both intervention and control groups. After 3 weeks, in both groups, pruritus was assessed by the same questionnaire like before the intervention. All of the 64 patients took their capsules regularly and completed the study. Thus, 64 patients were analyzed at the end of the clinical trial (Figure 1).

3.2. Ethical issues

The research followed the tenets of the Declaration of Helsinki. All patients signed a written informed consent form to participate in the study. This project was also approved by the Ethics committee of Ahvaz Jundishapur University of Medical Sciences (registration code# IR.AJUMS.REC.1396.631). This study was registered in the Iranian Registry of Clinical Trials website (identifier: IRCT20171220037968N1; http://irct.ir/trial/29363).

3.3. Statistical analysis

The results were presented as mean ± standard deviation (SD). To assess the normality of the data, the Kolmogorov–Smirnov test was applied. ANOVA test was used to eliminate the effect of age. To compare the pre- and post- intervention findings, the paired *t* test was used. To compare the changes between groups student's *t* test was used and a *P* value of less than 0.05 was considered significant. SPSS version 22 was applied to analyze the data.

4. Results

Sixty-four hemodialysis patients with uremic pruritus enrolled in the study. Thirty-two patients were allocated to

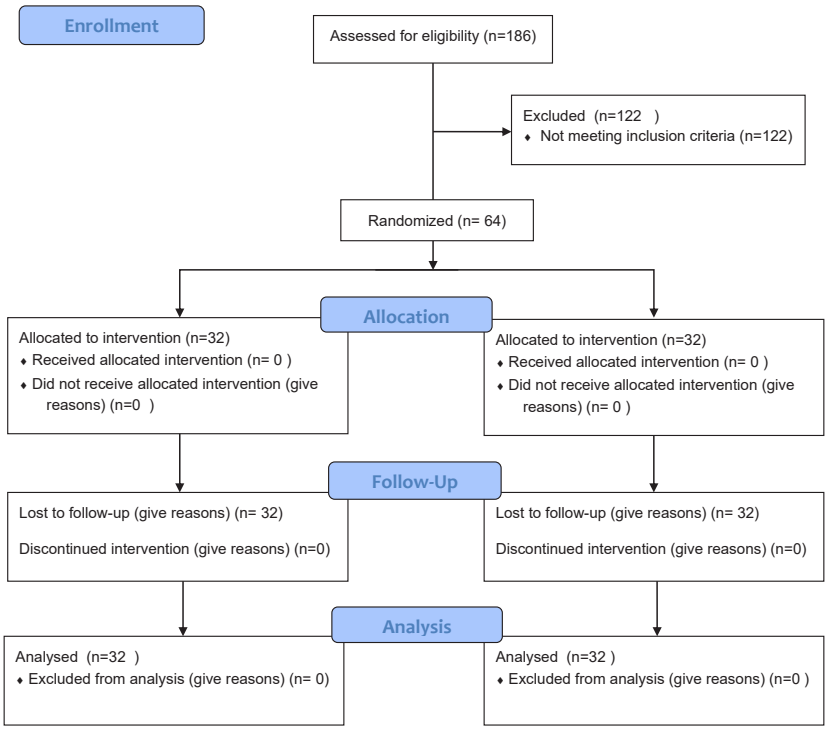

Figure 1. Assignment of patients in the study.

Table 1. The baseline characteristics of the patients

Age (y)	Intervention (n=32)	Placebo (n=32)
Mean	51.91	56.25
Standard deviation	6.586	8.865
Minimum	40	39
Maximum	67	73
Percentile 25	47.25	48.00
Percentile 50	51.00	56.50
Percentile 75	57.00	63.50

Table 2. ANOVA to eliminate the effect of age

Variable	*df*	*F* value	*P* value
Age	1	0.143	0.707
Degree	1	9.01	0.004
Group	1	44.26	<0.001
Corrected Model	3	20.53	<0.001

the control and treatment groups by allocation concealment method. There were 27 males and 5 females in the treatment group and 23 males and 9 females in the control group, respectively.

The mean score of age in the treatment group was 51.91 years and in the placebo group, it was 56.25. Tables 1 and 2 show the baseline characteristics of the patients.

The paired sample *t* test showed that the mean degree of uremic pruritus in the group treated with omega-3 was decreased from 3.56 to 1.7209 and in the placebo group from 3.63 to 3, respectively ($P<0.001$) (Table 3).

Statistically, the difference between the treatment group compared with the placebo group regarding the intensity of pruritus degree and duration and disability and direction before and after of the study was significant ($P<0.001$; Table 4).

All the patients tolerated omega-3. They were followed-up for three weeks before and after the study to assess any drug side effects or complications.

5. Discussion

In our study, the effect of omega-3 to reduce the uremic pruritus in chronic hemodialysis patients was detected. The treatment was without any side effect after treatment with 2 grams of omega-3 during three weeks (1,2).

While different mechanisms have been explained, the pathophysiological basis of the uremic pruritus has not fully been understood (5,6).

Inflammatory processes and increasing oxidants because of renal failure and eliminating anti-oxidants by a dialysis membrane affect more organs as well as skin. Decreasing anti-oxidant level in CKD because of loss or decrease of absorption and malnutrition in these patients are effective factors for organ damages (1,3,7).

Disorders of lipid profiles, especially disorders of fatty acids that occur in CKD patients is another matter (8,9). It

Table 3. Group treated with omega-3 versus placebo group

Pairs	Duration group	Number	Mean	SD
	Intervention			
1	Duration	32	3.41	0.911
	A-Duration	32	1.63	0.492
2	Duration	32	3.56	0.669
	A-Duration	32	1.72	0.634
3	Duration	32	2.97	0.782
	A-Duration	32	1.56	0.564
4	Duration	32	3.03	1.031
	A-Duration	32	1.75	0.762
	Placebo			
1	Duration	32	3.59	0.712
	A-Duration	32	3.13	0.833
2	Duration	32	3.63	0.609
	A-Duration	32	3.09	0.963
3	Duration	32	3.59	0.615
	A-Duration	32	3.22	0.906
4	Duration	32	3.56	0.801
	A-Duration	32	3.34	0.902

SD: Standard deviation.

Table 4. The difference between treatment group compared with placebo group regarding the intensity of pruritus degree and duration and disability and direction before and after of the study

Variables	*df*	Mean difference	95% CI		*P* value
			Lower	Upper	
Dif*- duration	62	-1.31	-1.79	-0.83	<0.001
Dif-degree	62	-1.31	-1.72	-0.90	<0.001
Dif-direction	62	-1.03	-1.48	-0.59	<0.001
Dif-disability	62	-1.06	-1.55	-0.58	<0.001

*Dif: difference.

has been shown that omega-3 supplements have protective effects against oxidative stress and lipid profile (10,11).

Fallahzadeh et al found that Th1 proliferative response to antigen decreased after the use of fish oil (11).

Additionally, it has a protective effect on other organs. Omega-3 supplements were found to be useful for decreasing blood pressures in adults in a meta-analysis study too (11).

There are a few numbers of investigations on the effects of omega-3 on uremic pruritus. In a clinical trial study conducted by Ghanei et al and Mortazavi et al, omega-3 decreased the degree of itching in CKD patients (1,3). These studies, as compared to our investigation, had a lesser number of cases (1,3). Additionally, in one of them, the doses of omega-3 were smaller. According to the study conducted by Begum et al, the percentage decrease in the total score of pruritus was greater for the fish oil group compared with the safflower oil group (5). This study had not control group. Besides, in four studies, there is not any standard questionnaire to evaluate pruritus (2,3,12-18). In both studies by Ghanei et al, and Mortazavi et al, omega-3 administration was three times a day while in our study, prescribing was as single-dose (2,3,19-23).

In our study, omega-3 administration decreased degree and duration and disability and direction of pruritus significantly in chronic hemodialysis patients without any side-effects or complications. Considering this finding, omega-3 supplement therapy could be encouraged in uremic pruritus (20-27).

6. Conclusions

In spite of limitations in this study, it is worth noting that only a slight decrease in itching may be useful for hemodialysis patients with uremic pruritus. Therefore, and considering another effectiveness of omega-3 in advanced hemodialysis patients, omega-3 intake can be advised to use to improve uremic pruritus. In this study, the omega-3 supplement was found to be more effective than the placebo to decrease of uremic pruritus in hemodialysis patients. Therefore, it seems that omega-3 supplement could be administered as an acceptable drug for the treatment of uremic pruritus in hemodialysis patients.

Limitations of the study

The sample size is low, and the measurement of serum omega-3 levels and oxidative stress markers also contributed to the validity of the study that could not be assessed in this study.

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Authors' contribution

PLR and SS conducted the research. SSBM and BC helped to prepare the manuscript. PLR and SS prepared the final manuscript. All authors read and signed the final paper.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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