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Clinical Trial

Effects of the Topical Application of *Lavandula Officinalis L.* Essential Oil on Reducing the Severity of Eczema Symptoms: A Randomized Clinical Trial

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Abstract

Background and Aim: *Lavandula Officinalis L.* essential oil (L.O) has different effects such as anti-inflammatory and soothing effects on skin diseases. The aim of this study was to examine the effect of L.O on the severity of eczema.

Materials and Methods: This research was conducted as an open-label, randomized clinical trial. The patients who were enrolled to participate in the present study were randomly divided into five groups. In groups A, B, and C, 15 patients in each group received lavender essential oil cream at a dose of 3%, 5%, and 8%, respectively. In groups D and E, 15 patients in each group received 1% topical hydrocortisone and cream base, respectively. All the patients used the cream twice a day for 14 days. Baseline characteristics of the enrolled subjects and illness severity were recorded at the baseline and during the 7th as well as 14th days.

Results: Generalized estimating equations (GEE) method showed that the interaction of the experimental group and time factor on the severity of eczema was significant (P = 0.011). Moreover, the relative chance of higher eczema severity in experimental groups was different, and it was a function of time. The relative chance of any increase in the severity of eczema in groups A, B, C compared with group E on the 7^{th} day of treatment was reduced by about 9.7%, 34.7%, and 73.9%, respectivelyt; while on the 14^{th} day of treatment, it decreased by about 79.2%, 82.4%, and 97.7%, respectively. The lavender oil significantly reduced the severity of eczema at the 7^{th} and end of the 14^{th} day ($p \leq 0.01$).

Conclusion: Lavender has dose-dependently beneficial effects on the treatment of eczema.

Keywords: Eczema, Lavender essential oil, Skin cream

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Introduction

Eczema is a chronic and common inflammatory disease of the skin. Histologically, it has been associated with spongiosis and various degrees of acanthosis with dermal vascular lymphohistiocytic infiltration. Clinically, it is associated with itching, red rash, cracking, scaling, and papulovesicular lesions. Eczema is caused by several factors, including intrinsic and acquired factors (irritating, or allergic) and the most common type is the irritation known as dry eczema (1). The incidence of hand eczema is about 2 to 10% of the world's population, while in the United Kingdom 15 to 20% of children develop this inflammation (2). This inflammation is one of the most common diseases which is considered a threat to public health and has a profound effect on the quality of life. It causes sleep disorders, and is a social stigma in different ages (3). The main treatment for dermatitis is the diagnosis and elimination of irritants, hydration, and reduction of inflammation and itching of the skin. Prescribing medication and other treatments based on the signs and symptoms of the disease are among the treatments. The main treatments are systemic and topical drugs, including corticosteroids, inhibitors, emollients, and doxepin (4). Excessive use of common treatments can cause adverse effects such as skin thinning and cause irritation and harmful side effects for a long time. The use of emollients for skin hydration also causes mucosal suppression. Doxepin also causes drowsiness. Patients with eczema often have a poor response to these treatments. It should be noted that the use of topical drugs is preferable to systemic. Medicinal plants have been used as an important part of traditional medicine for many years. The World Health Organization states that 74% of modern medicines are herbal. It also states that 65 to 80 percent of the world's population use traditional therapies as the first form of medicine and 85 percent use herbs and herbal products (5). The use of medicinal plants is also expanding in the West. Safety, availability, and affordability are some of the factors that have attracted people's attention. Lavender, scientifically named *Lavandula Officinalis*, is an aromatic, evergreen herbaceous plant. It is an analgesic, antispasmodic, and sedative plant. There are reports of lavender essential oil's soothing effect on some skin diseases such as psoriasis, dermatitis, and eczema. Moreover, it also has wound-healing effects (6, 7). The essential oil of this plant contains linalool 28-36% and linalyl acetate 29-46%. Linalool and linalyl acetate are the main components of essential oils and have antimicrobial and anti-inflammatory properties (8-9). According to the above-mentioned information, the present study aimed to determine the impact of topically applied lavender essential oil on reducing eczema symptoms.

Materials and Methods

Ethical Considerations

The study protocol was approved by the Ethics Committee of LUMS (IR.LUMS.REC.1396.169) at 2018. All patient information was confidential; the principles of confidentiality were fully considered in this study. If a side effect occurred in the patient, the patient was immediately excluded from the study and appropriate treatment was performed to eliminate the possible complication.

Extraction and Analysis of Essential oils of *Lavandula Officinalis L*.

Lavandula Officinalis L. with herbarium number 6221 was collected from nature around Lorestan in spring, and approved by a botanist from Jihad and Construction Center of Lorestan. Essential oil extraction was carried out in a laboratory using water distillation method. The aerial part of the herb was totally dried in the shade, and were then milled. Plant extraction was performed using a Clevenger device for 5 hours. Subsequently, dehydration was performed using sodium sulfate. The essential oil was maintained in a dark glass at 4 °C. The yields of essential oil of Lavandula Officinalis L. were expressed in g relative to 100 g of dry plant; and calculated according to Equation (1):

$$\text{Yield (\%)}=\frac{Amount\ of\ extracted\ oil\ (g)}{Amount\ of\ dry\ plant\ mass\ (g)}\times 100$$

The essential oil was examined with an Agilent 6890N gas chromatography instrument attached to the Agilent 5973 mass spectrometry. The essential oils were identified in the HP-5 column (30 m long, 0.25 m in internal diameter and 0.25 µm in constant phase

thickness) by injecting 0.2 µl of essential oil at 50°C, and subsequently gradually increased from 5 to 260°C. The identification procedure was carried out using a library method via RT Time and Wiley 7 N Library Information.

Preparation of Topical Cream

The cream containing *Lavandula Officinalis L*. essential oil was prepared in collaboration with Knowledge Enterprise Company, Kimia Daru Aflak (10845). The creams were prepared in three doses of 3, 5 and 8%.

Setting

This open-label, randomized clinical trial was conducted at Shohadaye Ashayer Hospital, affiliated to the Lorestan University of Medical Sciences (LUMS), Khorramabad, Iran. The study protocol was registered in the Iranian Registry of Clinical Trials (IRCT) with registry number IRCT20100420003760N4. The study began in September 2018 and it was not completed until October 2019. Written informed consent was obtained from all the patients.

Study Population

Patients referred to the dermatology clinic of Shohadaye Ashayer Hospital who were diagnosed with eczema by a dermatologist were assessed for eligibility. The patients taking corticosteroids and other topical, oral, and injectable anti-inflammatory drugs were excluded.

Intervention

The enrolled patients were randomly divided into the five groups using permuted block randomization method and a random numbers table. The patients in groups A, B, and C: 15 patients in each group received lavender essential oil cream at a dose of 3%, 5%, and 8%, respectively. Group D: 15 patients received 1% topical hydrocortisone (Daro. pakhsh Pharmaceutical Company, Iran). Group E: 15 patients received cream base (Eucerin). All the patients used the cream twice a day for 14 days. Baseline characteristics of the patients included in the study, including age, sex, past medical history, drug history, and illness severity were recorded.

Definitions and Outcome Measures

Lesion severity indexes were used to assess the severity of eczema at the first, 7th, and 14th days of the study. These indexes included clinical signs such as erythema, infiltration, vesicles, fissures, and edema. To measure the amount or extent of the lesion, a range of 1-4 stages, expressed as percentage, were used. The stages are as follows: 1 = 0-24%, 2 = 25-49%, 3 = 50-74%, and 4= 75-100. Moreover, mild to moderate classification equivalent to stage one and two, severe classification equivalent to stage three, and very severe classification equivalent to stage four were used.

Sample Size

As far as we know, this was the first clinical trial investigating the impact of topically applied lavender essential oil on the severity of eczema symptoms. The present study was designed as a pilot trial, and based on an expert opinion, each group was composed of 15 patients.

Statistical Analysis

Considering that no similar study was found in the previous literature review to determine the sample size, a pilot study was used to calculate the sample size and 15 subjects were randomly assigned to each treatment group. The data were analyzed using the Statistical Package for the Social Sciences (SPSS, version 19.0; IBM company, USA). The data were reported as means ± standard deviation (SD), and the P-value of < 0.05 was considered statistically significant. The method of repeated measurements (the Generalized Estimating Equations) was used to analyze the data obtained from the study groups.

Results and Discussion

The Yield and GC/MS Analysis of *Lavandula Officinalis L*. Essential Eils

Essential oil extraction efficiency was reported to be 4.5% after 5 hours. The results relating to the chemical composition of the essential oils of *Lavandula Officinalis L.* extracted by the hydrodistillation method have been summarized in **Table 1**. Linalool (25.99 %), eucalyptol (14.91 %) and borneol (17.51 %) were important compounds identified in lavender essential oil.

Table 1. Chemical composition of *Lavandula Officinalis L.* aerial part volatile oil.

No	RT	Peak Area %	Name of the Compound
1	3.32	0.36	2H-1,3-Benzoxazine, 6-bromo-3-c

2	4.10	0.72	alpha.-Pinene
3	4.33	0.30	Camphene
4	4.57	0.24	1-Octen-3-ol
5	4.66	0.41	Bicyclo[3.1.0]hexane, 4-methyle.
6	4.78	0.90	beta.-Pinene
7	4.88	0.55	beta.-Myrcene
No	**RT**	**Peak Area %**	**Name of the Compound**
8	5.39	0.35	3-Carene
9	5.53	0.53	1-methyl-2-(1-methylet
10	5.76	14.91	Eucalyptol
11	5.99	0.23	1,3,6-Octatriene
12	6.42	1.08	cis-.beta.-Terpineol
13	7.21	25.99	Linalool
14	7.88	0.24	2,4,6-Octatriene
15	8.09	8.71	Bicyclo[2.2.1]heptan-2-one
16	8.22	0.27	Bicyclo[3.1.1]hept-3-en-2-ol
17	8.85	17.51	Borneol
18	8.94	0.99	2-Cyclohexen-1-one
19	9.06	4.27	3-Cyclohexen-1-ol
20	9.23	1.06	Butanoic acid, hexyl ester
21	9.33	3.46	p-menth-1-en-8-ol
22	9.53	0.31	Bicyclo[3.1.1]hept-3-en-2-one
23	10.24	0.90	Bicyclo[2.2.1]heptan-2-ol
24	10.31	0.23	Benzaldehyde
25	10.38	0.41	Butanoic acid
26	10.84	1.95	1,5-Dimethyl-1-vinyl-4-hexenyl
27	11.65	1.39	4-Hexen-1-ol, 5-methyl-2-(1-met
28	12.66	0.18	Cyclobutanecarboxylic acid
29	13.91	0.28	2,6-Octadien-1-ol
30	14.09	0.16	Hexanoic acid
31	14.79	0.14	Tetradecane
32	15.34	0.56	Caryophyllene
33	16.01	2.35	1,6,10-Dodecatriene
34	17.12	0.51	beta.-Myrcene
35	17.49	0.13	Naphthalene
36	18.98	0.61	Caryophyllene oxide
37	19.49	0.28	Hexadecane
38	20.25	0.67	Bicyclo[4.4.0]dec-1-ene
39	21.15	3.53	alpha.-Bisabolol
40	23.75	0.24	Octadecane
41	34.03	0.48	Hexanedioic acid
42	36.20	0.45	1,2-Benzenedicarboxylic acid
43	56.47	1.17	2-(2-Phenoxythiinyl)imidazolo

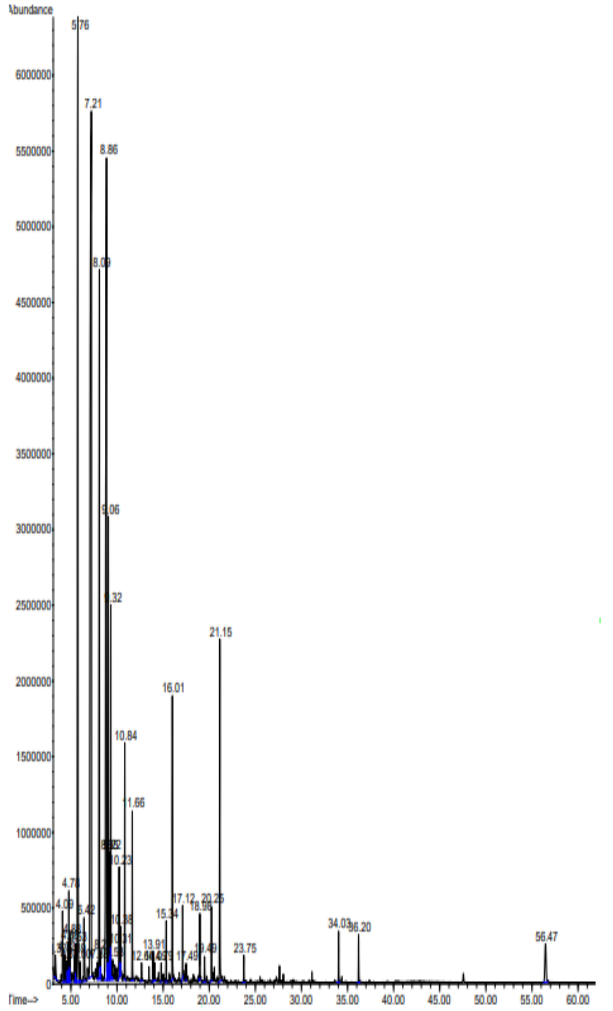

Figure 1. Chromatogram of *Lavandula Officinalis L.* Essential Oil Compounds using GC/MS method

Chromatographic profiles have been illustrated in Figures 1. Fourty three compounds were identified in lavender essential oil. A total of 75 patients completed the study. The flow of the participants through the study has been shown in Figure 2.

Table 2 shows baseline measurements for the five groups. Based on the results of the chi-square test with Monte Carlo simulation, there were no statistically noticeable distinctions between the experimental groups in terms of patient sex distribution.

Groups A, B, C: 15 patients in each group received lavender essential oil cream at a dose of 3%, 5%, and 8%, respectively. Group D: 15 patients received 1% topical hydrocortisone. Group E: 15 patients received

cream base (Eucerin).

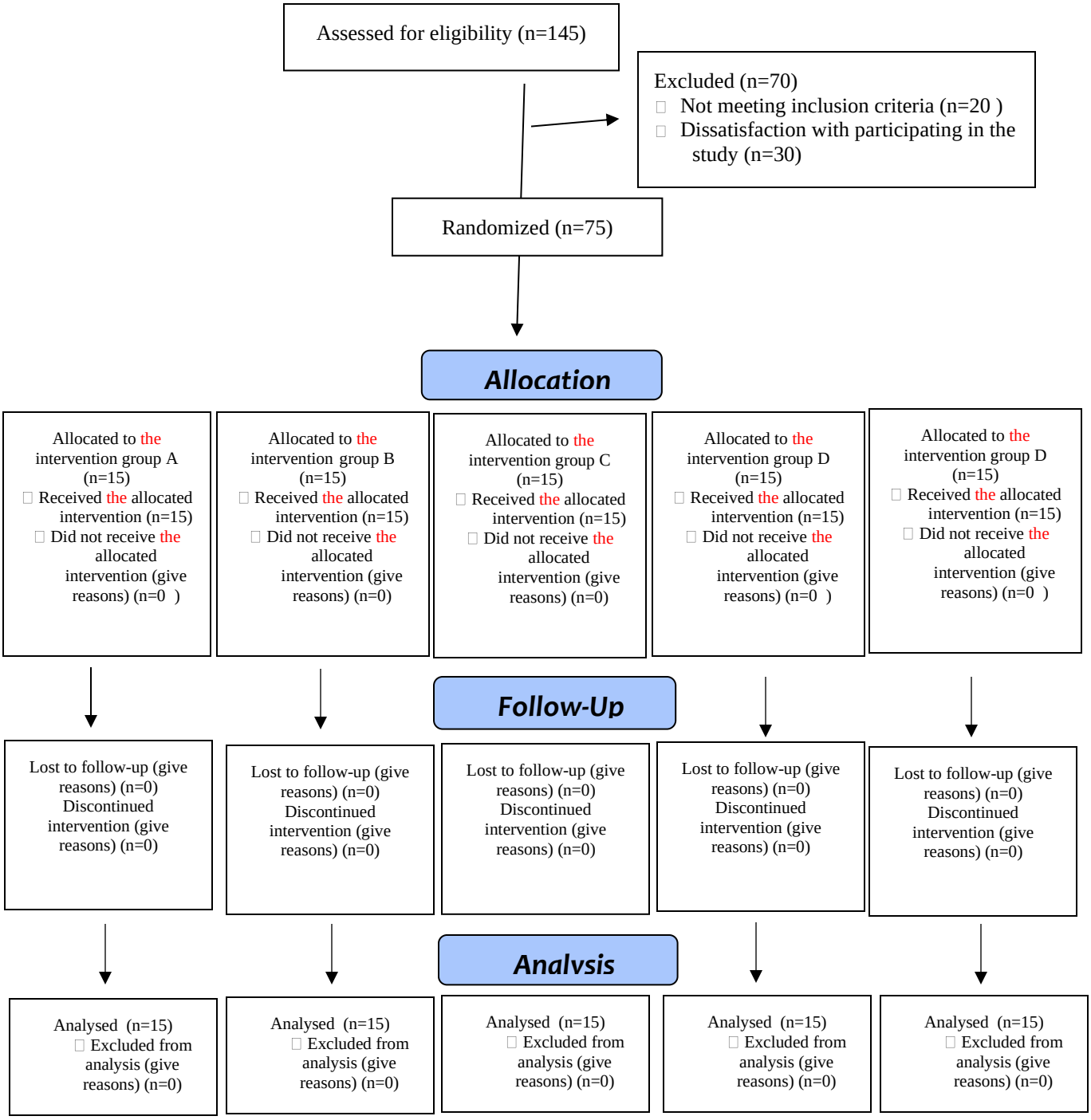

Figure 2. The Flow of the Study

In Table 3 and Figure 2, the marginal model and GEE estimation method showed that interaction of the experimental groups and time factor on the severity of eczema was statistically significant (X^2 = 13.106, df = 4, P = 0.011) so that the relative chance of higher eczema severity in the experimental groups varied and

Table 2: Comparison of the Experimental Groups in Terms of Patient Sex Distribution (n=15).

Groups	Female	Male	P value
A	13 (86.7 %)	2 (13.3%)	
B	10 (66.7 %)	5 (33.3%)	
C	11 (73.3%)	4 (26.7%)	0.443
D	10 (66.7%)	5 (33.3%)	
E	8 (53.3%)	7 (46.7%)	
Total	52 (69.3%)	23 (30.7%)	

Table 3: Comparison of Experimental Groups in Terms of Eczema Severity of Symptoms with the Passage of Time.

Groups	Eczema severity (%)	Time to check for symptoms		
		Beginning of the study	Seventh day	Fourteenth day
A	0-24	0 (0)	7(46.7)	7 (46.7)
	25-49	9 (60.0)	5 (33.3)	5 (33.3)
	50-74	6 (40.0)	2 (13.3)	1 (6.7)
	75-100	0 (0.0)	1 (6.7)	2 (13.3)
B	0-24	1 (6.7)	8 (53.3)	12 (80)
	25-49	10 (66.7)	0 (0.0)	0 (0.0)
	50-74	0 (0.0)	7 (46.7)	2(13.3)
	75-100	4 (26.7)	0 (0.0)	1 (6.7)
C	0-24	0 (0.0)	0 (0.0)	3 (20.0)
	25-49	11 (73.3)	3 (20.0)	0 (0.0)
	50-74	1 (6.7)	11 (73.3)	9 (60.0)
	75-100	3 (20.0)	1 (6.7)	3 (20.0)
D	0-24	2 (13.3)	3 (20.0)	5 (33.3)
	25-49	4 (26.7)	6 (40.0)	4 (26.7)
	50-74	5 (33.3)	4 (26.7)	5 (33.3)
	75-100	4 (26.7)	2 (13.3)	1 (6.7)
E	0-24	0 (0.0)	2 (13.3)	7 (46.7)
	25-49	6 (40.0)	10 (66.7)	7 (46.7)
	50-74	5 (33.3)	2 (13.3)	1 (6.7)
	75-100	4 (26.7)	1 (6.7)	0 (0.0)

Groups A, B, C: 15 patients in each group received lavender essential oil cream at a dose of 3%, 5%, and 8%, respectively. **Group D**: 15 patients received 1% topical hydrocortisone. **Group E**: 15 patients received cream base (Eucerin). P- value of interaction of experimental group and time factor was 0.011, P- value of the main effect of the time factor was 0.028, P- value of the main effect of the experimental group was 0.178.

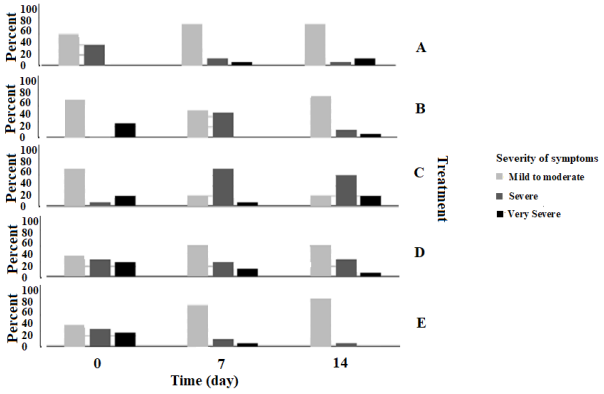

Figure 3. Comparison of Experimental Groups in Terms of Eczema Severity of Symptoms with the Passage of Time.

Table 4: Relative Chances of Higher Eczema Severity in Different Experimental Groups. *t: Time (day)

Type of comparison With group E	Odds ratio calculation formula Exp (n*t)	Odds ratio amount (Day)	
		Seventh	Fourteenth
Group A	1.368-0.210	0.903	0.208
Group B	0.883-0.187	0.653	0.176
Group C	1.094-0.348	0.261	0.023
Group D	1.053-0.166	0.330	0.103

It was a function of time, which has been explained in **Table 4**. According to the results of the marginal model, the relative chance of any increase in the severity of eczema in group A compared with group E on the 7th day of treatment was reduced by about 9.7% (OR = 0.903), while on the 14th day of treatment it decreased by about 79.2%. According to the results of the same model, the relative chance of any increase in the severity of eczema in group B compared with group E on the 7th day, decreased by about 34.7% (OR=0.653) while on the 14th day it decreased by about 82.4%. Moreover, the relative chance of any increase in the severity of eczema in group C compared with group E on the 7th day of treatment was reduced by about 73.9% (OR=0.261), while on the 14th day of treatment it decreased by about 97.7%. The relative chance of any increase in the severity of eczema in group D compared with group E on the 7th day of treatment was reduced by about 67.0 % (OR = 0.330), while on the 14th day of treatment it decreased to about 89.7%.

Groups A, B, C: 15 patients in each group received lavender essential oil cream at a dose of 3%, 5%, and 8%, respectively. Group D: 15 patients received 1%

topical hydrocortisone. Group E: 15 patients received cream base (Eucerin).

In this randomized clinical trial, we studied the impact of lavender essential oil on the recovery of symptoms of eczema. The sample groups matched concerning demographic and clinical characteristics. Our finding showed that the relative chance of any increase in the severity of eczema in the groups treated with L.O on the 7th and the 14th days of treatment reduced. It was also observed that the amount of this decrease was related to the dose of lavender, so that the highest effectiveness was observed in 8% concentration. Lavender is very used in perfumes, cosmetics, and cleaning products. The essential oil of lavender is rich in aromatic compounds such as cineole, borneol, camphor, monoterpene and phenols. Therefore, it has been used traditionally for psoriasis, dermatitis and eczema treatment. It has been shown in several studies that caryophyllene oxide, cineole, and terpenoid oxide have anti-inflammatory effects (10-11). In animal models of rats and mice, lavender showed anti allergic and inhibitory effects on histamine release from the mast cells (12-13). Linalyl acetate and linalool of lavender essential oils have local anesthetic effects. Findings of an animal model study revealed that linalyl acetate and linalool could improve in psoriasis-like conditions. These components have an anti-proliferative effect and can reduce epidermal hyperproliferation as well as hyperplasia that are very common in eczema patients (14-16). In a study, the effect of LO on the treatment of psoriasis in the rat model was examined, and its results showed that LO could significantly reduce symptoms of psoriasis. Young Mi et.al, showed that LO could reduce the symptoms of eczema in rats (17). Contrary to the findings of the present study the results of a study conducted on humans indicated that using a combination of lavender oil and other herbal essential oils for aromatherapy massage could not contribute to the improvement of skin irritation in children with itchy and inflamed skin (18). In another study, the impacts of topically applied 2% lavender oil on pain, healing, and safety in 115 patients with recurrent aphthous ulceration were examined. After four days, 100% of the lavender group experienced complete healing without any erythema, edema, and pain (19). So far, few clinical studies have investigated the effect of lavender essential oil in the treatment of eczema, and our study is the only randomized clinical trial that investigates the effects of lavender in the treatment of eczema in adults. The results of the present study showed that lavender oil could significantly reduce the severity of eczema with the passage of time. The only limitations of this study was low sample size. Further studies with a larger sampla size are recommended to be conducted.

Conclusion

Our findings showed that the relative chance of any increase in the severity of eczema in the groups treated with L.O was reduced. Lavender has dose-dependently beneficial effects on the treatment of eczema. It was also observed that the amount of this decrease was related to the dose of lavender, so that the highest effectiveness was observed in the concentration of 8%. With a concentration of 8%, it could have a better effect than hydrocortisone in treating eczema without any side effects.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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None.

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