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The effect of rosemary ointment on the pressure ulcer healing in patients admitted to the intensive care unit: A randomized clinical trial

Fatemeh Khoshoei Parizi[1], Tabandeh Sadeghi[2], Shahin Heidari[3]*

[1]Student Research Committee, School of Nursing and Midwifery, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[2]Department of Pediatric Nursing, School of Nursing and Midwifery, Non-Communicable Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran
[3]Department of Fundamental Nursing, School of Nursing and Midwifery, Geriatric Care Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

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***Corresponding Author:**
Shahin Heidari, Department of Fundamental Nursing, School of Nursing and Midwifery, Geriatric Care Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.
E-mail: kermanshah3252@yahoo.com

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ABSTRACT

Background & Aim: Pressure ulcers have been identified as one of the most important and challenging issues in patient's well-being. Based on the evidence, rosemary extract compounds can affect wound healing. The aim of this study was to determine the effect of rosemary ointment on pressure ulcer healing in patients admitted to the intensive care unit.

Methods & Materials: In this single-blind randomized parallel clinical trial, 70 patients who met the inclusion criteria were selected purposefully and assigned to the groups by stratified randomization method. In the intervention group, rosemary ointment was applied once a day for seven days. The control group received routine care. Data were collected using the Pressure Ulcer Scale for Healing before the intervention and on the third and seventh days after the intervention. Data were analyzed using independent t-test, chi-square test, and two-way repeated measurements ANOVA with SPSS 18 software.

Results: The mean scores of Pressure Ulcer Scale for Healing decreased significantly in the intervention group while remained unchanged in the control group (P=0.001) one week after the intervention. The effect of time and interaction effect was also significant (P=0.001). Comparison of the ratio of complete ulcer healing in the two groups showed a significant difference between the two groups (p=0.004).

Conclusion: Rosemary ointment facilitated healing and prevented the progression of grade I pressure ulcers in the Intensive Care Unit. Therefore, the use of this ointment as a low-risk, uncomplicated, available, and inexpensive intervention, is recommended in such patients.

Introduction

A pressure ulcer is a local skin injury caused by pressure or a combination of pressure and tensile forces on the bony prominences and is more prevalent in the sacrum, hips, and heels (1,2). Pressure ulcers form within 2 to 6 hours after the pressure is introduced onto the tissue. Therefore, to prevent it, the pressure on the tissue capillaries should be kept lower than 30 mmHg (1). Several factors such as age, inadequate nutrition, decreased mobility, decreased body mass, anemia, hypoalbuminemia, friction, decreased sensory perception, history of pressure ulcers, cigarette smoking, and vitamin A, C, and E deficiency are considered to be contributing factors in the development of pressure ulcers (2, 3). There are various reports on the prevalence of pressure ulcers. Their prevalence in the United States, Canada, and

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European countries are reported to be 17%, 25%, and 18%, respectively (4). The studies conducted in Iran have reported the rate of pressure ulcers to be 28.6% in internal wards and 12.9% in the general surgery wards (5). However, the prevalence of pressure ulcers is higher in Intensive Care Unit (ICU)wards, ranging between 8% and 40% (6). Changing the body position every 2 hours, cleansing the area around the wound, and avoiding contact with the patient's urine or stool can prevent the formation of pressure ulcers. Also, daily assessment of the site, length, width, and depth of the wound as well as the healing rate and the presence of smell, necrosis, scars, and infection, should be constantly recorded. If necessary, debridement should be performed to prevent bacterial growth (7). Pressure ulcers impose significant costs on both the health care system and patients (8). In addition to the pain and discomfort caused by cellulite and gangrene, these wounds can lead to amputation, impaired quality of life, and even death (9). There are various approaches to the treatment of pressure ulcers, such as cleaning the wound, debridement, optimized dressings, patient optimization, antibiotics, and reconstructive surgery. Also, newer treatment options such as negative pressure wound therapy, hyperbaric oxygen therapy, and cell therapy are provided (10).

Today, the tendency to use medicinal herbs in pressure ulcer treatment has increased due to the variety of effective compounds and their fewer side effects. Several studies have suggested the use of honey (11), fish oil (12), calendula officinalis (13), and aloe vera gel (14) to prevent and reduce the formation of pressure ulcers. Rosemary is a medicinal plant containing essential oils with anti-inflammatory, antispasmodic, antioxidant, antimicrobial, and muscle relaxing properties. The leaves of this plant contain flavonoids (apigenin), phenols, volatile oils (camphor), and terpenes (hidrosuricular and carnosol) (15).

Wound healing process involving epidermal regeneration, fibroblast proliferation, neovascularization, and synthesis. One of the factors that impair the healing process is free radicals that are generated at the site of injury causing damage to cellular membranes, nucleotides, proteins, and lipids (16). The wound healing effects of rosemary extract comes mainly from its antioxidant property (17, 18). This antioxidant effect is related to two phenolic diterpenes (Carnosic acid and carnosol) (19). Also, Carnosol, anthraquinones, terpenoids, oleanolic acid, and flavonoids are responsible for the anti-inflammatory effects of rosemary extract (17, 18).

Wound healing effects of Rosemary extract has been studied in throat ulcer after endotracheal intubation (20). angiogenesis and granulation tissue growth at the wound site in the diabetic male rats (21) mucosal ulcers of the mouth, lips, and gums in goats with small ruminant plague (22) and the rate of infection and increases the volume of collagen and production of epithelial tissue in the affected area (23).

Also, the anti-inflammatory and vasodilation properties of Rosemary extract have been discussed in a study. Results showed that rosemary extract positively affects the survivability of random-patterned skin flaps in rats (24).

Boyko et al. (2018), in a review of the current management of pressure ulcers, stated that despite a large number of treatments available, none of them is superior to the other, and pressure ulcers remain a debilitating and costly issue. They recommended additional research to develop products more effective in preventing and treating pressure ulcers (25).

Considering the possibility of the severe complications and additional costs of improper treatment of pressure ulcers and emphasis on the need for further research in review studies, this study was conducted to determine the effect of rosemary ointment on grade I pressure ulcers in ICU patients.

Methods

In this single-blind concurrent parallel randomized clinical trial, out of 500 patients assessed for eligibility, 70 patients with grade I pressure ulcers who met inclusion criteria were selected through purposive sampling.

The sample size was calculated using the formula for comparison of means, with a standard deviation of 1.1 cm^2 of the pressure ulcer area and an effect size of 0.9.

Various methods have been used to overcome the problem of unmatched trial groups, including minimization and stratification, with minimization providing more acceptable results. In the present study, minimization was made based on levels of age and BMI variables, which were predicted to have important effects on the study's primary outcomes. Levels of age were defined as 20- 40, 41-60, and ≥61 years. BMI categories were 20- 25 and >25. The first subjects were enrolled randomly into one of the groups/categories. The subsequent subjects were allocated to the group/category with fewer samples. The inclusion criteria were the presence of a grade I pressure ulcers (warmth, swelling, redness, and no change in the color of the pressure area 30 minutes after the pressure was removed), immobility, a moderate or severe reduction in consciousness (GCS scores< 8), over 20 years of age, no skin disorders such as dermatitis, no history of diabetes, not using corticosteroids, and no history of allergy to rosemary ointment. Patients were excluded from the study if they need to dopamine drip or their ulcer progressed to grade Π.

In the intervention group, the wound area was washed with normal saline, and then the rosemary ointment (2-3 mm) was rubbed over the wound and covered with a sterile gauze dressing once a day in the morning shift, for seven days. This study used 30 g tubes of rosemary ointment, each containing 2.4 g rosemary essence oil, 1.2 g caffeine, and 1.2 g menthol, prepared and sterilized by Gol Daru Company (Tehran, Iran). A preliminary sensitivity test was performed by applying a layer of ointment on the patient's inner arm. No allergic reaction was detected 30 minutes after use. The control group received routine care, including changing position every 2 to 3 hours and washing the wound area with normal saline once a day. The same nurse was responsible for pressure ulcer care in the morning shift for patients in the control group. The wound healing process was recorded three days and one week after the intervention. Data were collected by a nurse out of the research team.

Data collected by the personal information questionnaire (age, sex, location of ulcer, type of diet, laboratory indices, etc.) and the Pressure Ulcer Scale for Healing tool (PUSH). The PUSH tool was developed by the National Pressure Ulcer Advisory Panel (NPUAP) as a quick, reliable tool to monitor the change in pressure ulcer status over time. The first draft of the tool was presented at the Fifth National NPUAP Conference in February 1997. This tool is FREE for noncommercial use. Since its initial development, the tool has been validated by 2 multi-site retrospective studies. A pilot test conducted by CMS Data from two studies confirmed that the PUSH tool is a valid and sensitive measure of pressure ulcer healing (26).

In the present study, the instrument's content validity was measured through the qualitative content validity method by ten experts (including one methodologist, two instrument developing experts, five nurses experienced in wound care, and two wound care research experts). To assess the reliability, two observers completed PUSH separately for ten patients a few hours apart. The inter-rater Kappa was 0.9, which indicates a high degree of agreement between the data collected by the two examiners

The PUSH tool evaluates three items, including the extent of the wound area, the amount of exudate, and the type of tissue disorder. The size of the wound area was calculated by multiplying the largest length by the width; both were measured using a calibrated ruler with a precision of one millimeter. The scoring was conducted as follows:

The extent of the wound was scored on the 10-point ordinal scale from zero (no ulcer) to 10 (area over 24 cm^2), the amount of exudate on the 4-point ordinal scale from zero to three (absence of exudate, low, moderate, and high amount of exudate) and tissue impairment on the 5-point ordinal scale from zero to four (Closed, epithelial tissue, granular tissue, dead tissue, and necrosis).

The minimum and maximum total scores of the PUSH varies between zero and 17 (26).

Given the fact that there isn't any exudate or tissue destruction in grade I ulcers, these two items were scored zero. The total scores of the three measurements were recorded and compared to determine the wound healing process. A reduction in the total score in the final assessment indicated the effectiveness of the intervention. This study was registered at the Iranian Center for Clinical Trials with the IRCT20160503027736N3 code and was approved by the Ethics Committee of Rafsanjan University of Medical Sciences (RUMS) (IR.RUMS.REC. 1396.208). All procedures were performed in compliance with associated regulations and institutional guidelines. As the patients were unconscious, written informed consent was obtained from the patients' relatives after explaining the research goals and assuring them of the confidentiality of personal information and the safety of the intervention. None of the patients developed complications following the intervention.

In this study, the PUSH tool was completed by a trained fellow who was blind to the group allocations and was outside the research team, and the ointment was applied by a fixed individual of the research team for all patients.

Data were analyzed with SPSS software version 18 using descriptive statistics (mean and standard deviation). A Two-way repeated-measures ANOVA was conducted to compare the effect of rosemary ointment on the healing process of pressure ulcers before, three days, and one week after the intervention. The significance level for multiple comparisons was adjusted with Bonferroni adjustment. To get the Bonferroni corrected/adjusted p-value, we divided the original α-value (0.05) by the number of analyses on the dependent variable (3). The adjusted p-value was equal to 0.0160.

Results

A total of 500 patients hospitalized in the ICU were assessed for eligibility during the 6-month period from March to September 2019, 70 of whom met the inclusion criteria and completed the study (Figure 1).

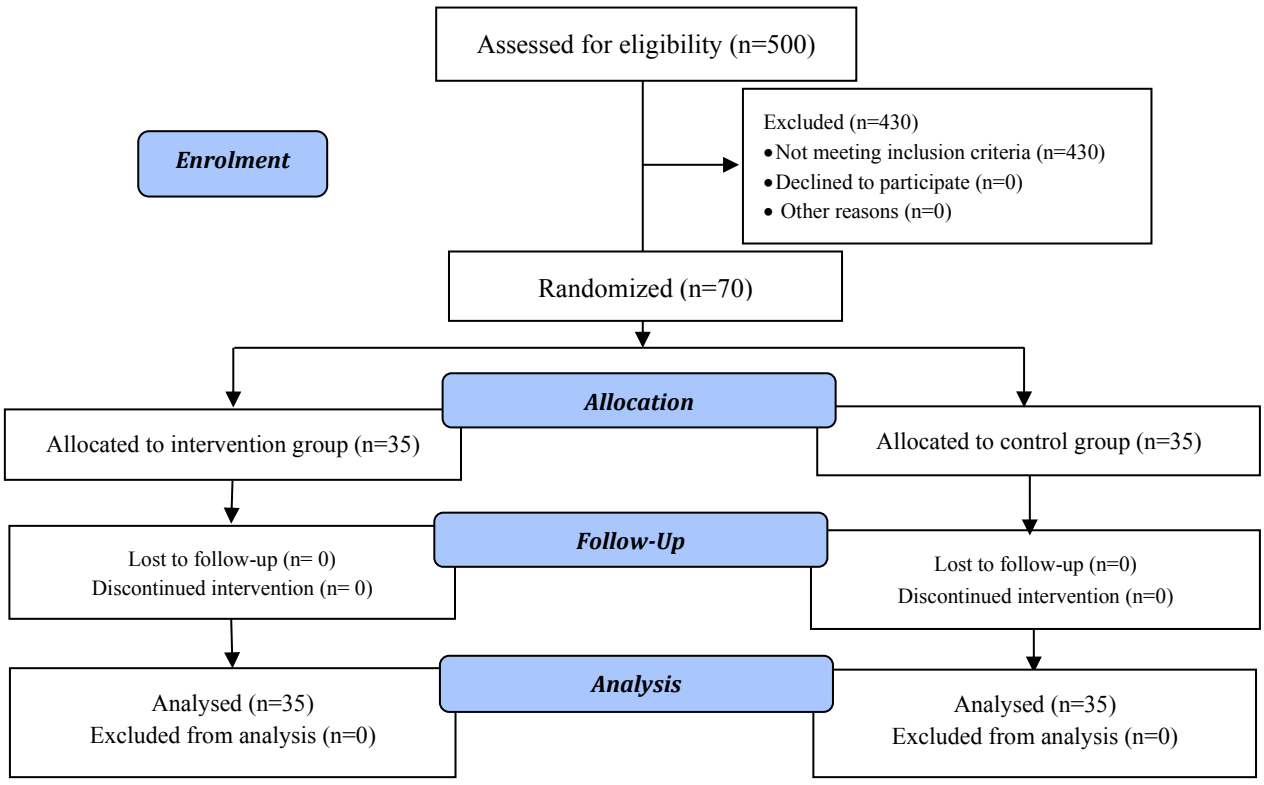

Figure 1. Consort flow diagram of the study

The mean age of patients was 67.94 ± 16.9 years in the intervention group and 68.45 ± 16.6 years in the control group. The patients of both groups were homogeneous in terms of demographic characteristics (Table 1).

To assure repeated measures ANOVA assumptions, independence of observations was met; participants did not interact in any way with other participants. The normality of PUSH scores was tested using the Kolmogorov-Smirnov test. Results showed that the data follow a normal distribution ($p > 0.05$).

Two-way repeated-measures ANOVA was used for group, time, and interaction of time and group effects. According to this test, all three results were significant (Table 2).

Table 1. Comparison of the demographic characteristics of patients in intervention and control groups

Variables		Intervention group (N=35)	Control group (N=35)	P-value*
		Mean ± SD	Mean ± SD	
Age		68.69±16.97	68.45±16.6	0.898
Laboratory Indices	ESR	38.62±29.44	27.50±25.02	0.242
	CRP	55.84±23.48	46±20.52	0.231
	WBC	1.058±4280.86	1.506±1339.24	0.64
	Albumin	4.96±7.26	3.05±0.36	0.443
	Creatinine	1.62±1.38	1.74±1.17	0.691
		N (%)	N (%)	P-value**
Sex	Male	13(37.1)	14(40)	1
	Female	22(62.9)	21(60)	
Method of nutrition	NGT	33(95.3)	31(88.6)	0.673***
	PEG	2(5.7)	4(11.4)	
Location of pressure ulcer	Shoulder	6(17.1)	8(22.9)	0.564**
	Sacrum	14(40)	14(40)	
	Heel	11(31.4)	7(20)	
	Auricle	4(11.4)	4(11.4)	
	Chin	0(0)	2(5.7)	
Inotropic drugs	Yes	8(22.9)	13(37.1)	0.148**
	No	27(77.1)	22(63.9)	

*Independent T-Test
** Chi-square
*** Fisher's exact test

Table 2. Comparison of the mean and standard deviation of PUSH scores of intervention and control groups in the time series of intervention

Groups	Time of assessment			Two-way repeated-measures ANOVA		
	Before intervention	Three days after the intervention	1 week after intervention	P-value*	P-value**	P-value***
	Mean±SD	Mean±SD	Mean±SD			
Intervention	8. 02 ± 1.99	6.01 ± 3.43	3.01 ± 3.63	0.001	0.001	0.001
Control	6.88 ± 2.82	6.34 ± 3.33	6.05 ± 3.57			

* Repeated measures ANOVA (inter-group comparison)
** Repeated measures ANOVA (intra-group comparison)
*** Repeated measures ANOVA (interactive effect)

Pairwise Comparisons between groups showed no significant difference before the intervention (P= 0.055) and three days after the intervention (P= 0.67), but the mean scores of PUSH between two groups one week after the intervention was significant (P= 0.001) (Table 3).

Considering the significance of the interactive effect, the average changes in each group over time were also examined, and based on the results, there was a significant difference between the mean, and standard deviation of the PUSH scores of the patients in pair comparisons (P= 0.001) and the mean score of PUSH was decreased during the time; however, these changes were not significant in the control group (P>0.05). (Figure 2). Comparison of complete healing in the two groups using chi-square for the goodness of fit test showed a significant difference between the two groups (Table 4).

Table 3. Comparison of the mean and standard deviation of PUSH scores between intervention and control groups before and after the intervention

Groups	Time of assessment					
	Before intervention		Three days after the intervention		One week after intervention	
	Mean difference	Std.Error	Mean difference	Std.Error	Mean difference	Std.Error
Intervention	1.14	0.58	-0.34	0.81	-3.05	0.86
Control						
P-value*	0.055		0.67		0.001	

* Repeated measures ANOVA (Adjustment for multiple comparisons; Bonferroni)

Table 4. Comparison of complete healing rate in two groups seven days after intervention

Groups / Wound condition	Intervention	Control	Chi-square test statistic	P-value
	N (%)	N (%)		
Complete healing	17(48.6)	5(14.3)	9.54	0.004
Incomplete healing	18(51.4)	30(85.7)		

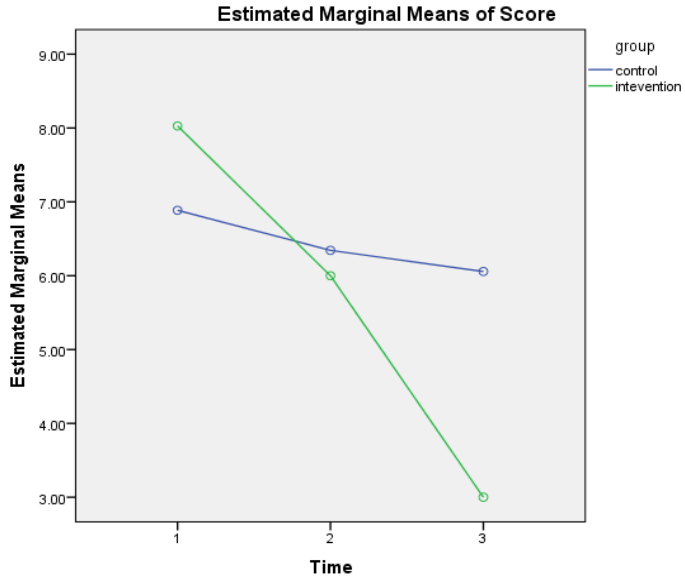

Figure 2. Comparison of PUSH score in both intervention and control groups before, three days, and one week after intervention

Discussion

Based on the results, there was a significant difference between the mean score of PUSH in the two groups one week after the intervention. The mean score of PUSH in the intervention group showed a significant decrease, while no change was seen in the control group. The effect of rosemary ointment on wound healing was more pronounced from the fourth day until the end of the seventh day.

According to available evidence, rosemary compounds inhibit the formation of inflammatory mediators such as prostaglandins, leukotriene, and cytokines in vitro (27).

Also, three phenolic diterpenes, including carnosic acid, carnosol, and rosmarinic acid, are responsible for antioxidant activity (Abdolghaffari). So, the significant differences between the two groups in the present study in terms of wound healing can be attributed to these properties.

Several studies reported similar results. Ince et al. (2015) reported that the use of rosemary extract twice a day for one week before and one week after removing the skin flap increased vascular dilatation, reduced inflammation, and necrosis, and ultimately increased survival of the flap skin (24).

Results of another study showed that rosemary extract could prevent throat ulcers after endotracheal intubation (28). In one study, rosemary essential oil increased angiogenesis and granulation tissue growth at the site of incisions in the diabetic male rats (21). In another study, mucosal ulcers of the mouth, lips, and gums in goats with small ruminant plague healed within 10 days of the use of rosemary essential oil (22). use of rosemary ointment significantly increases the volume of collagen and the production of epithelial tissue in the affected area (23).

Li et al. (2017) reported that the use of MEBO for one week did not significantly affect the improvement of pressure ulcer grades III and IV. This could be attributed to components such as esters, glycosylated flavonoids, and a fatty alcohol, which are also present in rosemary essence. MEBO increases the growth of new vascular tissues and vascular endothelial cells by incorporating compounds such as sesame oil, beta-sitosterol, and berberine (29). Both the study of Li et al. and our study use ointments with herbal bases, but there is a discrepancy between the results of the former and those of the present study, which can be due to the difference in the grade of pressure ulcers and duration of ointment use.

In the present study, at the end of seven days of intervention, the recovery rates in the two groups were significantly different. This finding coincides with the results of the study by Elahi et al (12), Hosseinrezaei et al (30), and Farsaei et al (31).

In this study, none of the patients had complications from the intervention. Extreme accuracy in the diagnosis of pressure ulcers of the first stage, implementation of all stages of intervention by a researcher, and evaluation of the wound healing process by someone outside the research team were other strengths of this study. However, due to the lack of evidence of the safety of rosemary ointment in open wounds, in this study, only patients with stage I pressure ulcers were considered, which is a kind of limitation, also due to the lack of studies. Similarly, in this study, rosemary ointment was used only once a day for a week, which may affect the results of the study.

Conclusion

Daily use of rosemary ointment for seven days significantly improved the healing of grade I pressure ulcer and prevented its progression to higher grades. So routinely use of this intervention can be recommended as a safe, effective and inexpensive measure to treatment of pressure ulcer and prevention of its progression.

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Conflict of interest

The authors declare that they have no conflict of interest.

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