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The effects of peppermint gel on prevention of pressure injury in hospitalized patients with head trauma in neurosurgical ICU: A double-blind randomized controlled trial

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ABSTRACT

Objective: This study aimed to evaluate the effect of peppermint gel on the prevention of pressure injuries in patients with head trauma admitted to neurosurgical intensive care units.
Design: This double blind, randomized, controlled clinical trial study was conducted on 150 patients with head trauma admitted to the ICU. Using sealed envelopes, patients were assigned randomly into two intervention (n = 75) and control (n = 75) groups.
Setting: The study was conducted in the ICUs of a university hospital and a general hospital in Shiraz, Iran.
Intervention: The intervention group received peppermint gel three times a day up to 14 days during the skin care as a layer on the skin areas exposed to the risk of pressure injuries. The control group used a placebo gel.
Primary outcomes: The expected outcome in this study was the incidence of pressure injuries stage I, which once daily was evaluated by pairs of observers with the National Pressure Ulcer Advisory Panel.
Results: The incidence rate of pressure injuries was 22.8% and 77% in the intervention and the control groups, respectively. The chi-square test result showed a significant deference between two groups ($P < 0.001$). Sacrum was the most common site for incidence of the pressure injuries.
Conclusion: The findings showed that the peppermint gel has a positive effect in the prevention of pressure injuries in the patients with head trauma admitted to ICUs. So, the use of this gel is suggested as an easy and low-cost method for prevention of pressure injuries in the patients admitted to ICUs.

1. Introduction

A pressure injury (PI) is localized injury to the skin or underlying tissue usually over a bony prominence because of pressure and shear.[1] The treatment and prevention of PIs consume large quantities of resources in terms of disposable equipment and nursing time.[2] The PIs have been described as one of the most costly and physically debilitating complications in the 20th century.[3] The PIs are the third most expensive disorder after cancer and cardiovascular diseases.[4] Up to 13% of patients during treatment develop the PIs in the intensive care unit (ICU). In fact, critically ill patients have twice risk factors of the PIs, and the patients admitted to the ICU are exposure to the PIs due to the nature of the disease and immobility.[5]

The PIs are associated with two to four times increased in mortality among the ICU patients.[6] The PIs are globally considered as an important indicator of quality of care and more ulcers are avoidable.[1,7]

The incidence rate of PIs varies in different studies. For example, this rate has been 40%–49% in a study by Shahin et al. (2008),[8] and 3.3% in ICUs in Shahin et al. (2009) survey,[5] and in a range of 10%–41% in Cooper (2013);[9] and the cumulative incidence of 15% and higher has been reported in studies by Black (2012),[10] Cuddigan (2012) and Goldberg (2012).[11,12]

In addition, based on the reports of studies conducted in Iran, the incidence rate of PIs has been found 35.3% by Mohammadi et al.,

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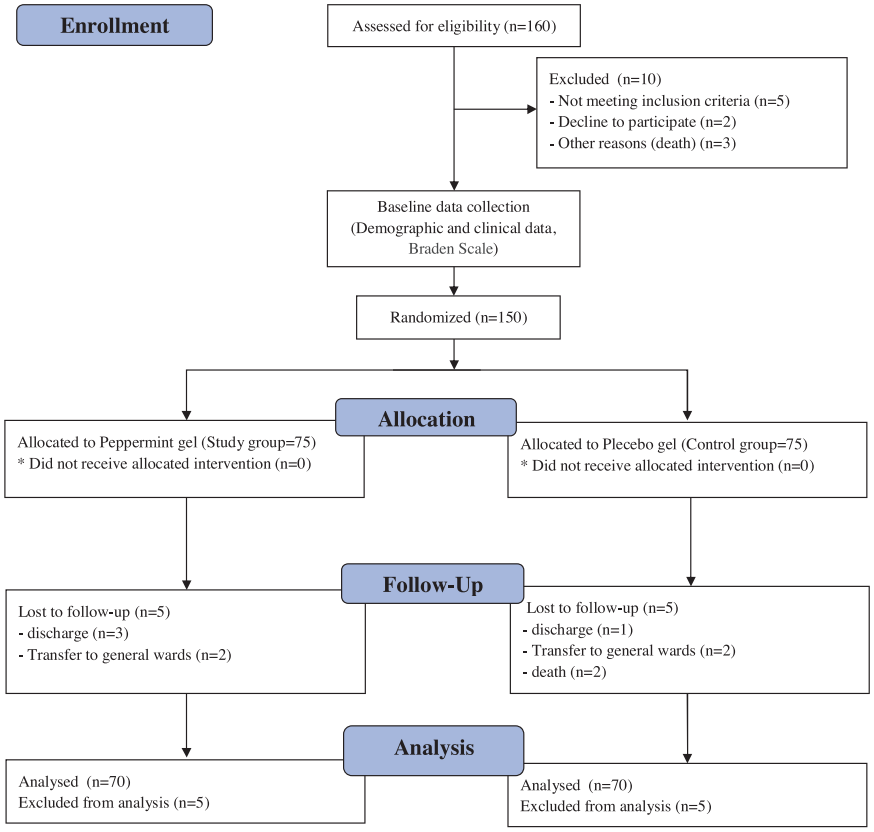


Fig. 1. Flow diagram of the study.

(2013) among patients receiving mechanical ventilation admitted in the ICU,[13] 22.7% by Reihani & Haghiri (2007) in patients with spinal cord and cranial injuries admitted in the ICU,[14] 22.6% by Amirifar et al. (2013) in hospitalization wards,[15] and 13.9% by Bolourchi et al. (2015) in orthopedic wards.[16]

The PIs in addition to the impact on the physical, psychological and social domains of patient well-being have a financial impact on all the families involved,[17,18,19] and reduce considerably the quality of life.[20]According to systematic review, cost of PI prevention per patient per day varies between €15.70 and €87.57. The average cost of PIs treatment differs between €1.71 and €470.49 per patient in all types of health care settings.[21] In the United States this cost have been reported 20900–151700 dollars per patient.[22] The costs of prevention and treatment of PIs include services, long-term hospitalization, complications of the wound and disposable materials. The cost of nursing services compared to the cost of disposables accounted for the highest degree.[23],[24],[25]

One of the main groups at risk of developing PIs, are patients with head and spinal injuries hospitalized in ICUs.[26]

Prevention of the incidence of PIs is considered as a first step due to adverse consequences and the high cost of treatment, because prevention is the most effective way to solve this problem and high quality nursing care is major key to solving this problem.[15]

In recent decades, several attempts have been made to improve the prevention of PIs in clinical areas, which have been based mainly on the implementation of evidence-based guidelines.[27–29] Systematic reviews that integrate the results of more than 20 studies have shown discrepancies in the areas of the use of preventive methods as well as facility-acquired PIs.[27–29] This heterogeneous results have been approved by experimental and quasi-experimental studies. While some trials have shown increase the number of patients receiving appropriate preventive methods but no significant reduction in the prevalence of PIs,[30,31] other trials haven't recorded significant changes in the use of preventive tools but reported a significant reduction in the incidence of PIs.[32],[33]

Various methods have been examined to prevent PIs in different studies. For example, the use of foam mattresses by Russell et al. (2003),[34] massage, fluid intake and adequate nutrients by Shahin et al. (2009),[5] and the use of pressure-reducing mattresses and planned repositioning in the study of Sving et al. (2016).[31]

Numerous studies have been examined the efficacy of novel approaches for treatment of PIs including; anodal and cathodal-anodal electrical stimulation on reducing the area of category II-IV PIs,[35] negative pressure-vacuum-assisted closure technology in rapid healing of chronic wounds,[36] extracorporeal shockwave therapy for the treatment of soft tissue ulcers, complete wound closure and reepithelialization, increased tissue granulation, increased blood flow perfusion and angiogenesis and reduced need for antibiotic treatment,[36,37] effect of laser therapy on angio and fibrogenic factors and cytokine concentrations during the healing process of PIs,[38,39] and application of stem cells in skin wound healing.[40] Nevertheless, so far no definitive method has been discovered to treat and prevent PIs.

The use of complementary medicines including medicinal plants is one of the proposed and potential cases in this regard that has been common since long ago. Recent approaches to medicine also have been welcomed by the public throughout the world for the prevention and treatment of diseases due to fewer side effects.[41] Peppermint plant can be mentioned on the application of medicinal plants; the essential oils of this plant have potent antibacterial and antifungal properties,[42] antiseptic effects,[43] as well as increase the elasticity of the skin and cause resistance against skin ulceration.[44]

The essential oil of peppermint plant, *Mentha Piperita L.*, is among the compounds that are generally regarded as safe.[42] The peppermint gel stimulates the skin receptors and dilates blood vessels, causing a sense of coolness and an analgesic effect.[45,46] The peppermint gel has average antimicrobial properties against gram-positive and gram-negative bacteria, *Candida albicans*, Aspergillus and Dermatophytic

fungi.[45] Menthol in peppermint is also a local vasodilator, which increases skin absorption of topical medications.[45,46] Several studies so far have been done on the effect of peppermint on the prevention of creating ulcers in other clinical situations, including nipple crack, aphthous stomatitis and oral mucositis.[42–44,47] Nevertheless, no study has examined the effect of peppermint gel in the prevention of PIs.

According to the positive properties of peppermint in stimulation of skin receptors, dilation of blood vessels and creation a sense of coolness and analgesic and anti-bacterial and anti-septic properties, this study was designed to evaluate the effect of peppermint gel for the prevention of PIs among the patients with head trauma admitted to the ICU.

2. Materials and methods

2.1. Study design

In this parallel double-bind randomized controlled trial, 150 patients from the ICUs of a university hospital and a general hospital were assigned randomly into the two intervention (n = 75) and control (n = 75) groups. Random sequence allocation was carried out using sealed envelopes (Fig. 1). Patients and relatives were blinded towards the assigned intervention, as well as outcome assessors and statistician.

2.2. The research community and setting

The research setting was the two ICUs in the city of Shiraz, Iran. These centers are under the strict supervision of a neurologist at Shiraz University of Medical Sciences. Quality care for patients is the same in both of the centers. Convenience sampling method was used to select patients with head trauma hospitalized in the two centers.

Inclusion criteria were: admitted to the ICU because of head trauma, endotracheal tube on admission to the intensive care unit, patients that are at risk of moderate to severe bedsores according to Braden scoring tool and scored less than 13–14, lack of systematic diseases such as diabetes, heart failure, kidney failure and cancer advanced phase,[48] lack of sensitivity to the mint family plants, the absence of PI on admission, Glasgow Coma Scale of 8 and less on admission, and no limit of changes in body position with multiple injuries. Exclusion criteria included: death or patient transmission in less than 48 h after admission to the ICU, unwillingness of family to cooperate, natural-conscious state in less than 48 h after inclusion, and the sensitivity to mint gel after use on a patient's forearm (area of 2 × 2 cm) and this area was evaluated for the presence of redness, swelling and warmth within 45 min.[45]

2.3. Intervention

The peppermint gel and placebo was made in Shiraz Ahura Darou Company, manufacturing of herbal medicines, specializing in the extraction of medicinal herbs, topical gels and preventive products. The peppermint gel formulations were prepared according to standard methods (Table 1). A brief description of how to prepare the peppermint gel has been presented in the appendix. The same formulation was prepared without peppermint oil as a placebo.

Nurses in each ICU received the necessary basic training on how to use peppermint and placebo gels.

The intervention lasted from January 2015 to June 2015. Nurses in each ICU used the peppermint and placebo gels, which were prepared in two quite similar tubes with the same color and smell and distinguished from each other only with A and B symbols. Only a study supervisor and a pharmacist were aware of the type of gels.

In the intervention group, peppermint gel was rubbed three times during the skin care as a layer on the skin of areas at risk for PIs, including the patient's hip area, and bony prominences such as both elbows, knees, heels and shoulder. This action was continued until the patient staying in the ICU (maximum 14 days); and if the patient was discharged from the ward, or transferred to the general wards, they would be excluded from the study. In the control group, all measures were similar to the intervention groups, except that the placebo gel was applied in this group. All evidence-based guidelines on the prevention of PIs such as change position, proper nutrition, skin examination, using foam and massage mattresses were similar for both groups.

2.4. Measuring outcomes and tools

The expected outcome in this study was the incidence of PIs stage I, which once daily was evaluated by the pairs of observers (nurse plus specialist) trained in the detection of PIs that was unaware of the groups of the patients. Measurement tool used in this study was National Pressure Ulcer Advisory Panel (NPUAP).

2.4.1. National pressure ulcer advisory panel

The NPUAP is staging system since 1989 as one of the most widely used classification systems for the PI that describes the depth of the wound caused by PIs.[49] In accordance with the panel, the PIs are divided into the original 4 stages and adding 2 stages on deep tissue injury and unstageable PIs.[49] In this work, skin redness without discoloration by finger pressure in area of interest was considered as PIs stage I (Fig. 2).

The reliability of this tool by inter-rater method in comparing PI staging among the nurses and specialists in the ulcers demonstrated 65% agreement between observers and Kappa of 0.514 for all stages of PIs.[50] Of the 235″potential PIs identified," 16.6% were eliminated from the study as they represented etiologies other than pressure (eg, candidiasis, maceration, denudement).[50] Comparatively, 44 PI experts were asked to classify lesions, using 56 photographs, as normal skin, blanchable erythema, PIs using the EPUAP grades 1 to 4, or incontinence lesions. The percentage of agreement was 94.5% and the multirater Kappa was 0.80.[51] In this study, the reliability coefficient of 74% indicated a high reliability between the two observers.

2.4.2. Braden scale

The Braden scale is a tool that considers the fundamental aspects of PI development, including the cause and severity of the ulcer and tissue tolerance to pressure.[9] The checklist of Braden scale includes sensory perception, humidity, activity, mobility, nutrition, friction and abrasion. The sensitivity of this scale was 83%–100% and the specificity was 64%–77%. Scoring was as follows: score equal or less than 9 is severe risk, scores of 10–12 are high risk, scores of 13–14 are moderate risk, and score of 15–18 indicates low risk.[15] This checklist was used for selecting patients that are at risk of moderate to severe PIs in admission time.

Validity of the tool was determined by content validity method and

Table 1
Composition in the formulations.

Formulation code	Carbopol 934 (%v/w)	Methyparaben (%)	Propyl paraben (%)	Triethanolamine (%v/w)	Glycerine (ml)	Viscosity
F1	0.1	0.1	0.2	0.07	15	Very low
F2	0.5	0.1	0.2	0.34	15	Low
F3	1	0.1	0.2	0.67	15	Moderate
F4	1.5	0.1	0.2	1.32	15	High
F5	2	0.1	0.2	1.90	15	Very high

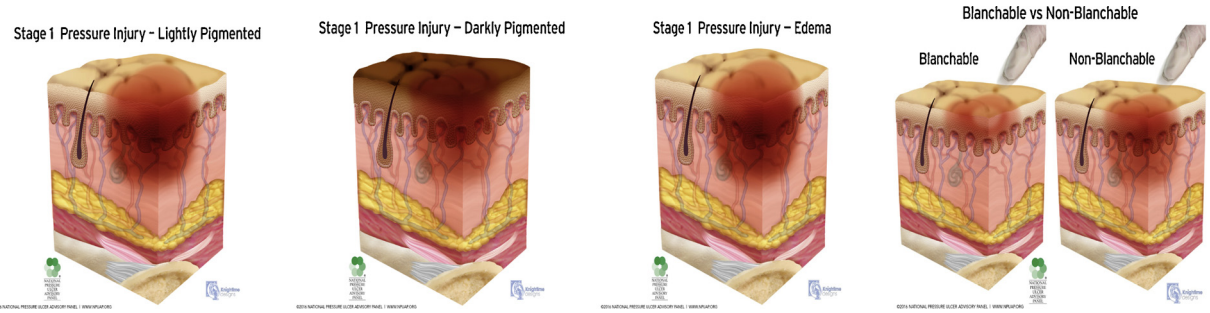


Fig. 2. Pressure injuries stage I illustrations (Adapted from NPUAP, 2016).

its scientific reliability via simultaneous observation. Two-observer agreement on using the tool to estimate the predictive power for PIs was evaluated by intra-class correlation coefficient that variation range was 84.1%–100%, indicating high reliability between the two observers.[15] In the present study, the reliability of the Braden scale was obtained by Inter-observer method, which was 86%.

2.5. Sample size estimation

The sample size was calculated using data from a pilot study of 30 patients (15 cases in each group). The sample size was estimated to be 54 cases for each group based on the cumulative incidence rate with confidence of 95%, power of 80% and one-sided test as well as by Sampsi order in STATA-9.2 software to compare the rates in the two samples, which were considered 75 participants in each group by taking potential dropouts. These patients were included in the final analysis from the two ICUs.

2.6. Method of data collection

A pre-test data collection was conducted before the intervention, including demographic information and past medical history such as age, gender, smoking history, alcohol, opium, psychoactive drugs, history of surgery and PIs, level of consciousness, oxygen, anemia, pharmaceutical and food allergies, type of damages and clinical information on the first day of hospitalization. The risk of incidence rate of the PIs in patients of both groups was assessed using the Braden scale and patients had moderate to severe risk for PI considered as potential samples. Patients were also evaluated for the presence of PIs.

Upon entering the patient into the ICU, the researcher or nurses trained on the study inclusion and exclusion criteria were introduced to the relatives of the patient (preferably the patient's guardian), and also the necessary explanations regarding the purpose and method of project were presented to them, and answered to their questions. The patients who had inclusion criteria were identified and their relatives were invited to participate in the study.

Signed informed consent forms were taken from these relatives of the patients. After collecting pretest data, the patients were assigned to the two groups using sealed envelopes containing letters A (the intervention group) or B (the control group) and chosen by the patients relatives.

The researcher or trained nurses carried out random sequence allocation of patients. After pretest data gathering and random sequence allocating, the peppermint or placebo gels were applied three times a day (once per shift) as a layer of on the skin of areas at risk of PI and this continued until the end of hospitalization in the ICU (maximum 14 days) and recorded in nursing reports. The pairs of observers (nurse plus specialist) who were unaware of the patient groups assessed daily the high-risk areas before the application of the gel in accordance with the NPUAP.

2.7. Data analysis

Data were analyzed by per protocol approach using STATA-9.2 software and assessed for the presence of missing quantities and normal distribution. Descriptive statistics (mean, standard deviation and frequency) and inferential statistics were applied to analyze the data. P-values less than 0.05 were considered significance in all tests.

Concerning the basic data, the differences in demographics, smoking, drugs, alcohol, psychotropic drugs, a history of anemia, acute illness, damages, blood transfusions, use of vasoactive drugs, tranquilizers, narcotics, and the presence or absence of PI on the first day of hospitalization were tested using Chi-square test between the two groups. The differences in drug usage, a history of hospitalization and history of drug or food allergy were assessed with Fisher's exact test. The *t*-test compared clinical information in both of the groups on the first day of hospitalization. The difference in the incidence of PIs was tested by Kaplan-Meier to show the preventive effect of peppermint gel.

2.8. Ethical considerations

The approval of this study was obtained from ethics committee of Semnan University of Medical Sciences (No. 92/408037 on 19.02.2014), Iranian Registry of Clinical Trials (IRCT201402098665N3) and Research Council of the university (No. 600). The approval of setting up a study was achieved from the managers of the hospitals and the intensive care units. The aim of the research and the relevant procedures were explained to the relatives of patients participating in the study. The relatives of the patients were assured that participate in the study is optional, and whenever they wish to continue the study or not, they can be excluded from the study. Written consent was obtained from relatives of patients to participate in the research. The confidentiality of information about the patient was reassured to their relatives.

3. Results

3.1. Response rate

In total, 140 out of 150 patients were evaluated by the fourteenth day of hospitalization (70 patients in each group). 16 patients (22.8%) of the intervention group and 54 patients (77%) of the control group were suffering from PI. PIs were not developed in 54 and 16 patients of the intervention and control group, respectively. The remaining patients were discharged, died or transferred to the general wards in less than 48 h after inclusion to study because of reaching to natural-conscious state; they were excluded from the analysis.

3.2. Baseline characteristics

The results showed that 81.3% of subjects in the experimental group and 78.7% of cases in the control group were male. The mean age of the patients was 34.06 years and 38.20 years in the intervention and the

Table 2
Baseline characteristics of the patients in the intervention and control groups.

Group Characteristic	Intervention N (%)	Control N (%)	p-value
Cigarette smoking			
Yes	17 (22.7)	27 (36)	0.073*
No	58 (77.3)	48 (64)	
Opium usage			
Yes	18 (24)	18 (24)	1.000*
No	57 (76)	57 (76)	
Alcohol usage			
Yes	7 (9.3)	5 (6.7)	0.547*
No	68 (90.7)	70 (93.3)	
Addictive substances			
Yes	3 (4)	8 (10.7)	0.117**
No	72 (96)	67 (89.3)	
Psychotropic substances			
Yes	4 (5.3)	2 (2.7)	0.117*
No	71 (94.7)	73 (97.3)	
Hospitalization history			
Yes	16 (21.3)	26 (34.7)	0.069**
No	59 (78.7)	49 (65.3)	
Anemia history			
Yes	1 (1.3)	1 (1.3)	1.000*
No	74 (98.7)	74 (98.7)	
Food and Drug Sensitivity			
Yes	0 (0)	4 (5.3)	0.12**
No	75 (100)	71 (94.7)	
Acute disease history			
Yes	34 (45.3)	32 (42.7)	0.742*
No	41 (54.7)	43 (57.3)	
Type of injury			
Accident	67 (89.3)	67 (89.3)	1.000*
Other	8 (10.7)	8 (10.7)	
Transfusion			
Yes	19 (25.3)	15 (20)	0.435*
No	56 (74.7)	60 (80)	
Vasoactive drugs			
Yes	8 (10.7)	1 (1.3)	0.016*
No	67 (89.3)	74 (98.7)	
Sedative drugs			
Yes	45 (60)	36 (48)	0.14*
No	30 (40)	39 (52)	
Narcotic drugs			
Yes	23 (30.7)	18 (27)	0.36*
No	52 (69.3)	57 (76)	

* Chi-square.
** Fisher Exact test.

control groups, respectively. Table 2 shows the baseline characteristics of the patients.

Clinical data of patients in the both intervention and control groups on the first day of admission involved level of consciousness, temperature, heart rate, systolic and diastolic blood pressure, arterial blood oxygen saturation, hemoglobin and hematocrit levels (Table 3).

The results of investigation on patients using the Braden scale on the first day of admission showed that high percentage of patients in both groups received a score of nine, and this means that they were at high risk for PIs (Table 4). 100% of each group had no PIs on the first day of hospitalization.

Table 3
Clinical information of the patients in the intervention and control groups on the first day of admission.

Group Clinical data	Intervention (n = 75) Mean ± SD	Control (n = 75) Mean ± SD	p-value*
GCS	5.56 ± 1.66	5.44 ± 1.42	0.072
Temperature	37.35 ± 0.92	37.44 ± 0.67	0.064
Heart rate	92.41 ± 19.36	91.58 ± 18.69	0.487
Systolic blood pressure	123.70 ± 18.27	124.28 ± 15.81	0.127
Diastolic blood pressure	74.76 ± 12.02	74.24 ± 11.07	0.202
O2sat	97.21 ± 2.75	97.24 ± 2.61	0.222
Hemoglobin	12.20 ± 2.88	12.29 ± 2.30	0.094
Hematocrit	35.84 ± 7.45	36.65 ± 6.14	0.131

* *t*-test.

Approach to survival analysis (Kaplan-Meier) showed that the total incidence rates of PIs were 21.3% and 72% in the intervention and the control groups, respectively. The chi-square test results showed significant difference between the two groups ($p < 0.001$). Fig. 3 shows the Kaplan-Meier diagram in the two groups.

This diagram displays the intervention group with blue color (A) and the control group with green color (B). Each stair drop means ulcer event and each vertical line means the censorship including death or discharge. The diagram shows the risk that means on the contrary of survival. The decline shows that the risk of developing ulcer becomes greater in both groups over time, especially for the control group, and the difference between the two groups is significant.

The most common positions of PIs in both groups were as follows: sacrum (48%), back (24%), hips (18%), shoulders (6%) and elbows (4%).

4. Discussion

4.1. Incidence rate

The results of this study showed a lower incidence of PIs in the intervention group than the control group. This finding was in line with Reihani & Haghiri (2007),[14] higher in comparison with the results of Shahin et al. (2009), and Hekmatpou et al. (2018),[5,52] and lower than other studies.[5,13]The reason for the low incidence of PIs in the study of Shahin et al. (3.3%) have been a short period (2–3 days) of patient hospitalization in ICUs. In addition, they are considered the incidence of ulcers in patients hospitalized in nephrology and cardiology wards, while the present study patients were hospitalized in the neurosurgical ICU, and PI incidence is higher among patients in other studies.[5,13]

The results of this study can be explained by the prolonged period of stay in the ICU (up to 14 days). In addition, the hospitals involved in the study had no recovery and intermediate wards. Therefore, all trauma patients would have admitted to the neurosurgical ICU. According to the researchers, the study had enough sample size to evaluate the possibility of the occurrence of PIs in the ICUs. This may be increases the ability to compare the results with other studies, elevating the generalizability of a study's results.

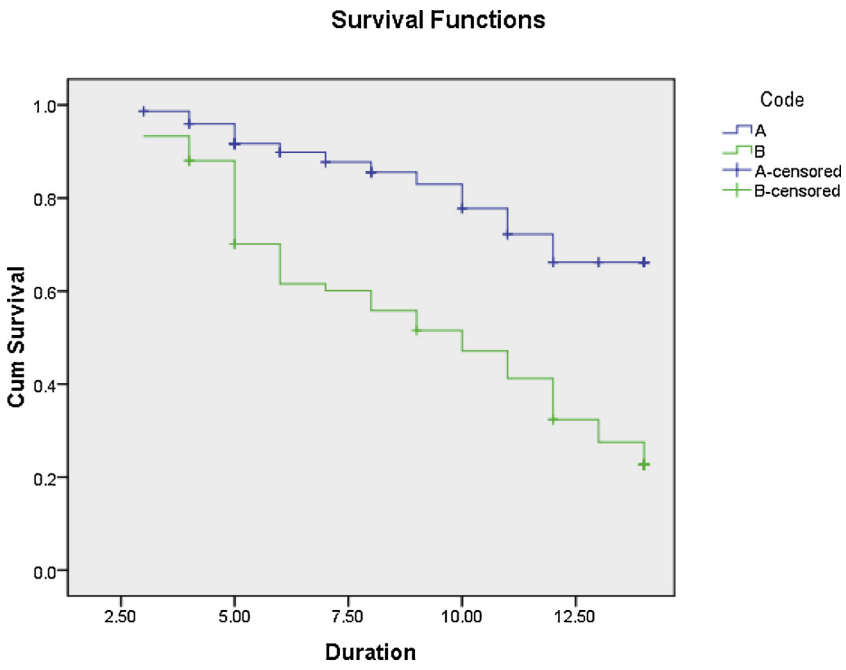
4.2. Impact of peppermint gel in prevention

The findings of the present research indicated that the use of peppermint gel in head trauma patients admitted to ICUs reduces the incidence of PIs. The peppermint plant that is also known under the other names such as Menthol, Mentha Piperita, Mentha balsamea is used in evidence-based pyramid with different purposes, such as relieving the symptoms of irritable bowel syndrome, nausea, headaches, colonic tension, bloating, irritability, breast fissures, pain, gastric emptying, subjective well-being, disseminated esophageal spasm, attention, calmness, memory, processing accuracy, processing speed, sedation and working memory. The correlation of the results has been very high.[45]

In this regard, Sayyah-Melli et al. (2007a) described the effect of peppermint gel, lanolin ointment and placebo gel to prevent breast fissure. A double-blinded, randomized trial study was carried out on two hundred and sixteen primiparous participants were assigned randomly to three groups. Each group applied only one of the above three preparations on both breasts for 14 days. The results showed that peppermint gel is effective as a natural remedy in preventing breast fissure.[44] These results completely were in line with our findings. Ashktorab et al., 2010 evaluated the effect of peppermint oil in the prevention of chemotherapy-induced oral mucositis. In a double blind clinical trial, 40 patients with colon or rectum cancers, who admitted for chemotherapeutic management, randomly divided in two equal

Table 4
Scores achieved by patients in the intervention and control groups in Braden Scale on the first day of hospitalization.

Subscales	Sensory perception		Humidity		Activity		Mobility		Nutrition		Friction and abrasion		Total
Group	score	percent	score	percent	score	percent	score	percent	score	percent	score	percent	
Intervention	2	70.7	2	61.3	1	100	1	77.3	1	97.3	2	36	9
Control	2	69.3	2	62.7	1	100	1	74.7	1	96	2	32	9



A=Intervention Group; B=Control Group

Fig. 3. Kaplan-Meier Diagram.

placebo and peppermint essence (PE) groups. PE and placebo groups were received 10 drops of oral rinse PE or placebo, three times a day, from the first day of chemotherapy up to the fourteenth day, respectively. The findings showed that peppermint oil is effective in preventing oral mucositis.[42] These results completely coincide with our findings even in terms of duration of treatment. Study of Mousavi and Akhavan-Tafti (1997) also indicated the effect of peppermint oil in improving oral aphthous ulcers.[43] In a single blind clinical trial, 60 patients with oral aphthous ulcers, randomly divided to two equal placebo and peppermint essence 2% groups. Placebo and PE groups were received 15 drops of oral rinse PE or placebo, three times a day for five minutes. The results showed improvement in oral aphthous ulcers after using Peppermint essence. These findings also were in accordance with our results, but in Mousavi and Akhavan-Tafti study, researchers have not described the duration of treatment (in our case, treatment lasted for 14 days), also random sequence generation, allocation concealment and losses to follow-up was not disclosed.[43]

Several studies have examined the impact of evidence-based guidelines on the prevention of PIs [27–29] Several preventive measures such as repositioning,[22] maintaining mobility and activity, proper nutrition and skin self-examination,[53] using foam and massage mattresses,[5] have been examined in several studies. However, it is known that, on the one hand, preventive use of these methods is dependent on the clinical judgment of nurses;[54] on the other hand, inconsistent effects have been shown on the use of preventive methods and incidence rate of acquired PIs.[27–29] No supportive study was found directly on impact of peppermint gel on PIs.

4.3. Common sites for the incidence of pressure ulcers

Sacrum, back, hip, shoulder and elbow were the most frequent sites of the appearance of the PIs in this study. The results of the present study was supported by Carlson et al. (1999) who stated that sacrum, coccyx and heel as the most common site for PIs.[55] In studies conducted by Moore et al. (2011) and Ahmadinejad & Rafiei (2011),[56,57] the sacrum was also mentioned as the most common site of involvement. Interpretation of these results leads to the conclusion that the sacrum is the most common site for PIs in patients hospitalized in the ICU. Shoulder and elbow were also other areas of PIs in this study. These results have not yet been confirmed by other studies and should be considered in future studies.

4.4. Factors affecting, the incidence of pressure ulcers

The results showed that patients in the intervention group had received more vasoactive drugs compared to the control group, which the difference was statistically significant ($p = 0.016$). The critical nature of the illness in intensive care patients with impaired ventilation and circulation affects the supply of oxygen to body tissues. Certain drugs such as norepinephrine may improve this problem. Norepinephrine by binding to adrenergic receptors leads to peripheral vasoconstriction and impaired tissue perfusion and ischemia, and is associated with an increased risk of developing PIs.[58] In a study of Tschannen et al. (2012),[59] patients receiving vasopressor were 33% higher at a risk of PIs than patients who had not received vasopressor. However, since according to

the results, the incidence of PIs in the patients of the intervention group (receiving vasoactive drugs) was less than anticipated rate. The researchers concluded that this could be due to the positive impact of peppermint gel in the prevention of PIs.

The results of studies of the patients using the Braden scale on the first day of hospitalization showed that a high percentage of patients obtained a score of 9 in both intervention and control groups and were classified as severe risk (≤ 9) based on the cumulative score of the Braden scale.[60] According to the researchers, despite the high risk of patients for the occurrence of PIs, lower incidence rate of PIs in the intervention group may be due to the use of peppermint gel, and not due to correct and timely use of preventive measures, because inconsistent effects have been shown on the use of preventive methods and incidence rate of acquired PIs. [27–29]

4.5. Study limitations

This study had several limitations. Firstly, duration of hospitalization in the ICU was unpredictable. Secondly, decreased level of consciousness, lack of systematic diseases such as diabetes, heart or kidney failure or cancer advanced phase, and head trauma of patients were the inclusion criteria causing prolonged time of sampling. Thirdly, in the case of informed consent, the consent was obtained from relatives of patients due to lack of their consciousness. Some relatives of the patients in the study were not willing to participate, because of their claim that they did not know that patients agree to participate in the study or not.

5. Conclusion

The positive findings obtained from this study suggest that the peppermint gel has an important role in reducing the incidence of PIs in patients. It is clear that the traditional medicine can be useful with applying plants and herbal extracts for wound management in certain circumstances. According to the escalating costs of health care in the treatment of ulcers, the use of traditional medicine will be cost effective for wound healing. However, large randomized clinical trials are necessary to provide supportive evidences for using the herbs, including the peppermint gel in the treatment of ulcers. The use of peppermint gel along with the adoption of appropriate and timely preventive measures and proper evaluation of patients at risk using the tools like Braden, Waterlow or Norton will be effective in preventing the incidence of PIs, reducing the length of stay in hospital, the treatment duration and costs as well as increasing the patient's quality of life.

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Ethical approval

This study was conducted under the approval of the Medical Ethics Committee, Semnan University of Medical Sciences (MEC Ref.No.92/408037).

Declaration of Competing Interest

None.

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Appendix A

Preparation of peppermint oil gel

The composition of the peppermint oil gel formulations used in this study is shown in Table 1. The gels were prepared by dispersing various concentrations of carbopol 934 in water containing 0.2% propyl paraben and 0.1% methyl paraben as preservatives and 15 ml glycerine (as a humectant) for a period of 2 h. Peppermint oil (0.2 ml) was added gently to the carbopol dispersion under continuous stirring (200 rpm) to produce a concentration of 0.2% v/w. As carbopol 934 is a free acid and soluble in water up to 5% and forms a solution of fairly low viscosity with a pH of around 3, carbopol polymers must be neutralized in order to achieve maximum viscosity and a transparent gel. Upon neutralization with a base (this is easily achieved by neutralizing the carbopol polymer with a common base, such as sodium hydroxide or triethanolamine) a highly viscous gel is formed. Optimum neutralization is achieved at a pH of 6.5–7.0. To obtain acceptable viscosity (neither too runny nor very viscose) for a topical gel formulation, different concentrations of carbopol 934 were used. The results showed that the concentration of 1% carbopol 934 produced acceptable viscosity (medium viscosity). The same formulation without peppermint oil was prepared as the placebo with the same color and smell (similar essence with mint smell without effective elements).

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