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A Comparative Study on the Effect of EMLA Cream and Diclofenac Gel on Pain Caused by Needle Port Placement in Patients Under Chemotherapy: A Clinical Trial

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Abstract

Background: Injections are common nursing interventions, which usually cause pain. The pain caused by injection causes anxiety, discomfort, and reduced patient confidence in nursing performance. Since applying methods that enhance patients' comfort is a nursing task, the aim of this study was to determine the effect of EMLA cream and diclofenac gel on pain caused by needle port placement in patients undergoing chemotherapy at the oncology department.
Methods: This cross-sectional clinical trial study was conducted on 40 inpatients of the Oncology Ward of Khatam-al-Anbia Hospital in Zahedan, during year 2017. Patients were selected by conventional sampling, based on the Inclusion criteria of the study. Patients were randomly assigned to use EMLA cream, diclofenac gel or the placebo. The severity of pain was measured immediately after injection, using the visual analogue scale (VAS). Blindness was done for pain the assessor and data analyzer. The SPSS 22 software was used for statistical analysis. First, descriptive statistics were used to determine the frequency, percentage, and mean, and then inferential statistics of paired *t*-test, for group comparison.
Results: The mean scores of the severity of pain in three groups of EMLA, diclofenac gel, and placebo were 5.49 ± 2.05, 5.88 ± 1.93, and 6.71 ± 1.96, respectively. Comparison between diclofenac gel and placebo showed that the mean decrease in pain intensity in the diclofenac gel group was far more than the placebo ($P < 0.0001$). Comparing EMLA cream and placebo, the mean reduction in pain intensity in the EMLA cream was far higher than the placebo ($P < 0.0001$). Finally, the EMLA cream was more effective than diclofenac gel in pain reduction, although the difference was not statically significant.
Conclusions: Although the use of EMLA cream and diclofenac gel can reduce pain at the injection site, applying diclofenac gel is recommended due to its availability, cost-effectiveness, and domestic production.

Keywords: EMLA Cream, Diclofenac Gel, Pain, Chemotherapy, Port, Injection, Oncology

1. Background

The increasing incidence of chronic diseases has become a challenge of the century in the healthcare sector. On the other hand, the spread of chronic diseases, worldwide, has led to increased financial costs and adverse social effects on patients and communities (1). Cancer is currently one of the most important health challenges (2). Cancer diagnosis is a very unpleasant and unbelievable experience for anyone, and causes physical problems for people with disruptions to their occupational, economic, and social and family life (3). Cancer, as the third most common cause of death in Iran, is estimated to involve more than 30,000 cases, annually (4). These statistics point to the importance of paying more attention to patients with cancer.

Chemotherapy is used as a systemic method in the treatment of cancer (5). Chemotherapy has a potent intravenous stimulus of more than 24 hours, which often results in phlebitis and loss of superficial veins (6). Different degrees of intravenous damage include pain, redness, swelling, warmth, stiffness of the venous region, and ultimately, fever (7). These side effects increase the risk of thrombophlebitis in patients and negatively affect the health status (8). Failure to properly control the side effects of chemotherapy can exacerbate adverse effects on the lives of patients and may have an adverse impact on any benefit obtained from this increase in survival, due to increased side effects (9).

Central venous catheterization is one of the basic tech-

niques for treating a large number of hospitalized patients (10). The use of vascular catheters is important in healthcare. Patients with cancer are among candidates for the use of central vascular catheters in various stages of the disease. The portal catheter is used for long-term needs, such as intravenous injection and also blood sample collection. Therefore, the portal catheter system limits the use of peripheral edema and improves the quality of life of patients (11, 12).

Pain is one of the most common causes of suffering in patients, which is found in about 50% to 80% of patients hospitalized for various reasons (13, 14). The pain caused by the introduction of needles and catheters to blood vessels, becomes problematic when it is repetitive and requires continuous use (15). Control of pain, at the time of its occurrence, plays a crucial role in the prevention of unwanted physical and psychological complications. The first step in controlling and reducing pain is the examination of pain and attention to its symptoms (16). Considering that pain management is an ethical commitment for caregivers, it is essential to use proper nursing interventions to alleviate the pain caused by injection (13, 17). Nurses are indifferent to the pain caused by injections, including the needle port that patients experience with pain over and over again. This is considered normal and inevitable, however, patients see nurses as people, who take care of them in an unfamiliar environment. Considering their own conditions and close relationship with patients, nurses need to consider measures to provide comfort to the patient (17, 18).

Pain relief methods are divided to two categories: Pharmacological and non-pharmacological. Non-pharmacological methods include distraction of thought, coldness, and topical heat treatment. Common analgesic drugs include: Opioids, non-steroidal anti-inflammatory drugs, and auxiliary drugs (13). In some cases, non-pharmacological methods are not effective in reducing pain, and so instead, drugs can be used either alone or in combination with non-pharmacological methods. In this regard, the use of local anesthetics is one of the methods used to reduce pain caused by injection (19). EMLA cream is a combination of two local anesthetics, lidocaine (2.5%) and prilocaine (2.5%), which are used for a variety of painful interventions on the skin (20). This cream penetrates in healthy skin and provides a few millimeters of anesthetics on the skin's surface layers. The cream should be used at the desired location, an hour before the intervention (21). To prevent the occurrence of prilocaine-induced methemoglobinemia, this drug should not be used in patients with 6-Phosphate-dehydrogenase deficiency (G6PD), congenital or idiopathic methemoglobinemia, infants under the age of 12 months, and those treated with sulfonamide, nitrate, and phenobarbital drugs (22). The use of diclofenac gel has a positive effect on reducing the pain associated with venipuncture and reducing the incidence of symptoms of peripheral thrombophlebitis. The use of diclofenac gel is recommended one hour before venipuncture, as an effective and safe method to reduce pain with the least skin and environment side effects (23, 24). Various studies in Iran and abroad have been conducted to determine the efficacy of EMLA cream or diclofenac gel on reducing the pain of injection site, yet some have compared one of these two drugs with the placebo (24). Also, some studies have compared the efficacy of EMLA cream on reducing the pain at the injection site by topical cooling (19, 25). Because cancerous patients, who are undergoing chemotherapy, consistently experience stress and pain of the needle port in addition to stress associated with the disease, all of these unfortunate conditions have reduced their quality of life.

One of the primary tasks of nurse is to resolve or minimize the pain of patients. Nurses should take every step to reduce pain caused by the needle port in patients undergoing chemotherapy. Considering the fact that research on the use of topical drugs in reducing the pain caused by a needle port in patients under chemotherapy has not been done in Iran, this study was conducted to determine the effect of topical EMLA cream and diclofenac gel on pain intensity caused by the insertion of needle port in patients undergoing chemotherapy.

2. Methods

This clinical trial study was conducted on hospitalized patients and outpatients referred to the oncology department of Khatam-al-Anbia Hospital, affiliated to Zahedan University of Medical Sciences, Zahedan, during year 2017. Khatam-al-Anbia Hospital is the second largest hospital for admitting and treating patients with cancer in Zahedan, even in Sistan and Baluchistan Province. Considering that the study of a prior and subsequent group was not found in the search for resources after the pilot study, the values obtained with 95% confidence intervals were calculated using the sample size formula for the paired data of 40 patients. Samples were entered in the study using a conventional sampling design and three stages.

The inclusion criteria were having verbal, mental and vision ability, not having acute mental disorder at present, lack of history of favism, methemoglobulinemia, congenital or idiopathic liver disease, skin allergy, skin dermatitis, lack of treatment with sulfonamides, nitrates, and phenobarbital, lack of diabetes, addiction, and use of analgesics over the past 24 hours. Information was obtained by asking the patient and their family, assessment of patients'

medical records, and asking questions from the patient's physician. Exclusion criteria were wound site location during the intervention, infection and secretion at the site during the intervention, and failure to place the needle in the first attempt. Data gathering tool was a demographic and clinical questionnaire. The degree of pain was measured by the visual analog scale (VAS). The accuracy of the measurement of pain severity and validity, and its reliability and sensitivity in acute, chronic, and cancerous pain were also confirmed by various studies and nursing literature (18, 26, 27). In one study, the criteria validity of VAS was estimated to be 76% to 86% (28). This study was approved by the ethical committee of Zahedan University of Medical Sciences (IR.ZAUMS.REC.1396.103). After obtaining permissions and referring to the oncology ward of Khatam-ol-Anbia Hospital, while expressing the goals of the study and how to conduct the research from patients, the researchers invited patients to participate in the study. Patients, who were willing to participate were selected based on the criteria for entry in the study and a written consent was obtained for participation in the study.

In the routine method, no specific action was taken prior to injection and the injection site was the same for all patients. The order of the study methods (using EMLA cream, diclofenac gel, and placebo) was randomly selected for each patient (by selecting a card from three cards in the first injection, then a card from the remaining two cards in the second injection, and then the third card in the third injection). For EMLA cream, 1 mL of 5% EMLA cream (25 mg of lidocaine and 25 mg of prelocaine per gram), manufactured by Astra Zeneca, was applied. The port site of the patient was coated by the researcher, 60 minutes before the chemotherapy, without the patient knowing the name of the drug and its nature, with the tube covered with a band. After 60 minutes, the band was removed and the position was placed by cotton and alcohol disinfection and then a needle. The needle gauge was the same for all cases. For diclofenac gel, 1 mL of gel was applied (manufactured by Razak Laboratories, Public Joint Stock Company). The exact same approach as Elma cream was applied here as well. For placebo cream, 1 mL of vitamin A + D cream was applied (produced by RahaCompany). Again, the same approach as above was applied. After each injection, the severity of pain was measured immediately after injection by one of the oncology ward personnel, who was double-blinded, using the visual pain scale. For this purpose, a 10-cm ruler was shown to patients and the patient was asked to show a degree of pain after each injection. All injections were done to minimize the incidence of errors by the researcher. The person, who assessed the pain and the data analyzer were blinded to the type of intervention. The SPSS software version 22 was used for data analysis. First, frequency, percentage, and mean was calculated using descriptive statistics. Inferential statistics was used to compare the mean values and T-pair test was used to examine the effect of variables on patient groups.

3. Results

The findings showed that the mean age was 54.10 years, and 60% of patients were female. The demographic and clinical data of patients are presented in Table 2. The mean pain intensity was 5.59 $\pm$ 2.10 in the EMLA cream method, 5.88 $\pm$ 1.93 in the diclofenac gel method, and 6.71 $\pm$ 1.96 in the vitamin A+D method (placebo) out of total score of 10 (Table 1). Paired T-test results showed a significant difference between the mean score of needle pain in patients when they applied diclofenac gel with the mean score of pain in patients receiving vitamin A + D (P = 0.0001). Also, the mean score of needle pain in patients with EMLA cream with the mean score of pain in the same patients receiving vitamin A and D was also significantly different (P = 0.0001). However, the mean score of needle pain in patients during diclofenac gel application was not significantly different from the mean score of the same patients in case of EMLA cream (P < 0.001).

Table 1. Patient's Demographic and Clinical Characteristics[a]

Variables	Value
Age	54.10 $\pm$ 13.16
The number of chemotherapy sessions	8.52 $\pm$ 7.67
Mean duration of use of port	5.55 $\pm$ 3.07
Gender	
Male	16 (40)
Female	24 (60)
Satisfaction of the port	
Yes	36 (90)
No	4 (10)

[a]Values are expressed as mean $\pm$ SD or No. (%).

Table 2. Comparison of Mean$\pm$ SD of Pain Severity After Intervention with EMLA Cream and Diclofenac Gel

Sequence	After Intervention
EMLA cream	5.49 $\pm$ 2.05
Diclofenac gel	5.88 $\pm$ 1.93
P value	0.075[a]

[a]Paired *t*-test.

Table 3. Comparison of Mean ± SD of Pain Severity After Intervention with EMLA Cream, Placebo and Diclofenac Gel[a,b]

Pain Severity	After Intervention
Sequence 1	
EMLA cream	5.49 ± 2.05
Placebo	6.71 ± 1.96
P value	< 0.0001
Sequence 2	
Diclofenac gel	5.49 ± 2.05
Placebo	6.71 ± 1.96
P value	< 0.0001

[a] Paired *t*-test.
[b] P < 0.05 is significant.

4. Discussion

The results of this study showed that there was a statistically significant difference between mean and decrease in pain intensity, when comparing each of the two groups. Comparison of diclofenac gel group with the placebo showed that the mean and decrease in pain intensity in diclofenac gel group was far more than the placebo. Comparison of EMLA cream and placebo showed that the mean and decrease in pain intensity in EMLA cream group was far more than the placebo. There was no significant difference between EMLA cream and diclofenac gel. However, in numerous studies, the effect of EMLA cream on pain control was obtained. In the study of Khalili Shomia and Safavi EMLA cream was effective in treating pain in females undergoing elective cesarean section (29). In Dollabi and Tavakollian's study, EMLA cream was effective on the pain of copper iodine placement (30). In the article by Taghavi and Tavakoli EMLA cream was effective in treating pain during the lithotripsy in patients with renal calculus (31). The study of Shahabi and Kalani examined the effect of EMLA cream and distraction of thought (by music) on the pain caused by venipuncture in children. The results showed no significant difference between these two control methods for pain. It was also concluded that the use of EMLA cream and distraction of thought (by music) greatly reduced pain during venipuncture, and each of these two methods can be replaced with each other (32). Therefore, considering the same effect of EMLA cream and music, one of these two methods can be used according to the situations and facilities. A study by Nory Shadkam et al. on the effect of EMLA cream on pain relief from vaccination, showed positive effects of the EMLA cream (33). The study of Mohseni and Malekshahi aimed at investigating the effect of Piroxicam and EMLA cream on the severity of pain due to fistula cannulation in patients on hemodialysis. The results of this study showed that the pain in the EMLA cream group was clearly higher than that of Piroxicam and placebo (34). The above-mentioned studies were consistent with the current study. In addition, the crossover design of this study is an advantage, and obtained more accurate results. Also, previous studies were single blinded as only patients did not know about the method used, however, the present study was double blinded as the patient and the pain assessor were blind to the study. Another difference between these studies and the current study was the duration of EMLA cream use. The time of EMLA cream application was 45 minutes before the procedure in some studies while the suggested time of application in the current study was 60 minutes before the procedure. In the current study, the researchers applied the drugs exactly 60 minutes before the procedure. In a study by Thomas et al. that examined the effect of EMLA cream on vasectomy pain, the results showed that EMLA cream does not affect vasectomy pain (35). This result may have been obtained because of not using proper bandage after applying the cream. The current researchers used proper bandage after application of cream in the current study. A study was conducted by Ghane et al. to investigate the effect of EMLA cream on pain caused by lumbar puncture. The use of EMLA cream was not effective in this study. He considered the difference in his study with other studies as the lack of EMLA cream bandage and he claimed that it is likely that the use of bandage can be effective on the relief of pain with EMLA cream (36). Lal et al. conducted a study comparing the effect of EMLA cream and placebo and distraction of thought in children aged four to eight on pain during venipuncture. The results showed no significant difference in the pain score between placebo and EMLA, therefore, they concluded it is likely that the similarity between the two groups is due to the effect of distraction of thought (37). It is important to mention that there are other factors influencing pain intensity, such as duration and time of injection, and doing research on this could enhance our knowledge.

4.1. Conclusion

The current findings showed that the mean and decrease in pain intensity in the diclofenac gel group was far more than placebo. Also, the mean reduction in pain intensity in the EMLA cream was far higher than the placebo and EMLA cream was more effective than diclofenac gel although the difference was not statically significant. Although more research is needed on the ease of needle-port pain with EMLA cream and diclofenac gel, based on the findings of this study, two topical creams, namely, EMLA cream and diclofenac gel, are effective in reducing pain, yet using diclofenac gel is recommended with regards to accessibility, cost effectiveness, and domestic production.

Therefore, health workers and clinical specialist nurses at oncology wards are recommended to relieve pain and improve the quality of health care services. Diclofenac gel should be applied as an effective drug in oncology patients undergoing chemotherapy.

4.2. Research Limitations

One of the limitations of this study was the mental nature of pain that varies from person to person and makes it difficult to generalize the results. Also, with regards to cultural and regional differences, carrying out a study like the present study in other areas of the country would be favorable in order to validate and generalize the results. Among other limitations was the limited number of patients.

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Footnotes

Authors' Contribution: Alireza Salar: Supervision of the project, participation in data analysis, scientific editor and final approval of the paper; Fatemeh Kiani: Supervision of the project, participation in data analysis, scientific editor and final approval of the paper; Ali Navidian: Statistical counseling and data analysis; Shima Mohammadi Nejad: Implementing the project, data collection and writing the first draft of the project.

Ethical Consideration: This study was part of the dissertation of an MSc student on medical-surgical nursing, which was approved by the Research Committee at Zahedan University of Medical Sciences with IR.ZAUMS.REC.1396.103 code of ethics.

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