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The Effectiveness of Local Combined Cold-Hot Application on Bruising of Enoxaparin Sodium

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Authors' contributions

This work was carried out in collaboration between all authors. All authors designed the study, performed the statistical analysis and wrote the protocol. Author FES wrote the first draft of the manuscript. Authors EKL and AAL managed the analyses of the study. Authors NJP and AAL managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Bruising is one of the most common adverse events following administration of enoxaparin sodium, which can lead to unpleasant consequences such as reduced access to various sites for injection, joint complaints, and reduced satisfaction of patients from the treatment and care provided. Therefore, in order to find ways to reduce this complication, the aim of this study was to compare the effectiveness of local combined cold-hot application on bruising caused by subcutaneous injection of enoxaparin sodium.

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Methods: This randomized controlled trial was conducted from July to December 2018. 74 patients hospitalized in Poursina Hospital in Rasht were selected according to inclusion criteria and assigned to intervention group 1 (37 persons) and intervention group 2 (37 persons) by randomized block design. In each intervention group, the left side of the abdomen was treated as control (without intervention) and the right side was treated with cold pack (intervention group 1) or cold-hot pack (intervention group 2). Data collection was done by two-part tools, including individual and clinical data, and related records of bruising. Evaluation of the incidence and severity of bruising was performed at 24, 48, 72 hours after the first injection. Data were analyzed by SPSS version 22 using descriptive and inferential statistics (Independity Test, Friedman, Wilcoxon, Mann-Whitney, Kolmogorosimerno).

Results: The majority of research samples were men (79.7%). The mean age of the patients was 21 ± 48 years. The mean and standard deviation of bruising in intervention group 1 at 24, 48 and 72 hours after injection was 24.44±1.09, 4.49±1.04 and 4.35±1.14, respectively. The mean and standard deviation of bruising in intervention group 2 at 24, 48 and 72 hours after injection was 1.65±0.63, 1.49±0.65, and 0.88±0.43, respectively. Differences in bruising size were statistically significant (P<0.001).

Conclusion: The findings of this study showed that use of local cold-hot pack compared to cold pack is more effective regarding the size of bruising in place of enoxaparin sodium injection, which is clinically important.

Keywords: Low molecular weight heparin; sodium enoxaparin; bruises; cold pack; hot pack.

1. INTRODUCTION

Drug therapy is one of the most important responsibilities of nurses in the field of patient care [1]. Patients are always at risk of illness and treatment. On the other hand, therapeutic interventions, such as drug administration, also expose patients to complications [2]. However, treatment of patients should be guided in such a way as to achieve the desired and beneficial effect of interventions with minimal side effects [1,3,4]. Therefore, it is essential that the nurses identify the complications, and accordingly choose their interventions and take preventive measures against potential hazards [2].

One of the most important though preventable complications in orthopedic patients is thromboembolism, which can occur following trauma or surgery. To prevent this complication, anti-coagulants such as heparin are prescribed subcutaneously in patients with complete bed rest following orthopedic surgery. Although the incidence of thrombocytopenia caused by the heparin in enoxaparin sodium is nearly 10 times lower than unfractionated heparin [1], side effects such as bruising and pain at injection site, purpura, blood in the feces and urine, osteoporosis, and reduced platelet count threaten patients. Bruising can be the most commonly reported adverse event, ranging from 6.6 to 88.9% after subcutaneous injection [5]. Available evidence suggests that the peak of bruising occurs 48 hours following injection, and after 72 hours it begins to heal [5]. This side effect, although benign, can cause discomfort to the patient.

In order to get the treatment with the least complication, it is necessary to apply procedures that have the least complications following the injection of sodium enoxaparin [1]. A review of the literature suggests that the use of cold pack reduces the bruising caused by the injection of enoxaparin sodium. It seems that cold prevents bleeding with the contraction of the vessels around the injection site and the reduction of blood pressure around the injection site [6,7]. However, in a study has been shown that cold pack application at the injection site of enoxaparin does not have any effect on bleeding [8]. On the other hand, hot pack can cause dilatation of blood vessels and increase the blood flow in that area and increase metabolism and eliminate blood cells accumulating under the tissue of the damaged site [9]. It seems that using a combination of cold and hot may reduce the incidence of bruising after injection of enoxaparin sodium. Nonetheless, only one study has been conducted that compared the combined application cold and hot with cold and hot application in tree group people. Their results was showed the combined application cold and hot was more effective than cold or hot alone on bruising in the subcutaneous injection site [10]. The patient's profile affects the incidence and extent of bruising after [11]. Thus, the use of the patient as control group modifies the effect of the patient's characteristics on the results. As well, it seems the bruising is dose-depended [12].

Due to limited studies in this area, it is necessary to conduct future researches on different doses of drug and as a self-control experimental design. Therefore, in order to get more evidence and determine of the best intervention for reducing of complications after injection of enoxaparin sodium, this study was conducted to compare the effects of local cold and cold-hot application on extent of bruising after subcutaneous injection of enoxaparin sodium.

2. METHODS

2.1 Patient and Study Design

This study was a randomized controlled trial that was performed on 74 patients admitted to orthopedics ward of Poursina Hospital in Rasht. Samples were selected on the basis of the inclusion criteria. After entering the sample size into the random block program on the computer and extracting the full list, in quadruple blocks (with regard to the two existent groups in the study) and with concealment, 37 individuals were allocated to intervention group 1 (local cold pack on right side of the abdomen) and 37 individuals to intervention group 2 (local cold-hot pack on right side of the abdomen). In both groups, each of the samples was their own control, and injection without intervention on the left side of the abdomen was considered as control. The required sample size with 95% confidence and 80% confidence interval of two domains were used to test the statistical difference according to the low sampling formula (z1- α / 2 = 1.96, z1- β = 84%, P1 = 75.3%, P2 = 45%) based on the information of previous study.

$$n = \frac{\left(Z1 - \frac{\alpha}{2} + Z1 - \beta\right)^2 [P1(1 - P1) + P2(1 - P2)]}{(P1 - P2)^2}$$

Inclusion criteria included: (1) attendance and need to continue hospitalization for further 24, 48, and 72 hours in the orthopedic ward, (2) The order of treatment with 4000-unit enoxaparin sodium in the by the physician, (3) The normal results of the latest coagulation tests, including the PTT (25-35 seconds), (4) Proper renal function (creatinine 1.5-0.5 ml / dL), (5) No widespread skin lesions in the abdomen such as extensive scarring from surgery or burn, (6) Lack of conditions preventing the correct administration of enoxaparin injection such as high levels of ascites, (7) Absence of bruising in the abdomen caused by previous injections, (8) Willingness to be involved in research by written consent. Exclusion criteria included the patients who: (1) in the event of any change in the clinical conditions, changes in the amount of the drug or its discontinuation in the patient, (2) injections by personnel on the right side of the abdomen, (3) reluctance of the samples to continue to participate in the study.

2.2 Data Collection Tools

The data collection form in this study was comprised of two parts. The first section included individual information (age, sex, circumference of the abdomen per cm) and clinical information (medical diagnosis, results of the latest coagulation tests and platelet count, history of associated illnesses and medications). The second part of the tool was a form for recording the information related to the assessment of the area of the injection in terms of the extent of bruising at 24, 48, 72 hours after injection, date, type of group (intervention 1, intervention 2, control 1 and control 2), time and site of injection.

2.3 Procedure

Samples in intervention group 1 (cold pack) were injected with sodium enoxaparin in the right region of the abdomen and the site was treated with cold pack for 20 minutes (15 to 18°C). In the intervention group 2 (cold- hot pack), besides the 20-minute treatment with cold pack, after 12 hours of the injection, a hot pack was applied on the site (40 to 43°C). A cold-hot pack contains a gelatin which should be placed in the freezer for 1.5 to 3 hours to reach the desired temperature (15 to 18°C). To use the hot pack, it should be placed in warm water to reach the desired temperature (40 to 43°C).

In this study, the packs were purchased from Dispotech, Italy. Its temperature was monitored and controlled during the study using a standard laser thermometer.

In this study, all measurements were made using a standard thermometer and ruler. The ruler's standardization was done in a pilot study on 30 cases of bruising with two measurements by a person. Then the data were evaluated by Intraclass correlation coefficient (ICC), its correlation reached 87%, which ultimately led to a sustained outcome.

2.4 Injection Technique

To prevent possible differences in the technique of injection and control all external factors affecting the bruising and its extent by the researcher, injection was performed using pre-

filled syringes prepared by a single pharmaceutical company (Alborz Drug), at a 90-degree angle with pinching the injection site using index finger and thumb without aspiration, the syringe content was injected at least 5 cm right side of the umbilicus and after the injection was performed, the needle was removed from the skin with the same 90-degree angle without any massage at the site. (Before injection, alcohol-impregnated cotton applied on the injection site, then removed, and after the alcohol evaporated, the injection was performed). The circle of the circle with a radius of about 2.5 cm was used. The circular site of injection in a radius of 2.5 cm was marked by a waterproof marker, then the training was provided to avoid tampering such as massaging scratching or touching the area.

Additionally, apart from placing a written caution against any injections on the right abdominal side, oral advice was also given to the nurses in order to avoid any subsequent injections in the indicated area and interference with the results of the study. In addition, in all groups, the duration of injection, which was measured using a Joerex chronometer, was approximately 30 seconds to reduce the incidence of any complications.

Data were collected by expert blinded person after observing the injection site for bruising and measuring its extent using a standard ruler.

2.5 Tools / Equipment

The equipment used in this study includes cold and hot flexible packs (size: 15 x 2 cm), a laser thermometer for measuring the temperature of the cold and hot packs, a chronometer to measure the duration of the injection of enoxaparin sodium and the length of time the packs were applied in place of injection, a waterproof marker for determining the injection site, a flexible transparent ruler to measure the extent of bruising and meter tape for measuring abdominal circumference.

2.6 Ethical Considerations

This study was conducted after receiving the written approval of the Ethics Committee of the Vice-Chancellor for Research of Guilan University of Medical Sciences with IR.GUMS.REC.1397.094 issue-dated 6.11.2018 and at the Iranian Center for Clinical Practice with IRCT20180623040206N1. Before starting the sampling, the research samples received descriptions in terms of the purposes of the research, the method of performing their job and their rights and their expectations at each stage of the research, and in case of willingness they sign the written consent for participation in the study.

2.7 Data Analysis

After data extraction, data were analyzed by SPSS software version 22. Due to lack of normal distribution of bruising size, Kolmogorov Sminov and Shapiro-Wilk tests, Friedman's nonparametric test and Wilcoxon test and Mann-Whitney test were used to compare the size of bruising in the two groups, by the time of measurement. Significance value for the results of this study was $P < 0.05$.

3. RESULTS

The findings of this study indicate that the majority of research samples were men (79.7%) and in the age range of below 40 (44.6%) (Table 1).

The mean and standard deviation of bruising size on the right abdominal side (intervention1) and in cold group at 24, 48 and 72 hours after injection was 4.35 ± 1.09, 4.49 ± 1.04 and 35.3 ± 1.14 respectively. Fried Man test showed no statistically significant difference between times in term of bruising size. The mean and standard deviation of bruising size on the left abdominal side (control 1) in cold group at 24, 48 and 72 hours was 7.68 ± 2.76, 7.84 ± 2.84 and 86/8 ± 2/83 respectively. Fried Man test showed statistically significant difference between times in term of bruising size ($P < 0.001$).

The mean and standard deviation of bruising on the right abdominal side (intervention2) in the cold-hot group at 24, 48 and 72 hours after injection was 1.65 ± 0.63, 49 ± 0.65 and 1.08 ± 0.43 respectively. Using Fried Man test, a statistically significant difference was found between times in term of bruising size ($P < 0.001$). The mean and standard deviation of bruising size on the left abdominal side (control 2) in cold-hot group was 5.54 ± 1.74 in 24 hours, 6.38 ± 1.93 in 48 hours and 6.38 ± 2.27 in 72 hours after injection. Fried Man test, showed a statistically significant difference between times in term of bruising size ($P < 0.001$).

Finally, Mann Whitney test was showed a difference significantly in extent of bruising on the right side of the abdomen (intervention 1 and 2) in 2 groups ($P < 0/001$).

Table 1. Characteristic of samples

Variables		Cold Group N=37(%)		Groups of localized cold-heat N=37(%)		P-value
Sex	Female	8(21.6)		7	18.9%	0.772
	Male	29(78.4%)		30	81.1%	
Age (Year)	-	50.57±23.82		45.46±19.20		0.313
History of associated illnesses	Yes	18	48.6%	21	56.8%	0.485
	No	19	51.4%	16	43.2%	
History of diabetes	Yes	6	16.2%	10	27.0%	0.259
	No	31	83.8%	27	73.0%	
History of other diseases	Yes	15	40.5%	19	51.4%	0.351
	No	22	59.5%	18	48.6%	
Taking anticoagulant and antiplatelet drugs	Yes	17	45.9%	21	56.8%	0.352
	No	20	54.1%	16	43.2%	
Abdominal circumference (cm)	-	120.19±18.30		115.22±20.07		0.410
The result of the last PTT	-	31.19±2.75		32.24±3.40		0.320
PT	-	13.00±0.00		13.06±0.22		0.079
The result of the last INR	-	1.01±0.05		1.01±0.03		0.558
Number of Platelet	-	210729.73±35017.1		190594.59±42689.7		0.002

4. DISCUSSION

The findings of this study showed that the use of cold-hot pack in place of enoxaparin sodium injection is more effective in the size of bruising in comparison with cold pack. In this regard, the size of bruising was reduced in the right side of the abdomen in intervention group 2 (The combined cold-hot application) which is consistent with findings of other studies showing reduced bruising following enoxaparin sodium in use of hot pack [10,13]. The use of local hot pack leads to an increase in blood flow in the area and removal of blood cell accumulation below the affected tissue site. Changes in bruising were not observed in the right abdominal side during the study in intervention group 1. In this regard, other researchers found similar results for patients admitted to the orthopedics, internal and cardiac departments that were treated with an injection of 6000-unit enoxaparin sodium [14]. However, the results of some studies indicate a significant reduction in bruising with the use of cold pack on the injection site [15,16,17,18]. The reason for this contradiction may be the difference in the number of study samples, diagnosis, location of drug injection, frequency of sex, and the method used for selection of samples compared to other studies. The majority of research samples in this study were men (79.7%). Sex hormones secretion such as testosterone in men seems to increase the thickness of the skin and the subcutaneous tissue and protein content in the non-muscular mass of the body [11]. The effect of the male sex hormones mentioned in men affects the amount of tissue damage, with more resistance and less vulnerability to the subcutaneous injection of enoxaparin, resulting in less bruising. While in the study by Amanian et al. [13] the sexes of the samples were equally distributed.

On the other hand, reduction in concentration of the injectable solution of the drug used in this study compared to others can be considered as another reason for the difference between findings of the present study and others. In this study, 4000-unit sodium enoxaparin with a volume of 0.4ml was used, while the drug used by Amanian et al. was 6000-unit enoxaparin with a volume of 0.6 ml. In addition to the above reasons, another factor in the findings can be different definitions of the main research variable. For instance, in the study by Amanian et al. [13] bruising was defined as a region with a skin color variation of more than two millimeters, while in the present study, any color variation was considered as bruising. Changes in the size of bruising on the left side of the abdomen were not observed in the intervention group 1 (cold pack). This finding contrasts with the results of many similar studies. For example, studies done by BlakkyAkpinar, Gaytri Batra, Sarah Abdulaziz Alabdalhai and Zubik and Khorshid demonstrated a significant decrease in bruising in control groups. The difference in the research findings with the above studies can be explained by the difference in the research environment, the injection site, the volume of the injectable solution, the size and diameter of the syringe, and the duration of the drug injection. In the present study, patients who were admitted to

orthopedics ward, were treated with 4000-unit sodium enoxaparin performed with pre-filled syringes by a single drug company (Alborz Medication), at a 90-degree angle with pinching the injection site using index finger and thumb without aspiration, the syringe content was injected at least 5 cm right side of the umbilicus and after the injection was performed, the needle was removed from the skin with the same 90-degree angle without any massage at the site. In all groups, the duration of the injection was 30 seconds to reduce any complication of the injection, while for the study of BlakkyAkpinar et al., the duration of injection was 10 seconds in the right and left arm for each COPD patients who were being treated with 5000 mg heparin [10,19,17,18]. Compared to the right side of the abdomen (cold and cold-hot pack), the changes in the size of the bruising on the left side of the abdomen (control 1, control 2) increased by 24, 48 and 72 hours, respectively. It seems that factors such as (research environment, and diagnosis of the disease) are related to the significant increase in the size of bruising in the control groups compared to intervention groups because patients with fracture have some degrees of poor concentration caused by pain in their fracture area. The result is not enough motivation to learn about the training provided, such as abstinence from massaging or scratching the site of injection of enoxaparin sodium. This seems to be associated with the extent to which preventive measures are taken for bruising following drug injection. This issue, nonetheless, is also a limitation in the present study.

The changes in bruising on the right side of the abdomen were less in the intervention group 2 (cold-hot pack) compared with the intervention group 1 (cold pack). In this regard, the findings of the study by Amanian et al. on acute coronary syndrome patients with injections of 6000-unitenoxaparin sodium, are in agreement with the results of the present study. Changes in bruising size on the left side of the abdomen in the intervention group 2 (cold-hot pack) were lower than in intervention group 1 (cold pack). However, the findings of the study by Amanian et al did not show such a significant relationship. Such a contradiction in the results can be attributed to the difference in the frequency of gender and the research environment. On the other hand, reduction of the concentration of the injectable solution of the drug used in this study compared to other studies can be considered as another reason for the difference between the present study and other studies. In this study, 4000-unit sodium enoxaparin with a volume of 0.4 ml, while the drug used by Amanian et al. was 6000-unit of enoxaparin with a volume of 0.6 ml. It seems that reducing the volume and concentration of drug in the injection can reduce the extent of bruising. On the other hand, considering the age group of patients admitted to the orthopedics wards, the majority of the samples in the intervention group 2 (cold-hot pack) were less than 40 years old, so it could be justified that the samples understanding of the training provided in relation to the avoiding massage or scratching of the injection site was greater. As a result, self-care was taken to prevent drug complications. Contrary to the study by Amanian et al. in which the sexes of the study samples equally divided, the samples in the present study patients were male-dominated. Additionally, in the present study patients who were admitted to orthopedic wards treated with 4000 units of enoxaparin sodium were selected based on a randomized block list, but in the study by Amanaian et al, Gaytri Batra and Sarah Abdulaziz Alabdalhai, samples were selected from wards wherepatients with coronary artery diseases who were treated by anticoagulant and vasodilator drugs, were hospitalized. It is clear that the risk of bleeding with co-administration of enoxaparin sodium and other anticoagulants increases in patients with acute coronary syndrome. This may be another reason for the contradictory results [13,17,18].

In this regard, it is suggested to carry out other studies concerning the effect of cold and cold-hot pack on the incidence of bruising after injection of 40 mg of enoxaparin sodium in the left and right arm and their comparison, the effect of local cold and cold-hot pack on the incidence of bruising for injection of 6000 or 8000-unit enoxaparin sodium in orthopedic patients, and comparing of the effects of cold and cold-hot pack on the incidence of bruising caused by subcutaneous injection of unfractionated heparin and low molecular weight heparin.

5. CONCLUSION

The findings of this study showed that cold-hot pack on the site of injection of sodium enoxaparin significantly reduces the size of bruising which is clinically important. In order to improve the quality of nursing care and minimize unpleasant and painful experiences of patients, the findings of this study can be used as a guide to reduce the bruising associated with

subcutaneous injection of enoxaparin sodium. Probably reducing bruising can lead to satisfactory outcomes such as increasing access to different places for injection, mental and physical health and ultimately satisfaction of patient with the treatment and care provided.

CONSENT AND ETHICAL APPROVAL

This study was conducted after receiving the written approval of the Ethics Committee of the Vice-Chancellor for Research of Guilan University of Medical Sciences with IR.GUMS.REC.1397.094 issue-dated 6.11.2018 and at the Iranian Center for Clinical Practice with IRCT20180623040206N1. Before starting the sampling, the research samples received descriptions in terms of the purposes of the research, the method of performing their job and their rights and their expectations at each stage of the research, and in case of willingness they sign the written consent for participation in the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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