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Novel subcutaneous low-molecular-weight heparin injection technique to reduce post-injection bruising

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Abstract

Objective: To investigate the efficacy of a novel low-molecular-weight heparin injection technique compared to the standard technique relative to bruising incidence, bruise size, and pain.

Methods: A randomized controlled trial was conducted in 44 patients with acute deep vein thrombosis. Patients who were randomized into the control group received a 10-s duration injection with immediate needle withdrawal, whereas study group patients received a 30-s duration injection with a 10-s pause before needle withdrawal. Two injection sites were assessed for pain and bruising between 48 and 60 h after injection.

Results: Bruises occurred in 50.0% and 18.2% of control and study group patients, respectively ($p = 0.03$). Mean bruise size between 48 and 60 h after injection was 172.73 ± 372.60 mm^2 and 28.18 ± 70.01 mm^2 in the control group and study group, respectively ($p = 0.026$). Pain scores were comparable between groups.

Conclusion: A 30-s duration injection with a 10-s pause before needle withdrawal resulted in significantly fewer and smaller bruises.

Keywords

Novel technique, low-molecular-weight heparin, subcutaneous injection, post-injection bruising

Introduction

Low-molecular-weight heparin (LMWH) is the anticoagulant commonly used for initial treatment of acute venous thromboembolism. Many patients have to self-inject LMWH as an outpatient treatment, especially in patients with cancer-associated thrombosis that require long-term LMWH injection therapy.[1] Subcutaneous LMWH often causes bruising, hematoma, induration, and pain at the injection site.[2] Bruising is defined as a color change in the skin of ≥ 2 mm^2 in size.[3,4] Bruising results from blood leakage from injured veins into the subcutaneous tissue. Bruises usually reach their maximum size within 48 h, with reduction in bruise size starting at 72 h after bruise formation.[2,5] Presence of bruising may lead to anxiety, loss of self-confidence, and rejection of treatment. Bruising may also compel a patient to avoid repeated injections at a bruised site, which limits the area available for injections.[6] Only a few published studies have evaluated the techniques used for subcutaneous administration of LMWH.[2,7]

A 10-s injection duration is widely considered to be the standard and proper method for injecting heparin subcutaneously.[2] Balci Akpinar and Celebioglu and Chan both reported that increasing the injection duration from 10 s to 30 s reduced injection site pain and bruising.[2,7] Those studies also compared the effects of

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different wait times before needle withdrawal on bruising after heparin injection.[7] Balci Akpinar and Celebioglu found that a 10-s pause before withdrawing the needle after heparin injection resulted in a smaller bruise size compared to immediate needle withdrawal after injection.[2] However and to the best of our knowledge, combined 30-s injection duration and 10-s pause before needle withdrawal have not been evaluated.

Accordingly, the aim of this study was to compare the efficacy between a novel subcutaneous LMWH injection technique consisting of a 30-s injection duration combined with a 10-s pause before needle withdrawal and the standard 10-s injection with immediate needle withdrawal technique relative to bruising incidence, bruise size, and pain in patients with acute deep vein thrombosis.

Methods

This randomized controlled study was conducted at the Vascular Surgery Clinic of the Division of Vascular Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Siriraj Hospital is Thailand's largest university-based national tertiary referral center. Patients aged 18–80 years who were diagnosed with acute deep vein thrombosis during the 1 January 2015 to 30 June 2016 study period were included. Patients with one or more of the following were excluded: creatinine clearance <30 ml/min, bleeding disorder, thrombocytopenia, concurrent antiplatelet or other anticoagulant therapy, and/or pregnancy. Patients who had been given any other medicine injections at the abdominal site, or who had any incision or fibrotic scar tissue at the abdominal site were also excluded.

Patients were randomized and equally allocated into two groups using computer-based randomization software. The study group (30/10 injection group) received injections that lasted a duration of 30 s, with a 10-s delay before removal of the syringe needle. The control group (10 injection group) received injections that lasted a duration of 10 s, with immediate removal of the syringe needle when the injection was completed.

Nurses in our unit provided instruction to patients in both groups regarding how to self-inject enoxaparin 1 mg/kg every 12 h subcutaneously. The injection sites were located at 12, 2, 4, 6, 8, and 10 o'clock around the umbilicus, as shown in Figure 1. The first injection was given at the 12 o'clock position, 5 cm from umbilicus. Subsequent injections were given at the 2, 4, 6, 8, and 10 o'clock positions – in that order, and all 5 cm from the umbilicus. The next set of injection sites used the same clockwise position and order, but the injection was made at 10 cm from the umbilicus. The entire length of the needle was inserted into the skin of a skin fold created by the non-injecting hand at a 90-degree angle to the surface of the skin. The skin fold was held in place throughout the entire duration of the injection process until the needle was withdrawn. As previously described, patients in the *10 injection group* received enoxaparin over a 10-s injection duration, with immediate withdrawal of the needle. Patients in the *30/10 injection group* received enoxaparin over a 30-s injection duration, with a 10-s delay before needle withdrawal. A digital stopwatch was used to measure the duration of injection time and delayed needle withdrawal time. Pain assessment was performed immediately after each injection using a visual analog scale (VAS) to assess the severity of pain, with a score of 0 representing no pain and a score of 10 representing the most severe pain. Two injection sites were assessed for pain score between 48 and 60 h post-injection.

Patients were asked to come to our clinic four or five days after the first injection so that the resultant bruising could be observed and recorded. Two injection sites were assessed for bruising between 48 and 60 h post-injection. A nurse measured the size of the bruise in

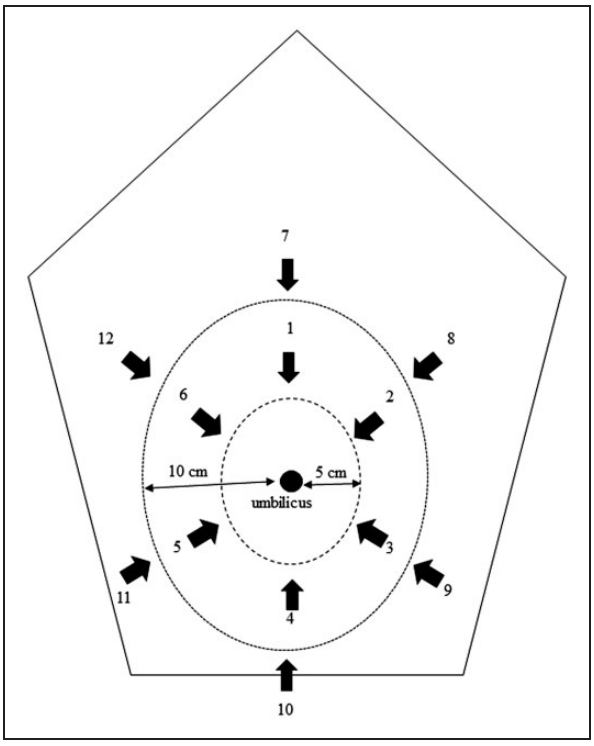

Figure 1. Diagram describing the injection site locations and order. The injection sites were located at 12, 2, 4, 6, 8, and 10 o'clock around the umbilicus. The first injection was given at the 12 o'clock position, 5 cm from umbilicus. Subsequent injections were given at the 2, 4, 6, 8, and 10 o'clock positions – in that order, and all 5 cm from the umbilicus. The next set of injection sites used the same clockwise position and order, but the injection was made at 10 cm from the umbilicus.

each patient. The size of bruising was measured using VISITRAK Digital Wound Assessment System (Smith & Nephew plc, London, UK). A bruise was defined as color change in the skin ≥ 2 mm^2 in size, which leads to pain and inflammation.[2,3]

The data collection form consisted of two parts. The first part of the form was used to collect demographic data about the patient that could affect the occurrence of bruising and/or pain. The second part of the form was used to collect data specific to the number and order of the injections, the location of injections on the abdominal wall, the pain score and duration of pain after each injection, occurrence of bruising, and bruise measurement values. Measured values were recorded on the data collection form between 48 and 60 h post-injection.

Ethical considerations

The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB) (COA no. 378/2557 [EC4]), and written informed consent was obtained from all study participants. This study complied with the principles set forth in the Declaration of Helsinki (1964) and was registered at the Thai Clinical Trials Registry (TCTR 20160426004).

Sample size calculation and statistical analysis

Power analysis and sample size calculations indicated that a minimum sample size of 19 patients per group would yield 80% statistical power to detect 45% change in bruising caused by LMWH injection between groups ($\alpha = 0.05$). Eight additional patients were recruited (four allocated to each group) to compensate for patients who had to withdraw from the study for any reason. Sample size calculations were performed using nQuery Advisor 5.0 (Statistical Solutions, Clearwater, FL, USA).

Data were prepared and analyzed using PASW Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA), and the level of statistical significance was set at a p-value of less than 0.05. Number and percentage were used to express categorical data, and mean $\pm$ standard deviation was used to describe continuous data. Independent samples t-test was used to analyze normally distributed quantitative variables, and Mann-Whitney U test was used to analyze non-normally distributed quantitative data. Qualitative data were compared using Pearson's chi-square test or Fisher's exact test.

Results

Of the 130 consecutive patients with acute deep vein thrombosis who were screened for eligibility during the study period, 44 patients were included in this study. Twenty-two patients were randomly allocated to each of the two study groups. Of the 86 patients who were excluded, 18 declined to participate, 25 were aged greater than 80 years, 4 were pregnant, 10 had abnormal coagulogram, 5 were taking antiplatelet drugs, 15 had received other anticoagulants, 3 had communication problems, 3 had recent surgical abdominal wounds, and 3 had abdominal skin fibrosis after radiation.

The mean age of patients was 50 ± 15 years, with a gender breakdown of 25 females and 19 males. The mean body mass index (BMI) was 24 ± 5 kg/m^2. The CONSORT flow diagram of the study protocol is shown in Figure 2. Patient demographic and clinical characteristics compared between the two injection technique groups are described in Table 1. No significant difference was observed between groups for gender, age, BMI, prothrombin time, activated partial thromboplastin time, platelet count, site of DVT, underlying diseases, or treatment for DVT.

At 48 h after injection, bruising occurred in eight (36.4%) patients in the control group and in three (13.6%) patients in the study group ($p = 0.08$). Between 48 and 60 h after injection, bruises occurred in 11 (50.0%) patients in the control group and in 4 (18.2%) patients in the study group ($p = 0.03$). No significant difference was observed between groups for pain score (Table 2).

The mean bruise size at 48 h after enoxaparin injection was 38.18 ± 103.03 mm^2 in the control group, and 2.23 ± 6.12 mm^2 in the study group ($p = 0.048$). The mean bruise size between 48 and 60 h after enoxaparin injection was 172.73 ± 372.60 mm^2 in the control group and 28.18 ± 70.01 mm^2 in the study group ($p = 0.026$) (Table 3).

Bruise size was classified into the following three categories: no bruise (<2 mm^2), small bruise (2–5 mm^2), and large bruise (>5 mm^2). The results of our analysis revealed that large bruises occurred at 48 h after injection in eight (36.4%) patients in the control group and in three (13.6%) patients in the study group ($p = 0.082$). Large bruises occurred between 48 and 60 h after injection in 11 (50.0%) patients in the control group and in 4 (18.2%) patients in the study group ($p = 0.026$) (Table 4).

Discussion

Bruising is an anticipated consequence of local tissue trauma that occurs during administration of subcutaneously injected LMWH. The results of the Chan's study demonstrated that the 30-s duration injection technique resulted in significantly fewer and smaller bruises compared with the standard 10-s duration

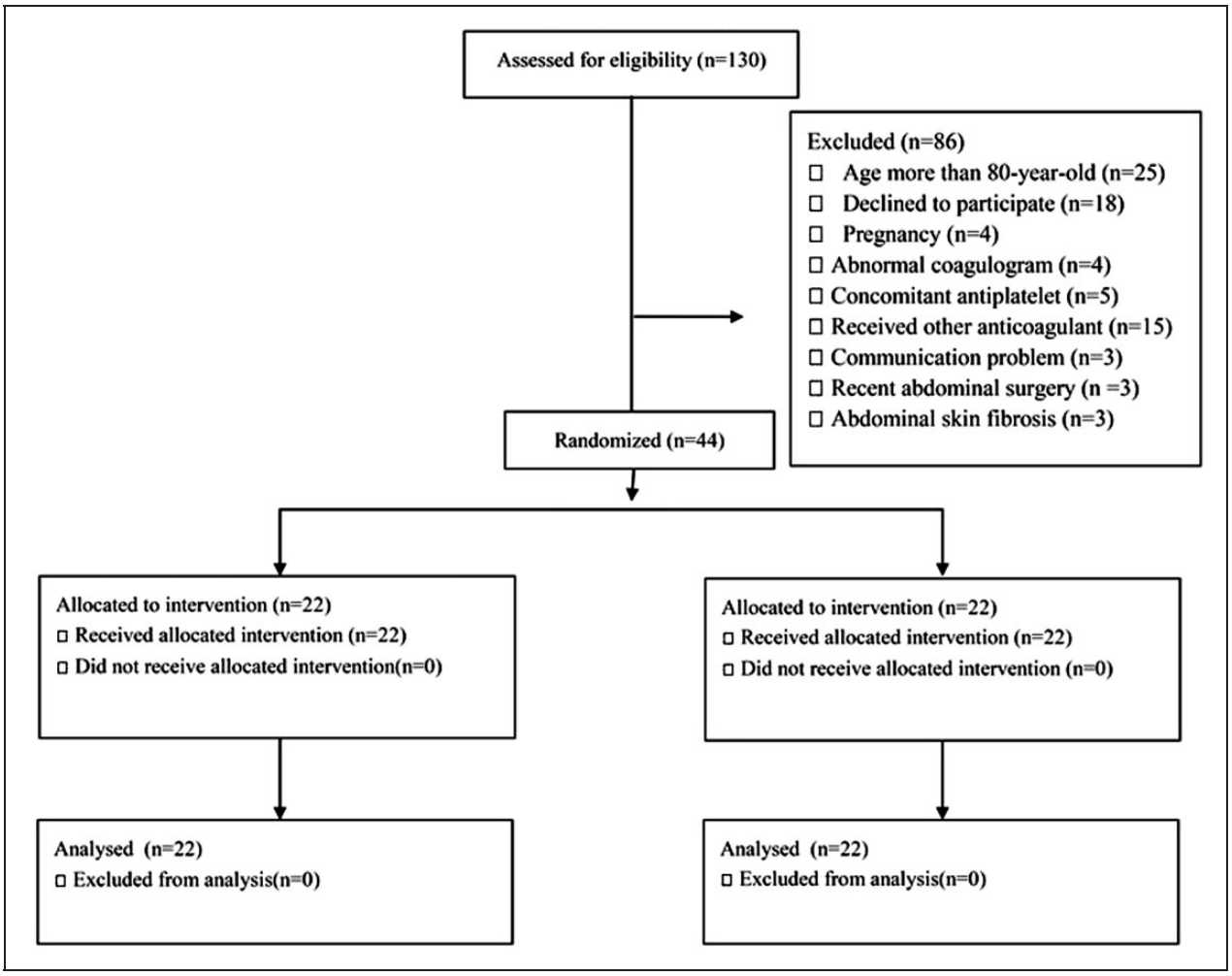

Figure 2. CONSORT flow diagram of the study protocol.

Table 1. Patient demographic and clinical characteristics compared between injection technique groups.

	Injection technique		
	10 Injection technique (n=22)	10/30 Injection technique (n=22)	p
Female gender, n (%)	11 (50.0)	14 (63.6)	0.36
Age (yrs), mean±SD	51.9±15.0	48.7±14.5	0.485
Body mass index (kg/m^2), mean±SD	24.3±4.7	23.9±4.8	0.824
Prothrombin time, mean±SD	12.2±0.7	12.4±0.8	0.564
APTT, mean±SD	25.5±2.9	26.8±2.6	0.113
Platelet count ($\times 10^3$), mean±SD	330.1±148.2	261.6±92.1	0.072
Site of DVT, n (%)			N/A
Ilio-femoral	3 (13.6)	3 (13.6)	
Femoro-poppliteal	18 (81.8)	19 (86.4)	
Subclavian	1 (4.5)	0 (0.0)	
Underlying diseases, n (%)			
Cancer	10 (45.5)	7 (31.8)	0.353
Hypertension	3 (13.6)	3 (13.6)	1.0
Diabetes	1 (4.5)	0 (0.0)	1.0
Others	2 (9.1)	3 (13.6)	1.0

(continued)

Table 1. Continued

	Injection technique		
	10 Injection technique (n=22)	10/30 Injection technique (n=22)	p
Treatment of DVT, n (%)			0.545
Enoxaparin	13 (59.1)	11 (50.0)	
Enoxaparin + warfarin	9 (40.9)	11 (50.0)	

Note: A p-value < 0.05 indicates statistical significance.
SD: standard deviation; APTT: activated partial thromboplastin time; DVT: deep vein thrombosis.

Table 2. Bruise incidence and pain score after enoxaparin injection compared between injection technique groups.

	Injection technique		
	10 Injection technique (n=22)	10/30 Injection technique (n=22)	p
Occurrence of bruise at 48 h, n (%)	8 (36.4)	3 (13.6)	0.08
Occurrence of bruise between 48 and 60 h, n (%)	11 (50.0)	4 (18.2)	0.03
Pain score at 48 h, median (min, max)	2 (0, 7)	2 (0, 8)	0.64
Pain score between 48 and 60 h, median (min, max)	2 (0, 7)	2 (0, 8)	0.69

Note: A p-value < 0.05 indicates statistical significance.

Table 3. Mean bruise size after enoxaparin injection compared between injection techniques.

	Injection technique		
	Control (n=22) Mean±SD	New technique (n=22) Mean±SD	p
Bruise size at 48 h (mm^2); (min, max mm)	38.18±103.03 (0, 460)	2.23±6.12 (0, 20)	0.048
Bruise size between 48 and 60 h after injection (mm^2); (min, max)	172.73±372.60 (0, 1,680)	28.18±70.01 (0, 260)	0.026

Note: A p-value < 0.05 indicates statistical significance.
SD: standard deviation; min: minimum; max: maximum.

Table 4. Number of patients in each bruise size category after enoxaparin injection compared between injection techniques.

	Injection technique		
	Control (n=22)	New technique (n=22)	p
At 48 h after injection			
Bruise categories			0.082
No bruise (<2 mm^2), n (%)	14 (63.6)	19 (86.4)	
Small bruise (2–5 mm^2), n (%)	0 (0.0)	0 (0.0)	
Large bruise (>5 mm^2), n (%)	8 (36.4)	3 (13.6)	
Between 48 and 60 h after injection			
Bruise categories			0.026
No bruise (<2 mm^2), n (%)	11 (50.0)	18 (81.8)	
Small bruise (2–5 mm^2), n (%)	0 (0.0)	0 (0.0)	
Large bruise (>5 mm^2), n (%)	11 (50.0)	4 (18.2)	

Note: A p-value < 0.05 indicates statistical significance.

injection technique.[7] In addition, Balci Akpinar and Celebioglu found that waiting 10 s before removing the needle after subcutaneous heparin injection resulted in less and smaller bruises than those produced by the standard immediate needle withdrawal technique.[2] In this study, we combined these two techniques (30/10 injection technique) and compared their combined efficacy with the standard 10-s injection with immediate needle withdrawal technique relative to bruising and pain.

We found heparin administration via the 30/10 injection technique to be significantly associated with both reduced bruising incidence and reduced bruise size between 48 and 60 h after injection. Local tissue trauma may be related to the magnitude of injection pressure on the affected tissues. Slower injection of LMWH may cause lower injection pressure and commensurately less tissue damage. In addition to less tissue trauma, slower injection may allow more time for tissue absorption of LMWH. Moreover and importantly, there was no difference in pain scores between patients who received the 30/10 injection technique and those who received the 10-injection technique in this study. Therefore, a longer injection was not more painful.

Although bruising was significantly reduced in our study group compared to controls, the latter group had a relatively large bruise size compared to controls in other comparable studies.[7] This represents a potential limitation of our study. A second limitation was the relatively small sample size. The post-hoc power of this study was 61%. That acknowledged, this study was still able to demonstrate statistically significant differences between the two compared techniques, and it yielded significant data that are valuable for clinical nursing practice. Future studies should be conducted in larger study populations and in different patient groups. The novel technique reported here should also be investigated in other injection applications that commonly result in bruising.

Conclusions

This study provides new information for clinical nursing practice about bruising that is associated with subcutaneous LMWH injection. Our findings revealed that a 30-s duration injection combined with a 10-s delay before withdrawing the needle resulted in significantly fewer and smaller bruises. A larger study is needed to confirm this result.

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Declaration of Conflicting Interests

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Ethical approval

The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB) (COA no. 378/2557[EC4]).

Guarantor

NS.

Contributorship

SJ contributed to the study design, data collection, and data analysis. RP, NP and ST took part in the data collection. NS contributed to the study design and writing. SJ and NS took part in revising critically for important intellectual content. All authors approved the final version to be submitted.

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References

1. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest* 2016; 149: 315–352.
2. Balci Akpinar R and Celebioglu A. Effect of injection duration on bruising associated with subcutaneous heparin: a quasi-experimental within-subject design. *Int J Nurs Stud* 2008; 45: 812–817.
3. Kuzu N and Ucar H. The effect of cold on the occurrence of bruising, haematoma and pain at the injection site in

subcutaneous low molecular weight heparin. *Int J Nurs Stud* 2001; 38: 51–59.
4. McGowan S and Wood A. Administering heparin subcutaneously: an evaluation of techniques used and bruising at the injection site. *Aust J Adv Nurs* 1990; 7: 30–39.
5. Vanbree NS, Hollerbach AD and Brooks GP. Clinical evaluation of three techniques for administering low-dose heparin. *Nurs Res* 1984; 33: 15–19.
6. Dehghani K, Najari Z and Dehghani H. Effect of subcutaneous enoxaparin injection duration on bruising size in acute coronary syndrome patients. *Iran J Nurs Midwifery Res* 2014; 19: 564–568.
7. Chan H. Effects of injection duration on site-pain intensity and bruising associated with subcutaneous heparin. *J Adv Nurs* 2001; 35: 882–892.