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Occurrence and Extent of Bruising According to Duration of Administration of Subcutaneous Low-Molecular-Weight Heparin

A Quasi-experimental Case-Crossover Study

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Background: Several authors have documented the role of low-molecular-weight heparin injection techniques in bruising. However, few researchers have measured the influence of injection duration on the occurrence and extent of bruising. **Purpose:** The aim of this study was to evaluate the influence of different durations of subcutaneous heparin injection on the occurrence and extent of bruising. **Methods:** A quasi-experimental case-crossover study design was adopted in 2010. A consecutive series of patients admitted to 2 orthopedic units in a large (600 beds) teaching hospital located in northern Italy were eligible for enrolment. Injections were administered following a standard procedure. The manipulated variable was the duration of the injection, 10 seconds (treatment A) and 30 seconds (treatment B). The evaluation of bruise occurrence and extension performed after 48 hours and data analysis were conducted in a blinded fashion. **Results:** A total of 150 patients receiving their first and second subcutaneous heparin injections (300 injections) were enrolled. Eighty-seven bruises were observed out of 300 injections (29%): 57 of 150 (38%) after injections lasting 10 seconds and 30 of 150 (20%) after injections lasting 30 seconds (relative risk, 1.50; 95% confidence interval, 1.21–1.86; $P = .00$). Of the 87 bruises that occurred, 69 (79.3%) were small (2–5 mm) and 18 (20.6%) were large (>5 mm), with no difference in size between 10- and 30-second injections (relative risk, 0.91; 95% confidence interval, 0.39–2.12; $P = .83$). **Conclusions:** Low-molecular-weight heparin injection should be administered over 30 seconds to decrease bruising. **Clinical Implications:** There is a need to reflect on the feasibility of such a practice because injecting low-molecular-weight heparin at 30 seconds requires accuracy, a steady hand, the absence of tremor, a calm environment, and the ability to administer an infinitesimally small amount of liquid (eg, 0.4 mL) per second.

KEY WORDS: administration, bruise, case-crossover, duration, injection, low-molecular-weight heparin, quasi-experimental

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Ethics adherence: We have respected the Italian law and principles of professional codes. The project was approved by the internal review board of the university and teaching hospital.

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Low-molecular-weight heparin (LMWH) is administered subcutaneously by nurses to patients at risk of developing thromboembolism or who have thromboembolic disease in both inpatient and outpatient settings.[1] The effects of LMWH are related to the ability to inhibit activated factor X (factor Xa), resulting in decreased thrombin and, ultimately, the prevention of fibrin clot formation. The routine use of thromboprophylaxis in surgical patients older than 40 years or undergoing major general surgery has been shown to reduce the risk of postoperative deep vein thrombosis.[2] The adverse effects of LMWH are bruising, nodules,[3] pain, melena, hematuria, thrombocytopenia, osteoporosis,[4–6] small-scale hemorrhagic manifestations, and alopecia.[7] Of these adverse effects, the occurrence of bruising is highly variable, from 20.6%[5] to 88.9%[8] of cases after subcutaneous administration. Bruises might affect subsequent procedures,

reducing the surface area available for abdominal administration and the opportunity for site rotation[5,6,9]; bruising might also lead to discomfort,[5,10] anxiety and concern,[9] and possibly refusal of treatment by patients because of reduced trust in nurses' competence to perform the injections.[3,5,6,11,12]

Several authors[9,10,13–15] have documented the influence of the injection technique on the occurrence of bruising. However, few researchers[5,8,10,16] have documented the role of injection duration on the occurrence and on the extent of bruising. The general aim of this study was to contribute to the advancement of knowledge in the prevention of bruising associated with the LMWH injection technique performed by nurses.

Review of Literature

There are no recommendations on the duration of subcutaneous LMWH injection in nursing textbooks,[4,17,18] information leaflets,[19–21] or most articles available that have documented the effects of different injection techniques on bruising.[6,9,12,22–31] Moreover, some authors[5,17,22,32–37] have reported the need to administer LMWH over more than 10 seconds with the aim of reducing pain and local trauma.[10] However, only 4 studies[5,8,10,16] have documented the influence of injection duration on the occurrence of bruising.

In a quasi-experimental study involving 34 patients affected by stroke, Chan[5] documented a reduction in the occurrence of bruising if the injection was performed over 30 seconds. The injection technique involved choosing the right or left side of the abdomen, cleansing the injection site with an antiseptic, removing the safety cap by pulling the needle in a straight line, pinching the skin at the site throughout the injection, inserting the needle at an angle of 90°, removing the needle quickly at the end using the same inclination and applying an antiseptic, and pressing gently for 10 seconds. Two techniques were used for 2 injections. The first injection (technique A) lasted 10 seconds, whereas the second injection (technique B), given 12 hours later, lasted 30 seconds. The occurrence of bruising was assessed at 48 and 60 hours after each injection and the risk of bruising was twice as high with the use of the 10-second technique (47.0% vs 20.6%). After the injection lasting 10 seconds, larger bruises appeared than with the 30-second injection: The average bruise size difference ranged from 23.16 to 24.67 mm^2. Wilcoxon signed-rank analysis demonstrated that injection technique A resulted in significantly larger bruises compared with injection technique B at both 48 and 60 hours after injection. However, in a subsequent study by Chenicek[16] based on a quasi-experimental design involving 34 patients admitted for neurological or cardiac intensive care or orthopedic, there was no difference ($P = .549$) in the bruising extension (in millimeters) measured 48 hours later between the 10-second injection (mean [SD], 0.41 [0.743]) and the 30-second injection (0.56 [0.549]), and no difference in the occurrence of bruising was reported.[16]

Balci Akpinar and Celebioglu[8] used 3 different injection techniques over 3 days in a quasi-experimental study involving 36 patients with chronic obstructive bronchopathy. The first injection was 10 seconds in duration (technique A), the second was 30 seconds (technique B), and the third was 10 seconds, with withdrawal of the needle after a further 10 seconds (technique C). The injection sites were circled with a marker and identified with their respective letters. After 48 hours of each injection, there was a higher incidence of bruising after technique A (88.9%) than after the other 2 techniques (technique B, 61.1%; and technique C, 63.9%). The researchers measured the diameter of the bruise using a plastic ruler, finding that injection technique A sites had significantly larger bruises (14.36–20.94 mm) than did injection technique B sites (4.66–10.20 mm) and injection technique C sites (4.69–77.88 mm).

More recently, a quasi-experimental study on a sample of 50 cardiological, neurological, and orthopedic patients[10] confirmed the positive effects on bruising of slow administration of the LMWH injection. Following a randomized sequence, 1 injection was performed at 10 seconds on the right side of the abdomen, whereas another injection lasting 30 seconds was administered into the left side of the abdomen. After 48 to 72 hours, bruising was apparent at 64% (n = 32) of sites receiving the 10-second injection and at 42% (n = 21) of sites receiving injections lasting 30 seconds ($P < .05$). The mean bruise size at 48 and 72 hours was 109.20 and 110.12 mm^2, respectively, with the 10-second injection and 18.76 and 21.72 mm^2, respectively, with the 30-second injection technique ($P < .05$).

On the basis of the small amount of evidence available, LMWH injections should be administered over more than 10 seconds,[5,8,10] although Chenicek[16] reported no difference between the 10- and 30-second injection duration. However, as mentioned also by the same authors,[5,8,10,16] there is a need to address new challenges emerging in the field and overcome some limitations of the available studies in the context of the new treatments. In particular, further research should consider the following:

a. The changes that have occurred in LMWH injection frequency. A systematic review of trials[38] found that 1 LMWH injection a day is safe and effective in surgical patient thromboprophylaxis.

Available research in the field of bruise occurrence and extension[5,8,10,16] was performed before this systematic review, from 1997–1998 in Kuzu and Uçar[6] to 2006 in Balci Akpinar and Celebioglu,[8] when the frequency was twice a day. The frequency of the injection might influence the occurrence of bruises because of differences in the amount of solution injected and in the number of injections performed daily. In a study assessing the risk factors for bleeding in patients with acute coronary syndrome receiving treatment with enoxaparin, the number of doses was identified as a possible risk factor (odds ratio, 2.15; 95% CI, 1.25–3.68).[39]

b. The need to involve large samples of patients, given that existing studies[5,8,10,16] have involved 50 patients or less.

c. The need to limit bias. Available studies[5,8,16] in which bruising differences were evaluated involved studies in which injection was performed first at the 10-second injection and later at the 30-second injection. Lack of randomization in the sequence of the injection duration might have influenced the outcomes because the second injection was exposed to the effect of the LMWH itself. Only Zaybak and Khorshid[10] have performed an injection duration randomized sequence. To increase the validity of the study, there is also a need to ensure that the evaluation of the bruising occurrence and data analysis are performed in a blinded fashion.[40]

d. The effects of some covariates on bruise occurrence. Patients' coagulation profile, obesity, and diabetes, which determine microangiopathy and capillary frailty, should be considered in the evaluation of bruise occurrence.[4,11,14,35]

Conducting repeated studies aimed at determining which technique is more effective is also needed to allow patients and their caregivers to safely self-administer LMWH.[41]

Aim

The aim of this study was to evaluate the influence of different durations of subcutaneous heparin injections (10 vs 30 seconds) on the occurrence and extent of bruising.

Methods

Study Design

A case-crossover quasi-experimental study design was adopted in 2010. This study design was adopted to control confounding factors that might influence the occurrence of bruising and to increase the internal validity of the study.[40]

Sampling and Sample

A consecutive series of patients admitted to 2 orthopedic units in a large (600 beds) teaching hospital located in northern Italy were eligible for enrolment. Patients were considered eligible if they were (*a*) 18 years or older, (*b*) admitted to the hospital for urgent or scheduled reasons, (*c*) candidates for or had already undergone orthopedic surgery, (*d*) required to maintain bed rest, (*e*) starting subcutaneous LMWH therapy, (*f*) monitored for at least 3 days after the first injection, and (*g*) had given their consent to participate in the study. Patients were excluded if they (*a*) were already receiving subcutaneous heparin injection(s) in the previous days, (*b*) were taking oral anticoagulants or antiaggregates, (*c*) had cardiological, hematological, or liver diseases or were following hemodialytic treatment for their effects on coagulation,[5] (*d*) were pregnant, or (*e*) had an altered integrity of abdominal skin (eg, for trauma).

Patients remained involved in the study until 48 hours after having received their first and second LMWH injections. After the follow-up evaluation of the occurrence and extent of bruising, patients were discharged from the study and continued to receive the prescribed LMWH injections following the standard procedure available in the units. In order not to influence the evaluation of bruise occurrence and extension, subsequent injections were done far from the initial injection site. Figure 1 demonstrates the flow of patients through the study.

Intervention

The first and second subcutaneous LMWH injections were administered to each patient by an expert nurse. These injections were administered according to the prescriptions made by the physician and following a standard procedure (Figure 2) based on the best evidence available.[4–6,8,10–12,17,18,22–24,26,28–31,38,42–44]

To maximize the difference in the effects on bruising occurrence, the manipulated variable was the duration of the injection. The standard injection duration, measured with a chronometer, was 10 seconds in treatment A and 30 seconds in treatment B. A homogeneous injection technique, in terms of site (lower abdomen, at least 5 cm from the navel), needle gauge (27.5 gauge, 5/8 in), syringe volume (0.4 mL), enoxaparin quantity (4000 IU), and timing between the first and second (24 hours),[38] was assured. The order to start with either treatment in each patient (A or B) was randomly selected.

Outcomes, Follow-up, and Rationale

The occurrence and extent of bruising were the outcomes. Bruising was defined as an area of discolored

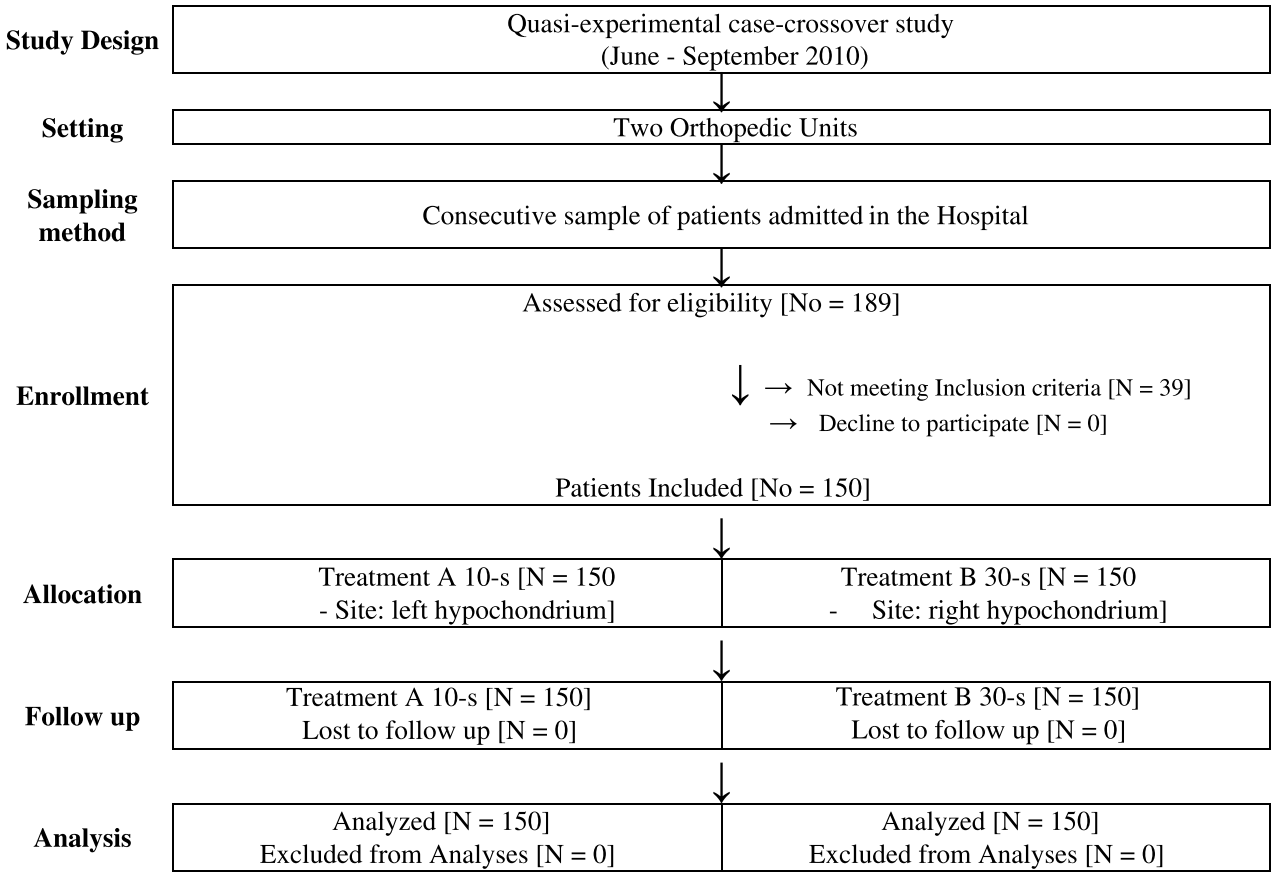

FIGURE 1. *Flow of patients through the study.*

skin of more than 2 mm appearing 48 hours after administration.[5] The tissue damage caused by the injection and bleeding from small capillaries of the dermis and hypoderm constitute the mechanism of bruising. According to the evidence available[5,6,8,10,16] indicating that bruises usually peak at 48 hours and begin to disappear within 72 hours after injection, the evaluation of bruising was performed exactly 48 hours after injection by expert nurses who received specific instruction. They scrutinized the skin at the circled site, at a distance of 1 cm with nontoxic water-removable coloured ink on both the left and right sides. When bruising was present, its extent was measured with a plastic ruler. The maximum horizontal extent (diameter) of the bruise was recorded (in millimeters) regardless of whether the bruise was regular or uneven in shape at the time of measurement.

Blinding Procedures

The site of each treatment was known only by the nurse administering the injection. The decision (treatment A, 10 seconds left hypochondrium; treatment B, 30 seconds right hypochondrium) was written in a paper and placed in an envelope and kept in a locked safe. Nurses evaluating the bruising did not know which treatment had been performed on the left and right side of the abdomen. The data analysis was also performed in a blinded fashion. The envelope containing this information was opened after analysis was complete.

Other Variables and Collection of Data

The following variables were collected: (1) patient demographics (age, gender), (2) patient dependency on activities of daily living (Barthel Index composed of 10 items, 0 = totally dependent to 100 = independent), (3) patient body mass index (<18.5 kg/m^2 = underweight, ≥30.0 kg/m^2 = obese), and (4) patient clinical profile (ie, comorbidity; in receipt of surgery or not; other medications taken; coagulation index ranges [international normalized ratio: normal, 0.8–1.2; higher, >1.2; lower, <0.8; and partial thromboplastin time values: normal, 12–15 seconds; higher, >15 seconds; lower, <12 seconds]). For the coagulation index ranges, normal, high, or low values indicating hemorrhagic risk were assumed according to the reference values indicated by the teaching hospital included. These data allowed the identification of covariates that might influence[5] the occurrence of bruising. Data on the time at which the injections were performed and on the outcomes measured after

FIGURE 2. *Low-molecular-weight heparin injections: Standard procedure adopted and manipulated variable.*

48 hours were collected on a sheet prepared for each patient involved. This was filled in both by the nurse performing the injection(s) and by nurses measuring the occurrence and extent of bruising.

In a preliminary analysis to assess reproducibility, 10 bruises were independently evaluated in terms of their occurrence (categorical data, Cohen κ coefficient[40]) and extent (continuous data, Pearson correlation test,[40] r) by 2 expert nurses involved later in the study in the bruise evaluation. There was complete concordance in the occurrence ($\kappa = 1.00$) and a strong correlation on the extension ($r = 0.97$).

Ethical Issues

The internal review board of the teaching hospital approved the study protocol. Patients were informed about the aims of the study. They were also informed about the evidence available on the LMWH administration procedure and were asked their permission to circle the injection with water-removable ink. They gave their written informed consent.

Data Analysis

Data analysis was conducted using the Statistical Package for the Social Sciences version 18 for Windows (SPSS Inc, Chicago, Illinois). Descriptive analyses (frequencies, percentage, mean ± SD, median and range) were used to describe the characteristics of the patients involved and the occurrence and extent of bruising. Two analyses were then conducted. In the first, we examined the occurrence of bruising by treatment (A vs B) and included all patients involved. The second excluded those cases where both treatments (A or B) caused bruising in the same patient. Differences in occurrence of bruising were evaluated by calculating the relative risk (RR) and 95% confidence

interval (95% CI). Differences in the average extent of bruising were calculated using the Student *t* test. Based on previous research,[5] bruise size data were analyzed according to 3 categories: no bruise (0–1 mm), small bruise (2–5 mm), and large bruise (>5 mm). Differences in the occurrence of large and small bruises between treatments were also calculated using RR and 95% CI. A multivariate analysis including demographic (ie, age, gender) and clinical (ie, diabetes, patient's coagulation profile) data and injection duration (A vs B) was performed. The level of statistical significance was fixed at $P = .05$.

Results

Participants

A total of 150 patients who were due to receive their first and second subcutaneous LMWH injections (300 injections) were included. Table 1 presents the main characteristics of the patients involved.

Bruise Occurrence

Of 300 injections, 87 (29%) bruises were observed: 57 of 150 (38%) after rapid subcutaneous injection (10 seconds) and 30 of 150 (20%) after slow subcutaneous injection (30 seconds) (RR, 1.50; 95% CI, 1.21–1.86; $P = .00$). Of 150 patients, 22 (14.6%) developed bruises after both treatments (10 and 30 seconds). Excluding these patients, 35 of 128 (27.3%) patients developed bruises after the 10-second injection, whereas 8 of 128 (6.5%) patients developed bruises after the 30-second injection (RR, 1.86; 95% CI, 1.51–2.30, $P = .00$).

Extent of Bruising

Of the 87 bruises that developed, 69 (79.3%) were small (2–5 mm) and 18 (20.6%) were large (>5 mm), with no difference between treatments (RR, 0.91; 95% CI, 0.39–2.12; $P = .83$). The average size of the bruise was 6.12 ± 9.4 mm (median, 3 mm; range, 2–50 mm): 6.4 ± 9.8 mm (median, 4 mm; range, 2–60 mm) after the 10-second injection and 5.7 ± 9.1 mm (median, 3 mm; range, 2–50 mm) after the 30-second injection. The average difference was 0.095 mm (95% CI, −3.253 to 5.102; $P = .661$).

The differences in average bruise size in those patients who developed bruises after only 1 treatment (10 or 30 seconds, 128 patients) were not statistically significant (4.71 ± 7.24 mm vs 2.89 ± 1.36 mm; average difference, 1.82 mm; 95% CI, −3.110 to 6.760; $P = .46$). The average bruise size in patients who developed bruises after both treatments (10 and 30 seconds, 22 patients) was 6.7 ± 5.8 mm and 7.2 ± 11.0 mm, respectively, a difference that was not significant (average difference, 0.50 mm; 95% CI, −6.48 to 5.48; $P = .83$).

TABLE 1 Patients' Characteristics (n = 150)

Patients' Characteristics	n (%)	Mean ± SD (Range, Median)
Age, y		74.8 ± 15.5 (27–98, 78)
Gender		
Female	102 (68)	
Male	48 (32)	
Undergone surgery	146 (97.3)	2.4 ± 1.6 d after hospital admission (0–6 d, 2.0 d)
Barthel Index (0 total dependent-100 total independent)		41.27 ± 28.2 (0–100, 41.2)
BMI		
Underweight (<18.5 kg/m^2)	2 (1.3)	
Normal (18.5–24.9 kg/m^2)	82 (54.7)	
Overweight (25–29.9 kg/m^2)	44 (29.3)	
Obese (30–≥40 kg/m^2)	22 (14.7)	
Comorbidities[a]	45 (30.0)	
Diabetes	16 (10.7)	
Insulin treated	6 (37.5)	
INR[b]		1.10 ± 0.09 (0.94–1.49, 1.1)
Normal	140 (93.3)	
High	10 (6.7)	
Low	0 (–)	
aPTT[b]		1.02 ± 0.19 (0.71–1.64, 1.0)
Normal	114 (76.0)	
High	16 (10.7)	
Low	20 (13.3)	

Abbreviations: aPTT, activated partial thromboplastin time; BMI, body mass index; INR, international normalized ratio.
[a]Hypertension, arrhythmia, gastric and intestinal disease, respiratory disease, gout, breast cancer, old transient ischemic attack, and neurological disorders, not associated with occurrence of bruising.
[b]Based on the ranges indicated by the laboratory unit of the teaching hospital involved.

Factors Affecting the Occurrence of Bruising

Two multivariate analyses were performed. The first evaluated the factors associated with the occurrence of bruising within the whole set of injections performed (300 on 150 patients), and the second excluded those injections performed following the 10- and 30-second scheme that resulted in bruises in the same patient (44 injections and 22 patients). In both multivariate analyses, the occurrence of bruises was not associated with gender (female), age, or the coagulation profile of patients, whereas 10-second injections increased the risk of bruise occurrence from 2.658 (95% CI, 1.567–4.508) in the first multivariate analysis to 5.111 (95% CI, 2.294–11.387) in the second multivariate analysis. In the latter, overweight/obesity emerged as a protective factor in bruise occurrence (RR, 0.445; 95% CI, 0.208–0.953). Table 2 presents the factors associated or not with bruise occurrence included in the multivariate analysis.

Discussion

Bruise Occurrence

Previous investigators exploring the influence of injection duration report varying incidences of bruising after LMWH injection. In one study, the rate was a 47% incidence of bruising after rapid injection versus 20.6% after slow injection[5]; in another, 88.9% versus 61.1%, respectively[8]; and in a third, 64% versus 42%, respectively.[10] Our findings, in which we corrected for limitations in previous studies, add to this body of literature and suggest that LMWH should be injected slowly. We note a bruising occurrence of 38% after rapid subcutaneous LMWH injection and 20% after slow subcutaneous injection. Excluding those patients who developed bruising after both treatments, the occurrence was 27.3% over 10 seconds and 6.5% over 30 seconds. In line with previous studies,[5,8,10] we found that performing the injection over 10 seconds increased the occurrence of bruises.

The overall lower occurrence rate of bruising documented after both treatments in our study, as compared with previous studies,[5,8,10] might be explained by a number of factors. One explanation may be the administration of smaller doses of LMWH in less concentrated solutions. In our study, 4000 IU/0.40 mL was administered, whereas 5000/0.25 mL was administered in Chan[5] and 4500/0.45 mL was administered in Balci Akpinar and Celebioglu.[8] As documented in a pharmacokinetic/pharmacodynamic study, the bruising likelihood after enoxaparin increases with the value of its maximum concentration.[47] It may be reasonably supposed that injecting higher doses of enoxaparin in more concentrated solutions (eg, 5000/0.25 mL) over the same time period, by producing higher maximum concentration, may provide higher probability of bruising. Another explanation may be the volume of injection. As documented by Chan,[5] injecting higher concentrations of enoxaparin (eg, 5000/0.25 mL) over 10 seconds reduces the tissue pressure by 50% of that produced by injecting 0.5 mL of enoxaparin over the same duration. Finally, a difference in follow-up times may be an explanation. Given that bruising peaks at 48 hours and healing starts at 72 hours after injection,[43] we evaluated bruising 48 hours after injection. Previous studies evaluated bruising after 8 hours,[8] after 48 and 60 hours,[5] and after 48 to 72 hours.[10] Further research in the field should standardize the follow-up times to increase the comparability of the results.

TABLE 2 Factors Associated With the Occurrence of Bruising: Multivariate Analyses

Variables	RR	95% CI	*P*
First multivariate analysis[a]			
Gender: female	1.319	0.705–4.014	.24
Age >60 y	1.682	0.705–2.470	.24
Overweight/obese (BMI ≥25 kg/m^2)	0.840	0.485–1.452	.53
Diabetes	1.627	0.703–3.769	.25
High INR values	0.405	0.121–1.351	.14
High aPTT values	1.713	0.730–4.023	.21
Intervention A (10 s)	2.658	1.567–4.508	.000
Second multivariate analysis[b]			
Gender: female	1.167	0.457–2.744	.52
Age >60 y	1.465	0.457–4.696	.52
Overweight/obese (BMI ≥25 kg/m^2)	0.445	0.208–0.953	.03
Diabetes	2.605	0.889–7.635	.08
High INR values	0.196	0.023–1.681	.14
High aPTT values	1.921	0.603–6.118	.26
Intervention A (10 s)	5.111	2.294–11.387	.000

Abbreviations: 95% CI, 95% confidence interval; aPTT, activated partial thromboplastin time; BMI, body mass index; INR, international normalized ratio; RR, relative risk.
[a]300 injections, 150 patients.

Extent of Bruising

Although there was much variability in the size of the bruise observed, no statistical difference emerged between treatments A and B, a finding demonstrated in previous work.[16] Nevertheless, the extension was, in general, smaller than that documented by Balci Akpinar and Celebioglu[8] and larger than that documented by Chenicek.[16] Unfortunately, Chan[5] and Zaybak and Khorshid[10] evaluated the bruise surface (in mm^2), whereas in our study, bruise diameter was evaluated. Variability, as emerged within the study findings, might be explained by different factors. First, there were different concepts of what constituted bruising extension. Balci Akpinar and Celebioglu[8] documented an average diameter extension including bruises at

minimum diameter (0 mm). Chenicek[16] considered also bruises bigger than 1 mm, whereas Chan[5] and Zaybak and Khorshid[10] evaluated the bruise surface (in mm^2). In our study, we excluded those bruises with a diameter smaller than 2 mm. Heterogeneity in the method of bruise extension evaluation (surface or diameter) and in the concept of bruise itself (at least 2 mm or including also those <1 mm or with 0 mm/0 mm^2) reduces the comparability of the available results. Another explanation of the difference observed in our study from those documented previously[8,16] may be the high rate of overweight and/or obese patients (44%) included.

Factors Affecting the Occurrence of Bruising

Multivariate analysis confirmed the association between the 10-second injection and occurrence of bruising. In contrast with previous studies,[7,9,10,23] but in line with others,[34,43] age and female gender were not associated with bruising. Burke and Walsh[48] reported that bruising is more common in women older than 60 years because the level of estrogen in the blood and capillary resistance are reduced. The reduction in estrogen levels can cause changes in the skin, including a reduction in collagen and elasticity, promoting increased capillary fragility. Such tissue changes may affect the rate of drug absorption and make the skin susceptible to bleeding and bruising after minor trauma caused by the injection of heparin. There is a need to note that previous studies (ie, Zaybak and Khorshid[10]) found that male participants had larger bruising size, but the method adopted in the bruising measurement, as aforementioned, was different than ours. Moreover, previous authors have performed a univariate analysis, whereas our results are supported by a multivariate analysis that takes in account the effects of all variables included in the model.[40]

Surprisingly, given previous evidence,[7,9,23,49] obesity seemed to be a protective factor against bruising in the adjusted analysis. Most of these studies did not report the total daily dose of heparin administered to the patients nor the patients' body weight. It is noteworthy that enoxaparin is a hydrophilic molecule that is distributed in plasma and lean tissue and predominantly eliminated renally. It has been recently demonstrated that dose individualization of enoxaparin in overweight/obese patients according to the lean and not to total body weight may significantly reduce the prevalence of bleeding and bruising events.[47] The lower incidence observed in our study in overweight/obese patients may be related to lower drug exposure after the conventional standard dosage. It is also possible that the discoloration of the skin that was assumed to indicate bruising[5] is less accurate in overweight/obese patients because it is difficult to detect.

Implications for Practice

Some patients receive LMWH injections for a lengthy time after hospital discharge.[2] With daily doses, administered for weeks, the risk of bruising is high. Any solution that reduces the risk of bruising is important for both patients and nurses. Although the results and those of previous studies favor performing the injection over more than 30 seconds, which can thus be considered best practice, there is a need to reflect on its feasibility. Administering a solution of 0.4 mL over more than 30 seconds is difficult. It requires accuracy, a steady hand, the absence of tremor, conditions of maximum cooperation from the patient, a calm ward environment, and the ability to administer an infinitesimally small amount of liquid per second. Whereas this could be difficult for nurses in some conditions (ie, when assisting confused patients, when managing staff interruptions), it could be even more difficult for patients and their caregivers.

The patients in our study were elderly (mean age, 78 years). Administering LMWH slowly could be very difficult in such patients because of the essential tremors that develop with aging, which may also lead to accidental removal of the needle from the skin. For this reason, it will be essential to measure the feasibility of the 30-second LMWH injection both at hospital and at home. More research on the effects of intermediate injection duration (ie, 20 seconds) is also needed. In fact, only 1 study available[8] introduced another variable in the evaluation of injection duration, showing the effectiveness of a dosing duration of 10 seconds followed by a 10-second delay before removing the needle. Moreover, even injecting and waiting require ideal conditions that are not always possible in the ward or at home. Adopting new technologies such as those developed for patients with diabetes with motor limitations[50] to maximize the accuracy of movements made during the injection and the ability to slowly inject small doses could make a further contribution to patients receiving LMWH treatments.

Strengths and Weaknesses

Although the sample size was larger than that of other studies that have addressed the same research objective,[5,8,10,16] it would be appropriate to examine these issues in even larger groups of patients with different health problems. Further limitations of this study include the lack of random sampling (only 1 Italian region was involved on the basis of its proximity to the researchers) and having included only 2 orthopedic units located in the same teaching hospital. In addition, given the high level of standardization of the injection procedure adopted and performed

What's New and Important

- Performing low-molecular-weight heparin (LMWH) subcutaneous injection for 10 seconds increases the occurrence but not the extent of bruising.
- In daily practice, LMWH subcutaneous injection should be administered for 30 seconds.
- Because slow injection requires accuracy, a steady hand, the absence of tremor, a calm environment, and the ability to administer an infinitesimally small amount of liquid per second, there is a need to measure its feasibility.

by expert nurses, the results should be generalized with caution because in daily practice, nurses perform subcutaneous injections with different levels of expertise and different compliance toward standard procedures. In addition, the injections were done according to the medical prescription of 4000 IU/0.40 mL every 24 hours, which expresses the best treatment for the patients involved[38] and whose results might be reliably generalized for similar quantities of international units and timing of administration.

However, this study has many strengths. Patients being treated with oral anticoagulants or antiplatelet drugs such as aspirin and warfarin were excluded because of possible interference with blood clotting. In addition, participants had not been subjected to heparin administration in the days preceding the study, the order of the treatment (A or B) was randomly selected, and patients' abdominal skin integrity was evaluated before inclusion in the study. Furthermore, only orthopedic patients were included because they have received little attention in the literature[10,16] even though they receive extended deep vein thrombosis prophylaxis after hospital discharge.[2] In the process of study development, we tried to address the limitations of previous studies by analyzing the effects of demographic and clinical variables (eg, gender, patient coagulation profile, obesity, and diabetes, which determine microangiopathy and capillary frailty), which have not generally been considered previously. To develop a more consistent approach, a blinded approach and 2 different analyses were performed, the first including all patients and injections and the second excluding those patients who developed bruises after both treatments. This might have reduced the bias and confounding factor effects, respectively.

Conclusions

This study provides a contribution to the prevention of bruising associated with subcutaneous administration of heparin. Reducing discomfort, anxiety, concerns, rejection of treatment, and the lack of confidence in the nurse because of the presence of bruising on the skin is an aim of the nurse. Based on our results, slowly performing (at least 30 seconds) subcutaneous administration of LMWH reduces the occurrence of bruising compared with injections given within 10 seconds. Evaluation of the feasibility of slow injections is, however, necessary to verify whether nurses and patients can really use this procedure in daily practice. Meanwhile, other research models that compare 20-second with 30-second injection duration and that include the combined assessment of multiple variables (eg, ice + injection duration) for developing new interventions preventing bruising related to LMWH are strongly recommended.

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