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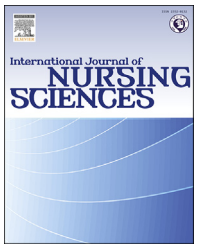

Original Article

The effect of subcutaneous injection duration on patients receiving low-molecular-weight heparin: Evidence from a systematic review

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ABSTRACT

To assess the effect of the injection duration of subcutaneous low-molecular-weight heparin (LMWH) on pain and bruising in patients. Randomized controlled trials and quasi-experimental studies were searched for in four electronic databases. The pooled effect size was expressed as relative risk (RR) and mean difference (MD) with 95% confidence intervals (CI) for dichotomous and continuous data. Cochrane Q and p value were used to assess heterogeneity and the I^2 statistic was adopted to quantify the level. Finally, eight studies involving a total of 532 participants met our inclusion criteria. The slow (30 second) injection was associated with a reduction in pain intensity and duration, and lower bruising occurrence at 48–72 hours and 48 hours post injection. The bruising area was also smaller at 48 hours and 60 hours post injection. No differences were identified between the slow and fast (10 second) injection in bruising area and bruising occurrence at 24 hours and 60 hours post injection. With present evidences, slow injection of LMWH is beneficial to the patient's well being, but further studies to identify the feasibility and standardization of the technique is recommended.

1. Introduction

Pharmaceutical administration is an extremely important component of daily nursing service and extensively applied in emergency and rehabilitation settings. Some medicines, especially those administrated via subcutaneous (SC), intradermal or intramuscular, put extra responsibilities on nurses to explore safe and standard injection techniques to minimize unnecessary pain and potential complications [1,2].

Abbreviations: SC, subcutaneous; LWMH, low-molecular-weight-heparin; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analysis; JBI-MASTARI, Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument; RR, relative risk; MD, mean difference; RCTs, randomized controlled trials.

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As a type of heparin, low molecular weight heparin (LMWH) is only administered subcutaneously [3]. LMWH is frequently prescribed for preventing or treating venous thromboembolism because of its high bio-availability and predictable anticoagulant effect [4,5]. However, just like any other drugs, the use of LMWH does not come without possible adverse reactions. SC heparin preparations often cause adverse effects (AEs) such as bruising, pain, induration and hematoma at the injection site [6,7]. In this regard, previous study has indicated that these local complications increased the patients physical and psychological discomfort and thus resulted in patients' distrust in nurses' efficiency [8,9]. In addition, the bruising can also restrict the possible area for future SC injection and reduce the opportunities for site rotation [10,11].

Literature related to the SC heparin injection have explored the potential factors which might minimize those side reactions and considered that the selection of syringe size and injection site, the application of ice and aspiration, and the injection duration can impact the occurrence of bruising and pain [12–15]. Among them, injection duration is an important influence factor. The researchers recommended giving SC LMWH injections over a 10-s duration [11,12], but which injection duration technique is ideal is far from clear.

Several Studies [16,17] previously have investigated the effects of injection duration on adverse outcomes at the injection site associated with SC administration of LMWH. Although exhaustive association trials have been undertaken to settle this issue, it hasn't yet been obtained a definitive conclusion, and those results haven't been recur. To provide more information for nursing practice, this systematic review examines existing knowledge to objectively assess the influence of two different injection techniques (10-s versus 30-s) on pain and bruising at the injection site in hospitalized patients who require LMWH therapy.

2. Material and methods

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement [18] and Cochrane Handbook for Systematic Reviews of Interventions were adopted to guide the systematic review and meta-analysis [19]. All pooled analyses were grounded on previously published literature, and thus no ethical approval and patient informed consent were required.

2.1. Inclusion and exclusion criteria

We pre-specified the inclusion criteria for our study according to the PICOS format (which describes the participants, intervention, comparison, outcomes and study design). The details of this criterion were as following: (1) **P**: participants were considered meet the inclusion criteria if they were (a) 18 years or older; (b) administered LMWH therapy subcutaneously in hospital. (2) ***I*** and **C**: Two techniques of 30-s SC administration of LMWH in the one site of the abdomen as the intervention and 10-s SC administration of LMWH in the other site of the abdomen as the control were performed. (3) **O**: the pain intensity, the incidence of bruising and the size of bruising at the injection site were listed to be as primary outcome of measures and bruising dimensions and the site-pain duration were viewed as secondary outcomes. (4) **S**: Randomized controlled trials (RCTs) and quasi-experimental methodology would be appraised and included in the review.

It was ineligible for the study if the patients were currently on any other anticoagulant therapy. Study without a comparison group were excluded. Language of publication was imposed into English or Chinese through August, 2015.

2.2. Search strategies

We searched PubMed, EMBASE, the Cochrane Library, and the China National Knowledge Infrastructure (CNKI) to collect potential relevant randomized controlled trials (RCTs) and quasi-experimental studies through August, 2015. The search strategies utilized are shown in Appendix A. Next, the reference lists of included articles were manually searched to include any eligible studies.

2.3. Data abstraction

Two investigators (L-JY and TS) independently extracted the following basic information and essential continuous and binary data for expected outcome of interest from each included study using the predesigned data extraction form (Table 1): study ID which included first author and publication year, country, number of participants, demographics of subjects (age and gender), intervention, reported outcome of interest. The author would be contacted to acquire the complete data when necessary. If researchers provided inconsistent data for same outcome, we would obtain the most rational one. Any divergences between authors concerning the eligibility of a study were resolved by consulting a third author until a consensus was obtained (XT).

2.4. Quality appraisal

Risk of bias was assessed for RCTs using the Cochrane Risk of Bias Assessment tool (19) and for quasi-experimental study using the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MASTARI) (see Appendix B) independently by two investigators (ZZ and LM). Disagreement was resolved by consulting a third investigator (G-MS). The Cochrane Risk of Bias Assessment tool addresses six specific domains as follows: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other issues. The risk of each included study was rated as 'low bias risk', 'unclear bias risk' or 'high bias risk' in accordance with the adequate degree of information extracted. The JBI-MASTARI tool based upon a quantity of critical questions fastened on the aspects of study design that research has shown to affect significantly the validity, for example, randomization, allocation, blinding and reporting. Each study was thus evaluated for quality utilizing the below checklist.