Femoral nerve blocks for the treatment of acute prehospital pain: a systematic review with meta-analysis

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Author contributions

All the authors designed the study. LR and VM performed the literature search, screened the studies and performed the quality assessment. GV performed the statistical analysis and generated the plots. All the authors participated in the preparation of the manuscript.

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Conflicts of interests

Authors do not have conflicts of interests.

Abstract

Background: Pain management is one of the most important interventions in the emergency medical services. The femoral nerve block (FNB) is, amongst other things, indicated for pre- and post-operative pain management for patients with femoral fractures but its role in the prehospital setting has not been determined. The aim of this review was to assess the effect and safety of the FNB in comparison to other forms of analgesia (or no treatment) for managing acute lower extremity pain in adult patients in the prehospital setting.

Methods: A systematic review (PROSPERO registration (CRD42018114399)) was conducted. The Cochrane and GRADE methods were used to assess outcomes. Two authors independently reviewed each study for eligibility, extracted the data and performed risk of bias assessments.

Results: Four studies with a total of 252 patients were included. Two RCTs (114 patients) showed that FNB may reduce pain more effectively than metamizole (mean difference 32 mm on a 100 mm VAS (95% CI 24 to 40)). One RCT (48 patients) compared the FNB with lidocaine and magnesium sulphate to FNB with lidocaine alone and was only included here for information regarding adverse effects. One case series included 90 patients. Few adverse events were reported in the included studies. The certainty of evidence was very low. We found no studies comparing FNB to inhaled analgesics, opioids or ketamine.

Conclusions: Evidence regarding the effectiveness and adverse effects of prehospital FNB is limited. Studies comparing prehospital FNB to inhaled analgesics, opioids or ketamine are lacking.

Introduction

Pain is common in the prehospital setting but is often undertreated,[1-3] much of which can probably be attributed to the negative respiratory, haemodynamic and emetic side effects of opioids. Adequate pain management not only improves patient comfort but also allows emergency medical service (EMS) providers to perform necessary treatment such as fracture reduction and evacuation from the scene.[4] Peripheral nerve blocks are an alternative to systemic analgesics for managing pain from extremity injuries. They are considered safe for the management of trauma patients, with minimal effects on breathing and circulation.[5] Potential complications are rare but include the masking of compartment syndrome, vascular puncture, haematoma, nerve damage and infection.[6] Several studies have shown that the femoral nerve block (FNB) is a useful technique in the emergency department (ED).[4,7,8] FNB has been reported to be superior to fentanyl alone for patients with femoral fracture when used in the pre-operative setting.[9] A recently published systematic review on fascia iliaca compartment blocks (FICB) concluded that this technique is suitable for prehospital management of pain from femoral fractures. Only minor side effects were reported and FICB can be administered by providers with varying backgrounds.[10] The FNB may be a more familiar technique than FICB for most anaesthesiologists, but to our knowledge no systematic review has been published on the use of FNB in the prehospital setting. A recently published systematic review (SR) focused on the effect of FNB the pre-operative setting included only one pre-hospital study. [11]
The aim of our systematic literature review was to assess the effect and safety profile of the FNB compared to systemic analgesia (or no treatment) in the management of prehospital patients with acute lower extremity pain.

Methods

We conducted this systematic review according to international standards[12] (PROSPERO registration (CRD42018114399)). The current review was performed as part of a comprehensive series of literature reviews of studies on prehospital analgesia, these are intended to lay the foundation for an updated guideline on pre-hospital pain management by the Scandinavian Society of Anaesthesia and Intensive care medicine (SSAI).

Inclusion criteria

Inclusion was made according to the PICO-criteria stated below:

Population	Adult patients (≥ 18 years) with acute pain in the prehospital setting
Intervention	Femoral nerve block
Comparison	Other analgesics or no analgesics
Main outcomes	Pain reduction, serious adverse events (as defined in the studies)
Other outcomes	Success rates (as defined in the studies), time on scene, relevant adverse effects such as nausea/vomiting, unintended sedation, hypoventilation, hypotension and others that have been reported

We included adult patients with acute lower-extremity pain after trauma managed in the prehospital setting. We also sought to identify patients in whom a FNB might be of particular benefit or harm. The following study designs were considered eligible for inclusion: Systematic reviews (SR), randomized controlled trials (RCT)s, cohort studies with a control group, interrupted time series, and controlled before and after-studies. Case series were also included for information pertaining to safety.

Exclusion criteria

Children under the age of 18 were excluded. We excluded studies performed in-hospital. Conference abstracts, posters and publications without results available in full text were also excluded.

We deviated from the protocol by including safety information from one study that also included some patients below the age of 18 years (19% aged under 18). We also deviated

from the protocol by including success rates (as defined in the studies) and time on scene as other outcome measures.

Search strategy

The authors in collaboration with experienced research librarians developed a search strategy based on the inclusion criteria. The following databases were searched from inception: PubMed, EMBASE, Cochrane Library and Epistemonikos.

The most recent update of the search was conducted in September 2019, and the full search strategy is presented in Appendix 1. The search was limited by language to include only: Danish, English, Norwegian, and Swedish.

Study selection

LR and VM independently assessed all titles and abstracts identified from the search according to the inclusion criteria above. References considered potentially relevant were collected and assessed independently in full text by these two assessors using the same inclusion criteria. If agreement was not reached, a third author was consulted. Study selection based on title and abstract, full text assessment, and risk of bias assessments were conducted using Covidence (Covidence systematic review software, Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org).

Assessment of risk of bias

LR and VM independently assessed risk of bias for included RCTs.[12] The following items were assessed (RCTs): i) sequence generation; ii) concealment of allocation; iii) blinding of participants and personnel; iv) blinding of outcome assessor; v) incomplete outcome data; vi) selective outcome reporting; vii) other risk of bias. All items were rated either as high, unclear or low risk of bias. The case-series were assessed using the check list proposed by Mural and co-workers 2018.[14]

Data extraction and analysis

LR and VM independently extracted data from each included study including; full reference, study design and country in which the study was conducted; characteristics of the

population (number of patients; age; gender; cause of pain; setting and context); type and dose of analgesics given; cadre/competency of the health care personnel; comparison/control intervention; attrition; outcomes and follow up times.

Dichotomous outcomes are presented as risk ratio (RR) with 95% confidence interval (CI). Continuous outcomes are presented as mean difference between the groups (MD) with 95% CI. We used Review Manager 5.3 (RevMan, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) to generate forest plots. We used intention-to-treat analysis. We used the random effects model, and evaluated statistical heterogeneity using the Q test and I^2 statistics.

We have, on request from the editors, deviated from the protocol to conduct a post-hoc trial sequential analysis (TSA, http://www.ctu.dk/tsa/) on the main outcome: change in pain score from place of accident to hospital.

Grading the confidence in the evidence

We assessed our confidence in the evidence for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.[12] This is presented as “high”, “moderate”, “low” or “very low”.

The evidence across each outcome was assessed by eight criteria, five that could lower our confidence in the evidence: i) risk of bias/ methodological limitations; ii) consistency between studies (statistical heterogeneity); iii) directness (similar study participants, intervention, comparator and outcome measures in the included studies for the population, interventions and measures we are considering); iv) precision of results; v) reporting bias. Three criteria were assessed to consider upgrading of evidence from observational studies that had not been downgraded: vi) strong or very strong association between intervention and outcome; vii) large or very large dose response; viii) situations where all plausible confounders would have reduced the effect. For questions of effect of interventions, RCTs start at high- and observational studies start at low confidence.

Ethical considerations

This being a systematic literature review, we did not need approval from The Committee for Research Ethics.

Definition

Toxic effects of the local-anaesthetic medication, anaphylaxis and disturbances in vital functions were defined as systemic side effects. Further, because of the risk of nerve damage and systemic side effects with each nerve block performed, an unsuccessful FNB was also labelled as an adverse event.

The PRISMA checklist was used. (Appendix 2)

Results

A total of 806 studies were identified by the search, of which sixty were considered to be potentially relevant based on title and abstract and were assessed in full text. Two RCTs were included for the analysis of effect. [15,16] One case series and one RCT where all patients received FNB were included for information regarding safety (Figure 1).[17,18] We also identified an RCT performed by Büttner and co-workers, comparing various ultrasound-guided nerve blocks to systemic analgesia in patients with isolated extremity injury that required reduction, splinting or technical rescue.[4] This study included only four FNBs and had a different focus and was therefore excluded.

Characteristics of the trials

In at least three of the four included studies, the FNB was performed by physicians. [15-17] In the remaining study[18], the authors did not specify the profession of the health care provider performing the FNB. Both RCTs included for the analysis of effect were conducted in Austria[16,16], while the prospective case series[17] was conducted in France and the remaining RCT in Tunisia.[18]

The two Austrian RCTs included 62 patients with trauma in the femoral region[15] and 52 patients with trauma around the knee.[16]

The case series included 90 patients with suspected femoral shaft fracture. Of these, 73 patients had been involved in road traffic accidents, eleven in industrial accidents and six had sustained injuries from falls.[17] Since the majority of the patients (81%) were adults we deviated from the protocol and included this study to avoid missing information regarding safety. The Tunisian study on diaphyseal femoral fracture with 48 patients compared the FNB with and without magnesium sulphate (Mg) as adjuvant. [18]

In both the Austrian RCTs, a nerve stimulator was used and the local anaesthetic was L-bupivacaine.[15,16] In the French case series, the FNB was performed using lidocaine hydrochloride without nerve stimulator or ultrasound.[17] In the Tunisian study, lidocaine was

used either with or without magnesium sulphate and no nerve stimulator or ultrasound was used.[18]

The included studies are briefly presented in Table 1. The excluded studies are listed in Appendix 3 with reasons for exclusion.

Risk of bias assessment

Our risk of bias assessment for these studies was based on information in the publications. The risk of bias was largely determined by the lack of certainty regarding blinding of participants, personnel and outcome assessor (Figure 2). One of our main outcomes was change in pain score (in addition to serious adverse events), a subjective measure that may be influenced by lack of blinding. This factor seriously reduces our confidence in the results presented in these studies, which is reflected by downgrading the level of evidence (see GRADE evaluation, table 2). Tables 3 and 4 summarize our judgements for the risk of bias assessments.

Comparisons

The following comparison was included:

- FNB versus metamizole

Two RCTs compared the use of femoral nerve block versus intravenously administrated metamizole.[15,16]

Femoral nerve block versus metamizole

The RCTs compared FNB with L-bupivacain to 1 g metamizole: 1) in femoral trauma and 2) in knee trauma.[15,16] In both studies the trauma had occurred indoors. Pain and anxiety scores were measured using a 100-mm Visual Analogue Scales (VAS) at the site of accident, during transport and on arrival to hospital. We compared scores on arrival at hospital. The patients were moved to a vacuum mattress after the treatment. Heart rate, oxygen saturation and blood pressure were recorded before therapy at the site of the accident, during transport and upon arrival at hospital. FNB provided a larger reduction in pain and anxiety than metamizole in knee trauma. In the FNB group, pain and anxiety were reduced by half from that measured on-scene and the heart rate was significantly reduced. In the metamizole group, pain and anxiety were not significantly reduced. However, the results for the metamizole group were neither presented in the publication, nor did the authors respond to our request for this information. [16] Because of this, our analysis of change in pain score and anxiety from the scene to hospital are derived only from the 62 patients in the study of FNB in femoral trauma.[14] There was significantly greater reduction in pain score (mean

difference 32 mm on the 100 mm VAS scale (95% CI 24 to 40)) with FNB than after treatment with metamizole. Because there is only one study, there is no TSA monitoring boundaries (Appendix 4). From this study with 62 participants, TSA calculated an information size of 12. Anxiety was also reduced in FNB group (mean difference 43mm on 100 mm scale (95% CI 34 to 52)) compared with metamizole.

All studies reported on adverse events.[15-17] In the two Austrian RCTs, no adverse events were observed during the procedure or follow-up. Barriot and co-workers reported two patients (out of 90) who experienced femoral artery puncture during the FNB. This patient population included 17 children, but the age of the patients who experienced femoral artery puncture was not noted in the publication.[17] No side effects were reported in the Tunisian study with 48 patients who received FNB.[18]

Three of the 31 patients who received a FNB for femoral injury and two of the 26 patients who received FNB for knee injury [15] did not benefit from the treatment (VAS level remained unchanged).[16] In the case series, treatment with FNB was unsuccessful in three of the 90 patients who received FNB, with little or no change in pain scores.[17]

Both RCTs addressing FNB *vs.* metamizole reported treatment time.[15,16] The following definition for treatment time was used: period from preparation of the medication or the set for the femoral nerve blockade until movement of the patient onto the vacuum mattress. [15] The meta-analysis shows that the mean time of administration of metamizole was 7.4 minutes (95% CI 6.2 to 8.6 minutes) faster than administration of the FNB (Figure 3).

Confidence in the outcomes for the comparisons involving FNB for the treatment of prehospital acute pain was assessed according to the GRADE principles.[13] Confidence was downgraded for high risk of bias due to lack of blinding in both RCTs, and downgraded for imprecision because of few studies with few participants. Table 2 presents a summary of findings for femoral nerve block versus metamizole.

Overall safety information about the use of FNB is derived from four studies. Of the 195 patients who received FNB, two patients experienced femoral artery puncture and eight patients did not achieve pain relief.

Discussion

In this systematic literature review we identified four studies on prehospital use of FNBs, three RCTs and one case series, with a total of 252 patients. [15-17] The number of patients is low and the results reported in one of the included studies are incomplete. In all of the studies, success rates were reported to be high. In three out of four studies, the FNBs were performed by physicians with training in regional anaesthesia, which may have contributed to the high success rates. One study did not report the level of training of the providers.

Both of the Austrian RCTs reported change in pain scores upon arrival at the hospital.[15,16] The effect of FNB was superior to metamizole, which is a non-opioid analgesic with anti-inflammatory effect but has limited availability worldwide[19]. It remains unclear how FNB performs compared to opioids, ketamine or inhaled analgesics, which are the treatments normally used for extremity trauma in most EMS systems. Our findings are consistent with the results of a recently published SR that reported that FNB reduced pain in the pre-operative setting but the quantity and certainty of the evidence was low.[11] One of the Austrian studies was included in both the pre-operative SR and our pre-hospital SR, although our review included only pre-hospital pain management.

No systemic or neurological adverse events were reported in the included studies. In general, using ultrasound may reduce the number of adverse events such as arterial puncture and using nerve stimulator may prevent nerve damage.[20-22] The effect of adding additional procedural equipment to on-scene time is unknown.

The use of FNB prolonged the time spent on scene compared to IV administration of metamizole.[15,16] However, if the patient has an isolated femoral fracture and stable vital signs and life-threatening injuries are not suspected based on clinical examination, the clinical implications of prolonged scene time may be minimal. Peripheral nerve blocks such as FNB may reduce the need for other types of analgesia later in the clinical course as reported by Büttner and coworkers[4]. Peripheral nerve blocks have also been shown to reduce the risk of pneumonia after hip fracture and to facilitate early mobilization after hip surgery.[23]

None of the included studies reported a case of compartment syndrome, which is a rare but devastating complication of certain extremity injuries. Concerns have been raised regarding the risk of peripheral nerve blocks preventing or delaying the recognition of compartment syndrome. However, the role of pain in the diagnosis of compartment syndrome is controversial. Clinical suspicion, regular assessment and compartment pressure measurement are important for the patients at risk.[24] If the patient has received opioids before FNB, the possibility for respiratory depression should be kept in mind.[25] Because of these challenges with nerve blocks, we suggest that eventual implementation in EMS systems should be done in close cooperation with ED physicians, orthopaedics and other relevant professions involved in pain management in the receiving hospital.

Studies from other settings

Although the studies on FNB are few and small, there is more data on FICB in the prehospital setting as outlined in a recent review.[26] The target in FICB is more lateral to the neurovascular bundle than in FNB and performing the block does not require special equipment, which may contribute to its popularity in the prehospital setting. The efficacy of the FICB and FNB have been reported to be similar in post-operative patients.[27, 28] FNB may nevertheless be more suitable for femoral shaft fractures since it does not require as large a dose of local anaesthetics.

Peripheral nerve blocks such as the FNB have also been suggested and used as a treatment option in war casualty medevacs and other austere circumstances where evacuation time is long.[29-31] However, no studies in these settings qualified for this SR.

Strengths and limitations of this review

A strength of this review is the systematic and transparent approach used to collect the evidence for prehospital pain management by FNB and the exclusion of studies performed under different conditions. Although we conducted a wide literature search, we cannot rule out the possibility that there may be other studies that we did not identify. Furthermore, there may be new studies published after the last update of the literature search. Another limitation of this systematic review is the language restriction that only includes studies published in Danish, English, Norwegian or Swedish. We are aware of one case series

published in French with 44 patients who all received FNB, no complications were reported.[32]

Limitations of the evidence

The main limitation of this review is the small number of included studies and patients. Administering nerve blocks in the prehospital setting presents unique challenges compared with performing the same procedure in-hospital. Also, extrication and transportation expose patients to greater forces and motion, with greater risk of pain, compared with that which would be expected in-hospital. This makes studying FNB in the prehospital setting relevant, but very few studies on FNB have been conducted in this setting and therefore the number of studies included in this review is low.

In both RCTs blinding of participants, personnel and outcome assessors was limited (no placebo injection). Furthermore, each outcome was only measured in relatively few patients.

A further limitation of the included RTCs is the lack of applicability to the Nordic countries (and most western EMS systems), due to use of metamizole as a comparator. Studies comparing prehospital FNB to ketamine, opioids and inhaled analgesics would be more relevant but none were identified in our search. Furthermore, much larger sample sizes are called for to document the safety of prehospital FNB, but studies of such a calibre are unlikely to ever be performed in this setting.

Finally, the few studies included have not all fully reported their datasets.

Conclusions

There is limited evidence available regarding the effect and safety of femoral nerve block in the prehospital setting. The efficacy of FNB compared with other relevant options for treating prehospital pain is currently unknown.

Further studies are required to determine the feasibility of FNB administration by EMS providers with varying levels of training; to assess the effect of FNB compared to opioids,

ketamine and inhaled analgesics; and to determine the risk of adverse effects of FNB in the prehospital setting.

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