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RESEARCH ARTICLE

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Pain relief after major ankle and hindfoot surgery with repetitive peripheral nerve blocks: A feasibility study

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Abstract

Background: Major ankle and hindfoot surgery (e.g., ankle, triple and subtalar arthrodesis) typically causes severe postoperative pain, especially the first two postoperative days. Current modalities of postoperative analgesic treatment often include continuous peripheral nerve blocks of the saphenous and sciatic nerves via catheters in order to extend the duration of pain- and opioid-free nerve blockade to 48 h. Unfortunately, the 48 h-efficacy of continuous infusion via a catheter is reduced by a high displacement rate. We hypothesised that one-time repetition of the single injection peripheral nerve blocks would provide effective analgesia with a low opioid consumption the first 48 postoperative hours.

Methods: Eleven subjects preoperatively received a popliteal sciatic and a saphenous single injection nerve block with a protracted local anaesthetic mixture. Surgery was performed under general anaesthesia. The one-time repetition of the single injection nerve block was carried out approximately 24 h after the primary nerve block. The main outcomes were pain and cumulative opioid consumption during the first 48 postoperative hours.

Results: Nine of the 11 (82%) patients had effective analgesia without opioids during the first 48 postoperative hours. Two patients each required a single dose of 7.5 mg of oral morphine equivalents after 43 h.

Conclusion: One-time repetition of single injection saphenous and sciatic nerve blocks consistently provided effective analgesia practically without opioids for 48 h after major elective ankle and hindfoot surgery.

KEYWORDS
major elective ankle and hindfoot surgery, pain, repetitive peripheral nerve block

Editorial Comment

To relieve the severe pain following major ankle surgery, continuous catheter-based nerve blocks of the saphenous and sciatic nerves are regarded as the best option. However, these

catheters often displace. This study investigated the one-time repetition of these nerve blocks in 11 study participants and found it to be feasible and to provide effective pain relief.

1 | INTRODUCTION

Major ankle and hindfoot surgery (e.g., ankle, triple and subtalar arthrodesis) causes severe postoperative pain for several days, underlining the importance of optimising postoperative pain relief in order to allow rapid rehabilitation and thus reduced risk of comorbidity.[1–3] Current modalities of postoperative analgesic treatment include peripheral nerve blocks (PNB)—either as single injection or continuous peripheral nerve blocks (cPNB) combined with paracetamol, NSAIDs and opioids.[3–5] Opioids are a major component of conventional post-surgical multimodal strategies, which may have negative perioperative consequences due to the numerous adverse effects such as sedation, respiratory impairment, postoperative nausea and vomiting (PONV) and constipation.[4–7] This can impede early ambulation and prolong the length of stay.[5] In addition, opioids are relatively ineffective in alleviating postoperative pain compared to PNBs, especially during mobilisation.[8]

Patients typically undergo major elective ankle and hindfoot surgery in general anaesthesia (or spinal anaesthesia). Continuous infusion via a popliteal sciatic nerve catheter is a widespread standard procedure to treat postoperative pain following this kind of surgery and, at some centres, supplemented by a saphenous nerve catheter.[4,8,9] The disadvantages of the catheter technique are the relatively high cost, extra time expenditure for the procedure, expert skill level needed and the high incidence of secondary displacement.[9–11]

In order to prolong the duration of the PNB, a possible alternative to cPNB would be to treat the postoperative pain with a one-time repetition of a single-injection PNB for a popliteal sciatic and a mid-thigh saphenous PNB. The primary single-injection PNB should be performed preoperatively on the awake patient with a protracted mixture of local anaesthetic. The single-injection PNBs should be repeated in the morning of the first postoperative day. Existing evidence indicates that the average duration of effective analgesia of a saphenous and a popliteal sciatic single-injection PNB after major ankle and hindfoot surgery is approximately 30 and 26 h, respectively, when using a bupivacaine-epinephrine-dexamethasone mixture.[12,13]

We hypothesise that one-time repetition of single-injection mid-thigh saphenous and popliteal sciatic PNBs can provide effective analgesia (Numeric Rating Scale [NRS] score ≤3) without opioids during the first 48 postoperative hours.

2 | METHODS

This study was a non-randomised and unblinded clinical feasibility trial. All subjects underwent major ankle and hindfoot surgery under general anaesthesia and received repetitive PNBs with a protracted mixture of local anaesthetic.

2.1 | Ethics

The study was approved by the Danish Medicines Agency (EudraCT nr. 2020–000294-24), the Central Denmark Region Committee on Biomedical Research Ethics (Project-ID S-20200090) and the Danish Data Protection Agency and was monitored by the Good Clinical Practice (GCP) Unit at Odense University Hospital. Written informed consent was obtained from all subjects. The study complied with the Helsinki II declaration.

2.2 | Subjects

Subjects were recruited at Lillebaelt Hospital, Kolding, Denmark, from February 2021 to October 2021. Eligibility criteria for the study included patients over 18 years of age with an American Society of Anesthesiologists (ASA) score of 1–3 who were scheduled for ankle arthrodesis, subtalar arthrodesis or triple arthrodesis in general anaesthesia. The exclusion criteria were inability to cooperate, being a non-Danish speaker, allergy to any drugs used in the study, daily intake of glucocorticosteroids, diabetes mellitus (requiring medical treatment), preoperatively reduced sensation in the areas innervated by the common peroneal nerve, tibial nerve and saphenous nerve, intake of opioids (dosing more than once daily) and pregnancy.

2.3 | Preoperative femoral triangle and popliteal sciatic nerve blockade

In all subjects, an intravenous (IV) line was placed and standard monitoring including pulse oximetry, electrocardiography and non-invasive blood pressure measurement was initiated.

A local anaesthetic mixture was prepared. The mixing ratio was 19 mL bupivacaine-epinephrine (Marcain adrenalin 5 mg/mL + 5 mcg/ml, Aspen Pharma, Dublin, Irland) added preservative-free dexamethasone 1 mL = 4 mg (Dexavital 4 mg/mL, Vital Pharma Nordic, Hellerup, Denmark). In total 20 + 10 mL of this mixture was used.

Popliteal sciatic PNB: The ultrasound (US) probe was placed transversely in the popliteal fossa. The bifurcation of the sciatic nerve in its two main branches (common peroneal nerve and tibial nerve) was identified using a 15-6 MHz linear US probe (SonoSite, X-Porte, Bothell, Washington, USA). The needle (22 G 80 mm, Pajunk, Geisingen, Germany) was inserted in-plane and 20 mL of the local anaesthetic mixture (see above) was injected targeting the common peroneal nerve and the tibial nerve under continuous US visualisation of correct perineural spread of the local anaesthetic mixture deep to the paraneural sheath.

Distal femoral triangle PNB: The US probe was placed transversely at the mid-thigh level. The intersection of the medial borders of the sartorius and adductor longus muscles was identified ultrasonographically. This ultrasonographic landmark is a consistent proxy marker of the apex of the femoral triangle and the proximal end of the adductor canal (i.e., the proximal border of the vastoadductor membrane).[14] The transducer was slid 2–3 cm proximal and the hyperechoic saphenous nerve visualised anterolateral to the femoral artery. The needle was introduced in-plane from the lateral end of the transducer and during the injection of 10 mL of the local anaesthetic mixture (see above) the correct perineural spread was continuously monitored by US.

The primary single injection popliteal sciatic and femoral triangle PNBs were carried out 60 minutes prior to surgery. The one-time repetition of the single injection popliteal sciatic and femoral triangle PNBs were carried out during the morning of the first postoperative day (approximately 24 h after the primary PNBs).

All PNBs were performed by two experts in regional anaesthesia (KEH and RWH).

2.4 | Anaesthesia and postoperative pain management

General anaesthesia was induced and maintained with propofol (Fresenius Kabi, Bad Homburg, Germany) and remifentanil (B. Braun, Melsungen, Germany) according to the standard local protocol of the hospital. After surgery, oral paracetamol 1000 mg (GlaxoSmithKline, Broendby, Denmark) was administered four times daily. No NSAIDs were administered perioperatively due to the preference of the surgeons. Glucocorticosteroids were not administered perioperatively. Ondansetron 4 mg IV (Hameln Pharma Plus GmbH, Hameln, Germany) was administered 30 minutes prior to emergence from anaesthesia.

Opioids were not administered intraoperatively. On arrival at the post anaesthesia care unit (PACU), the patients were instructed to request the PACU nurses for morphine IV (Amgros I/S, København, Denmark) for relief of pain present in the ankle or hindfoot in case the NRS score was above 3 (0–10).

2.5 | Surgery

Surgery was performed by three consultant orthopaedic surgeons specialised in ankle and hindfoot surgery. A thigh tourniquet was employed for all surgeries.

2.6 | Outcome measures

The main outcomes were pain NRS scores 0, 6, 12, 24 and 48 h postoperatively and the cumulative morphine equivalent oral consumption during the first 48 postoperative hours. Time zero was defined as the time of patient arrival at the PACU.

Other outcomes were: (1) Length (hours) of time interval of effective regional analgesia (defined as no need for opioids and NRS score ≤3/10) during the 48 h follow-up; (2) PONV scores (no, mild, moderate, severe) at 0, 6, 12, 18, 24 and 48 postoperative hours; (3) incidences of vomiting at 0–48 postoperative hours; (4) ondansetron administration at 0–48 postoperative hours; and (5) Cumulative morphine equivalent oral consumption during postoperative days 3–7.

2.7 | Assessment of outcomes

Before and after performing the PNBs, the anaesthesia of each target nerve (saphenous nerve, peroneal nerve and tibial nerve) was assessed by testing the sensation on a 3-point-scale (2, normal sensation, 1, diminished sensation and 0, no sensation) compared with the contralateral side in each of the relevant cutaneous areas of innervation. The sciatic nerve branches were tested on the dorsal side proximal to the second toe (superficial peroneal nerve), on the first web space (deep peroneal nerve) and on the plantar side proximal to the second toe (tibial nerve). The saphenous was tested proximal to the medial malleolus. Study eligibility required a baseline score of 2 (normal sensation) in all four territories of innervation. Thirty minutes after PNB completion re-testing was carried out in each of the four territories of innervation. A score of zero on the re-test indicated successful PNB placement, whereas scores 1 or 2 warranted a rescue PNB and renewed testing after additional 30 minutes.

The pain NRS score (0, no pain and 10, worst pain imaginable) was reported by the patient at 0, 6, 12, 18, 24 and 48 h postoperatively.

2.8 | Data capture

The data for the consumption of opioids was captured from the electronic patient record. Patients recorded NRS scores directly on the PCA pump (Rythmic Evolution infusion pump, Micrel Medical Devices S.A., Athens, Greece) during the first 48 postoperative hours. The patients used the PCA pump only for electronic NRS score capturing, therefore no infusion was connected. The patient recorded the median NRS score on the third postoperative day and opioid usage in the first week after discharge from the hospital on a questionnaire. These data were captured in Redcap by the investigator at the time of the telephone call 1 week after discharge.

PACU nurses collected data concerning PONV scores as well as incidences of vomiting and ondansetron usage.

2.9 | Sample size estimation

We estimated that 16 patients undergoing major elective ankle and hindfoot surgery (ankle arthrodesis, triple arthrodesis, subtalar arthrodesis) would be sufficient to satisfy the aim of the feasibility

TABLE 1 Patient characteristics ($n = 11$).

Age (y)	61 (13)
Sex (F/M)	8/3
BMI (kg/m^2)	26.6 (25.5–29.8)
ASA (I/ II/III)	1/10/0
Type of surgery (ankle−/subtalar−/triplearthrodesis)	5/4/2

Note: Values are presented as mean (SD), median [IQR] or count as appropriate.
Abbreviations: ASA, American Society of Anesthesiologists Classification; BMI, body mass index; F, female; M, male; y, year.

study, which was to produce observational evidence that one-time repetition of a single injection PNB would provide effective analgesia (NRS score ≤3/10) with minimum need of opioids (median zero and IQR 0–0) during the first 48 postoperative hours with a success rate approximating 100%.

2.10 | Statistical analysis

Only descriptive statistics were employed in this single-arm clinical study. The results are presented as mean (SD), median [IQR] or count as appropriate.

3 | RESULTS

Eleven patients were enrolled per protocol. Demographics are shown in Table 1.

Sixteen patients were scheduled to participate in the study per protocol. The early termination of the study was due to external circumstances unrelated to the study (both principal investigators became employed in a different hospital).

The median [IQR] pain NRS score was zero [0–0] for postoperative hours 0, 6, 12, 18, 24 and 48 (Table 2). Two patients had pain NRS-scores of three and five, respectively, at 48 postoperative hours (Table 3).

Nine of the 11 enrolled patients (82%) did not require opioids during the first 48 postoperative hours (Table 4). Two patients each required a single dose of 7.5 mg of oral morphine equivalents. During the following five postoperative days (postoperative days 3–7) 6 out of 11 patients required zero opioids. The median consumption of oral opioids during postoperative days 3–7 was zero [0–75] (Table 4). Six of 11 patients (55%) did not require any opioids during the first seven postoperative days (Table 4).

The median time to first opioid intake in the subgroup of five patients who required any opioid during the entire follow-up period was 54.3 h [43.4–68.1]. The individual values of the length in hours of the time interval of effective regional analgesia during the 48 h follow-up period are listed in Table 5.

No PONV, episodes of vomiting or ondansetron requirements occurred during the entire follow-up period (0–7 postoperative days) for any of the 11 patients (Table 2).

No serious adverse events were observed.

4 | DISCUSSION

The study shows that one-time repetition of saphenous and popliteal sciatic PNB effectively controls pain with minimum consumption of opioids for 2 days after major ankle and hindfoot surgery with a high success rate.

Postoperative pain after major elective ankle and hindfoot surgery (ankle arthrodesis, subtalar arthrodesis, triple arthrodesis) is often severe for several days—especially the first two postoperative days.[1,3,4,6] Daily mean in-hospital opioid consumption has been reported at ranges of approximately 10–30 mg oral morphine-equivalent doses[15] (with much higher doses in intermittent or long-term preoperative opioid users), despite multimodal analgesic regimes including single-dose PNB or cPNB.[6,9,16] Either single-dose PNB or cPNB is conventionally recommended as a component of multimodal analgesia in order to alleviate postoperative pain after major ankle and hindfoot surgery.[4] Both include a femoral triangle PNB, which anaesthetises the anteromedial aspects of the ankle including the ankle joint capsule,[12,17] and a popliteal sciatic PNB, which anaesthetises the entire lower leg, ankle and foot, except the area innervated by the saphenous nerve.[4,17] A femoral triangle PNB is relatively motor-sparing compared to a femoral PNB.[9,18]

The problem with single-dose saphenous and popliteal sciatic PNB is that even protracted local anaesthetic mixtures only prolong the duration of PNB to approximately 24 h on average.[4,12,13] This is too short to alleviate severe pain after major ankle and hindfoot surgery, as the duration of severe pain is typically 48 h.

One-time repetition of single injection PNB with a protracted local anaesthetic mixture is an effective, feasible and cost-effective way of providing long-lasting reliable pain relief. Bupivacaine is the longest-acting local anaesthetic amongst the commonly used and widely available long-lasting local anaesthetics and is thus chosen to provide the longest possible duration of analgesia with single-shot PNB. The conventional maximum analgesia time after PNBs can be increased by approximately 1 h with perineural adrenaline and an additional 8 h with perineural dexamethasone.[19] Perineural dexamethasone as an adjuvant to bupivacaine effectively prolongs the duration of analgesia and the time to the first opioid beyond 24 h, which has been shown previously in major elective ankle and hindfoot surgery.[4,13] Perineural administration of dexamethasone prolongs the duration of analgesia compared to IV administration by approximately 4 h.[20] Although the optimal perineural dosage of dexamethasone is unknown, 2–10 mg have been shown to be effective.[11] We opted for a relatively small dose of 4 mg based on existing published evidence.[11] Perineural dexamethasone is an off-label medication.[19] It has been associated with increased postoperative blood glucose concentrations,[19] although no delayed wound healing, increased rate

TABLE 2 Pain NRS score, PONV score, number of vomiting, ondansetron consumption during the first 48 postoperative hours.

	0 h	6 h	12 h	18 h	24 h	48 h
Pain NRS score	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]
PONV (no/slight/moderate/severe)	11/0/0/0	11/0/0/0	11/0/0/0	11/0/0/0	11/0/0/0	11/0/0/0
Vomiting (n)	0	0	0	0	0	0
Ondansetron (mg)	0	0	0	0	0	0

Note: Pain NRS scores (0–10) are presented as median [IQR]. Values for PONV and episodes of vomiting are presented as count.
Abbreviations: IQR, interquartile range; NRS, numeric rating scale; PONV, postoperative nausea and vomiting.

TABLE 3 Individual pain NRS scores.

Patient	0 h	6 h	12 h	18 h	24 h	48 h
1	0	0	0	0	0	0
2	0	0	0	0	0	3
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0
7	0	0	0	0	0	0
8	0	0	0	0	0	0
9	0	0	0	0	0	0
10	0	0	0	0	0	0
11	0	0	1	1	1	5

TABLE 4 Individual postoperative oral morphine equivalent doses (mg).

Patient	0–48 h	POD 3–7
1	0	0
2	0	0
3	0	0
4	0	127.5
5	7.5	22.5
6	0	0
7	0	0
8	0	0
9	0	97.5
10	7.5	30
11	0	75
Median [IQR]	0 [0–0]	0 [0–75]

Abbreviations: IQR, interquartile range; POD, Postoperative day.

TABLE 5 Length (h) of time interval of effective regional analgesia (defined as no need of opioids and NRS ≤3/10) during the follow-up period (0–48 h).

Patient	Number of effective regional analgesia (0–48 h)
1	48
2	48
3	48
4	48
5	43.2
6	48
7	48
8	48
9	48
10	43.6
11	48
Total, Median [IQR]	48 [43–48]

Abbreviation: IQR, interquartile range.

of infections[19,21,22] or increased occurrence of neurological complications have yet to be reported in human trials.[19,23] Vigilance is advisable since the one-time repetition of a single injection PNB in the present study is performed in a patient with partially anaesthetized target nerves.

Other potential adjuvants prolong analgesia for a shorter time compared to dexamethasone and are more rarely used.[19]

The main problem with cPNB is the high frequency of displacement of the inserted catheters.[11–13] Hauritz et al performed a literature search comprising 2711 catheters and calculated an overall failure rate of 21% during the first 24 postoperative hours.[11] This is a critical clinical problem, especially considering that the duration of a single injection PNB is approximately 24 h with a failure rate close to zero. In a clinical trial, the displacement of catheters was assessed by MRI control: The displacement rate of sciatic cPNB was 10% after 48 postsurgical hours when the catheter was inserted parallel to the nerve (out-of-plane) compared to 40% when the catheter was inserted perpendicular (in-plane) to the target nerve.[10] Catheters carry a higher risk of infection, a higher risk for Local Anaesthetic Systemic Toxicity (LAST) and a higher risk for local anaesthetic-induced myotoxicity.[11,24–26] Risk factors for myotoxicity include higher concentrations of local anaesthetic and adjuvants and duration of exposure of the target nerve to local anaesthetic.[26] Local anaesthetic in itself is neurotoxic, and in animal studies, injury has been shown to depend on the exposure time and concentration of local anaesthetic and the lowest possible concentration is advisable.[27]

Liposomal bupivacaine (Exparel®, Pacira BioSciences Inc., Parsippany-Troy Hills, USA) is a sustained-release drug delivery

system. Theoretically, it provides a continuous analgesic effect up to 48–72 postoperative hours after a single injection.[28] Emerging evidence unfortunately does not support additional benefits compared to conventional non-liposomal bupivacaine for perineural injection.[28–30]

Focus on optimal postoperative pain management may also be paramount for the reduction of chronic postsurgical pain since clinical studies have shown a strong association between acute and chronic postsurgical pain.[4,16,31] The incidence of chronic postsurgical pain is 10%–50% and may be much higher in specific populations of patients—for example, post-amputation.[31] One year following major elective ankle and hindfoot surgery, moderate to severe pain may be as high as 21% at rest and 43% while walking.[4,16,32] It remains to be clarified whether the observed association between severe acute and chronic pain is due to non-causal confounding or causation.

The validity of the present study was limited by the lack of a control group, randomisation and blinding. The primary purpose, however, was generating observational outcome data for the initial assessment of the method of one-time repetition of single-injection nerve blocks and qualifying the design of a future randomised controlled double-blinded trial. The early termination of the study is a limitation and theoretically might have influenced the final results. The results, however, are unambiguous and consistent in the 11 enrolled patients with a high success rate for effective analgesia and minimum opioid consumption during the first 48 postsurgical hours. We, therefore, believe that it would be very unlikely that the additional enrollment of five patients (in order to reach 16 enrolled patients as planned per protocol) would have changed the results significantly.

In conclusion, this feasibility study indicates that the one-time repetition of single injection saphenous and popliteal sciatic PNBs provided effective pain relief with minimum consumption of opioids during the first 48 postsurgical hours after major ankle and hindfoot surgery. Conclusive evidence would require further studies.

AUTHOR CONTRIBUTIONS

KEH involved in performing the procedures, drafting and revising the article. RWH involved in performing the procedures and revising the article. SB, HIJ, CWH and CJ involved in revising the article. TFB involved in drafting and revising the article.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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