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REVIEW

Systematic Review and Meta-analysis of the Efficacy of Perineural Local Anaesthetic Catheters after Major Lower Limb Amputation

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WHAT THIS PAPER ADDS

Perineural catheters, placed alongside the transected sciatic nerve (for transfermoral amputations) or tibial nerve (for transtibial amputations), have been used to provide targeted local anaesthetic during the postoperative period. Various studies have suggested this may reduce postoperative pain, opioid use, and long-term phantom limb pain. This systematic review and meta-analysis demonstrated that postoperative opioid consumption is approximately halved, without affecting immediate postoperative pain, mortality, long-term phantom limb or stump pain. However, the quality of included papers is generally low, and further research is required to confirm these findings.

Objective: The aim of this systematic review and meta-analysis was to evaluate the effects of using an intraoperatively placed perineural catheter (PNC) with a postoperative local anaesthetic infusion on immediate and long-term outcomes after lower limb amputation.

Methods: A systematic review of key electronic journal databases was undertaken from inception to January 2015. Studies comparing PNC use with either a control, or no PNC, were included. Meta-analysis was performed for postoperative opioid use, pain scores, mortality, and long-term incidence of stump and phantom limb pain. Sensitivity analysis was performed for opioid use. Quality of evidence was assessed using the GRADE system.

Results: Seven studies reporting on 416 patients undergoing lower limb amputation with PNC usage ($n = 199$) or not ($n = 217$) were included. Approximately 60% were transtibial amputations PNC use reduced postoperative opioid consumption (standardised mean difference: −0.59, 95% CI −1.10 to −0.07, $p = .03$), maintained on sensitivity analysis for large ($p = .03$) and high-quality ($p = .003$) studies, but was marginally lost ($p = .06$) on studies enrolling patients with peripheral arterial disease only. PNC treatment did not affect postoperative pain scores ($p = .48$), in-hospital mortality ($p = .77$), phantom limb pain ($p = .28$) or stump pain ($p = .37$). GRADE quality of evidence for all outcomes was very low.

Conclusion: There is poor-quality evidence that PNC usage significantly reduces opioid consumption following lower limb amputation, without affecting other short- or long-term outcomes. Well-performed randomised studies are required.

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INTRODUCTION

Major lower limb amputation remains one of the highest mortality procedures performed in the UK.[1] Any intervention to reduce morbidity or mortality is therefore high on the agenda for vascular surgeons.[2] Improving the management of postoperative pain in such a high-risk population would potentially reduce morbidity associated with the stress response to surgery, and minimise opioid use.[2,3]

Immediate postoperative pain management commonly involves epidural or intravenous patient controlled analgesia

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(PCA), which are both reliant on opioid-based agents. The pharmacokinetics of opioids are altered with increasing age, deteriorating renal function, and polypharmacy;[4] attributes commonly encountered in patients with peripheral arterial disease (PAD). This potentially leads to adverse drug effects and interactions. Opioid use is associated with the development of postoperative side effects such as nausea, vomiting, respiratory depression, drowsiness, and delirium, of which the latter is known to contribute to increased rates of mortality, reduced functional ability, and longer lengths of hospital stay.[5]

Phantom limb pain occurs in up to 83% of patients,[6,7] and is known to impair quality of life, impede rehabilitation,[8,9] delay psychosocial adjustment,[10] and reduce the chance of return to employment.[11] Factors thought to increase postoperative phantom limb pain include acute postoperative pain,[12] pre-amputation pain,[12] noxious intraoperative inputs and female sex.[13–15] Although many pharmacological agents are available for treatment of phantom limb pain, their efficacy is variable,[16] and better or alternative postoperative analgesia may prevent hyperplastic peripheral changes and central neural sensitisation.[17,18]

The American Society of Anesthesiologists recommends using multimodal analgesic strategies for managing postoperative pain.[3] This includes the use of opioid-sparing agents (such as nonsteroidal anti-inflammatory drugs, or acetaminophen), anticonvulsants, and other adjuncts to reduce pain. One such adjunct is the use of a perineural catheter (PNC), inserted at the time of surgery to provide a continuous infusion of local anaesthetic for up to 7 days postoperatively. First described for amputees by Malwer et al. in 1991,[19] the PNC is inserted adjacent to either the sciatic nerve for above-knee amputations (AKAs) or the tibial nerve for below-knee amputations (BKAs), and has been used as a method of reducing both immediate postoperative and stump/phantom limb pain. However, data are conflicting as to its efficacy for both short- and long-term outcomes, and utilisation of this treatment modality varies.

The aim of this systematic review and meta-analysis was to evaluate the effect of PNCs on immediate postoperative opioid use and pain, postoperative mortality, and long-term phantom limb and stump pain in patients undergoing lower limb amputation.

METHODS

Data sources, search strategy, and selection criteria

The Cochrane collaboration specified protocol[20] was utilised for this systematic review, which is reported as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for the conduct of meta-analyses of interventional studies.[21] The following sources were searched without date restrictions: PubMed, Embase via OVID, the Cochrane Library Database, and the Current Controlled Trials register. The search strategy, including MeSH terms utilised, was drafted and refined by two authors (DCB and CT, online supplement 1). An extensive search was also conducted of articles to be included in the analysis using the "Related Articles" function in PubMed, and reference lists checked for other papers suitable for inclusion. In addition, the *European Journal of Vascular and Endovascular Surgery*, *British Journal of Surgery*, and *Journal of Vascular Surgery* websites were searched individually. There was no search restriction based on language. The last search date was January 14, 2015. Outcomes were captured when given in two or more included papers. When papers were suitable for inclusion, but presented non-abstractable data for included outcomes, the corresponding authors were contacted for further data.

Randomised controlled trials (RCTs), cohort studies, and case series detailing adult patients undergoing major (hindquarter, transfemoral, through-knee, or transtibial) lower limb amputation were suitable for inclusion. All included papers utilised a cohort of patients with an intraoperative placement of a PNC for a postoperative infusion of a local anaesthetic (intervention group), compared with either a placebo control (i.e. containing normal saline), or alternative anaesthetic regimen without a PNC (control group). Studies detailing nerve catheters placed distant to the site of the operation (i.e. transgluteal sciatic nerve catheters placed under ultrasound guidance), and those giving a single intraoperative perineural injection of local anaesthetic without a PNC, were excluded.

Data extraction, outcome measures, and assessment of study quality

A data abstraction proforma was designed by one author (DCB) and piloted before refinement from all data abstractors (DCB, JCDG, CT). Data abstraction (DCB and JCDG) and assessment of methodological quality (DCB, AS) was performed independently by two authors with reference to the senior author (CT) on matters of disagreement. Extracted demographic and baseline data included: first author, year of study, study type (RCT, cohort, or quasi-experimental) and design (including whether retrospective or prospective, single or multiple centres, and if consecutive patients were enrolled), number of patients, primary anaesthetic given to both intervention and control groups, local anaesthetic used in the treatment group, and study quality as assessed using the Downs and Black score.[22] This checklist is used to score both RCTs and observational studies for scientific rigor, and thus permits quality comparisons between these study types. It scores studies on five methodological criteria: reporting (10 questions, 11 points), external validity (3 questions, 3 points), bias (7 questions, 7 points), confounding (6 questions, 8 points) and power (2 questions, 5 points), with a maximum score of 34.

The outcome measures collected were:

1. Postoperative opioid consumption;
2. Postoperative pain;
3. Postoperative mortality;
4. Phantom limb pain (pain experienced where the limb used to exist) incidence at follow-up; and
5. Stump pain (pain localised to the residual portion of the limb) incidence at follow-up