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TITLE:

The Role of Regional Anesthesia in Treatment of Chronic Phantom Limb Pain

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Chronic pain accounts for 11-40% of people in the United States and is a major contributor to healthcare costs.1 It is a precursor to narcotic abuse/dependence, depression, and suicide.[1] Phantom limb pain (PLP) and chronic stump pain (CSP) are specific chronic pain forms affecting limb amputation patients. There are nearly 200,000 amputations performed in the United States annually.[2] Of those patients, 95% report amputation-related pain, with 79.9% reporting PLP and 67.7% reporting CSP.[3] Anesthesia providers play an integral role in minimizing acute surgical pain and the development of a chronic pain condition. Regional anesthesia (RA) is a common component of pain management and enhanced recovery protocols.[4]

The etiology and pathophysiology of PLP/CSP are not well understood but are believed to be multifactorial (Figure 1). Peripheral and central components are involved in the development and persistence of these specific chronic pain conditions. Trauma to peripheral nerves causes hyper-excitability of the local nerves and leads to the formation of painful neuromas. Central sensitization in the spinal cord is due to increased nociceptive signals coupled with a reduced function of the descending inhibitory pathway. Cortical reorganization in the brain results when neighboring regions take over the area of the somatosensory and motor cortex of the amputated region. PLP, as well as any chronic pain condition, is associated with a psychological component and can be triggered by stress, depression, and anxiety.[3]

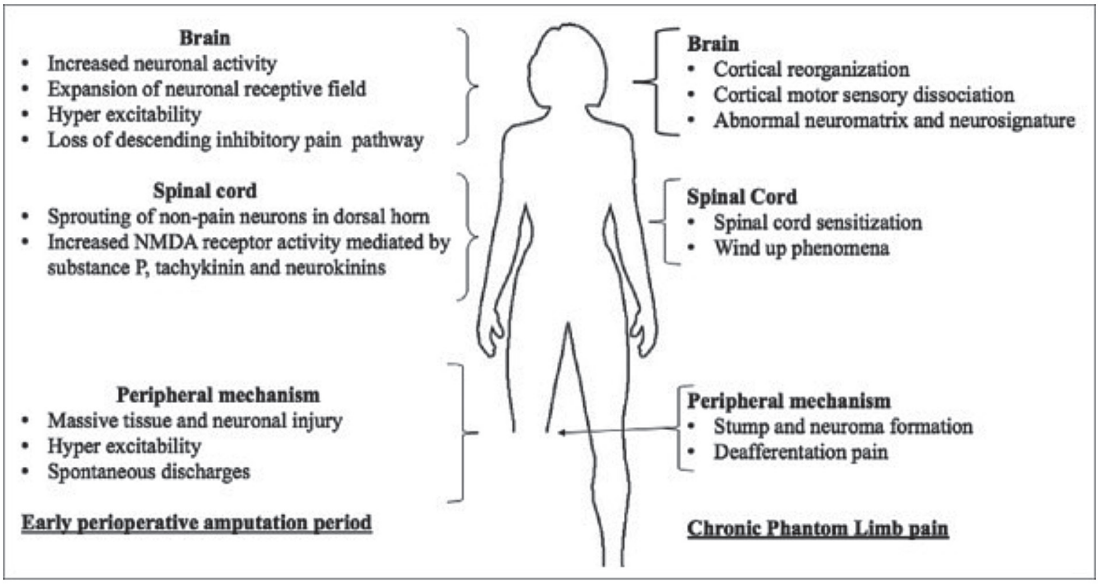

Figure 1. Pathophysiology and mechanism of initial and established phantom limb pain.[5]

One contributing factor to chronic pain after surgery is the effectiveness of perioperative pain management. This review aims to evaluate the role of RA in developing and treating chronic pain in post-amputation patients.[6] Two systematic reviews have

evaluated RA using perineural catheters within the last decade, with the second building on the first.[7,8] However, the primary focus of the prior reviews was to evaluate the immediate postoperative effects of RA, with the long-term effects being a secondary outcome measure. This review has modified the inclusion criteria from previous reviews to focus on the long-term effects of RA on post-amputation pain and will focus on evaluating RA's impact on the transition of acute surgical pain to chronic postoperative pain in limb amputation and its role in treating existing PLP and CSP.

This review aims to identify available evidence and evaluate the current literature findings to determine the effects of regional anesthesia in the perioperative period on the development and treatment of PLP. The PICO question guiding the framework of this review was: In patients with acute limb amputation and established PLP (P), does regional anesthesia (I) reduce the development or improve the treatment of phantom limb pain (O)?

Methodology

A search was performed using PubMed, CINHAL, Google Scholar, and Cochrane Library databases. The articles were appraised for level and quality of evidence utilizing the Johns Hopkins Evidence-Based Practice for Nurses and Healthcare Professionals Appraisal Tool.9 The literature was restricted to articles in English, and the language limitation could have excluded articles with important information on different techniques to reduce PLP. The search was limited to publications within the last ten years; using a more comprehensive time range could have given more information, but we wanted to ensure the information was current.

Results

Eleven articles met inclusion criteria; two systematic reviews with meta -analysis7,8, three randomized controlled trials[11–13] two narrative reviews[5,14], one quasi-experimental evaluation[15], one pilot study[16], one retrospective cohort study[17], and one retrospective observational study[18]. Four studies examined regional anesthesia (RA) to treat phantom limb pain (PLP).[11–13,16]Seven studied the effects of perioperative anesthesia techniques, including neuraxial, regional, and general anesthesia, on PLP. [5,7,8,14,15,17,18] This review included 10,220 patients; 6,561 received RA. Of the subjects that received RA, 3,507 had epidurals, and 3,054 had peripheral nerve blocks (PNB).

Various anesthesia techniques were examined in the studies, comparing anesthesia techniques and effects on PLP. Evaluation of the long-term impact of perioperative RA on the development of PLP or chronic stump pain (CSP) ranged from 6 months to 4.4 years.[5,8,14,17,18] Additionally, three studies examined regional anesthesia's effects 24-72 hours postoperatively on PLP, including postoperative pain scores, opioid requirements, and the development of PLP.[7,8,15]

RA as a treatment for existing PLP was reported in 160 subjects in this review, with 84 receiving RA.[11–13,16] The effectiveness of continuous peripheral nerve catheters in place for six days on treating PLP was examined in two studies.[12,16] Two additional studies examined a single injection PNB effect on PLP immediately after block placement and up to four weeks after treatment. Of these two, one studied the impact of 2% Lidocaine 30 minutes after the peripheral nerve block was administered, and the other studied the effects of a single shot injection at 4-6 weeks post-injection.[11,13]

Five authors reported the effects of RA on pain score and opioid usage 24 to 72 hours postoperatively with contrasting results. According to three studies, including one systematic review, decreased pain scores and decreased opioid requirements were reported in the first 72 hours postoperatively[8,14,15]; however, other researchers found no difference in pain scores or opioid consumption with RA in the 24-72 hours postoperative period. [5,7]

The effects of RA on the development of PLP or CSP were examined at times ranging from 6 months to 4.4 years after amputation.[5,7,8,14,17,18] Several studies, including two systematic reviews and a retrospective study, showed low to no evidence supporting using RA or single catheters to prevent PLP or CSP.[7,8,14,18] Others demonstrated a decrease in PLP and CSP at six months to a year.[5,17] The clinical narrative review reported patients who received epidurals 48 hours before surgery had decreased PLP at six months.[5] A separate study found that PNBs decreased PLP at one-year post-surgery. [16] A single PNB demonstrated no change in the development of PLP or CSP; however, patients with two simultaneous peripheral nerve catheters (PNC) were less likely to develop PLP. Benedetti et al,[18] found that patients with concurrent catheters perioperatively, such as femoral/sciatic or epidural/sciatic, were six times less likely to develop PLP than patients with one or no catheter. According to one retrospective study of 7,613 subjects, the incidence of PLP at 90 days and 1 year after peripheral nerve block, neuraxial, or general

anesthetic techniques was lowest with peripheral nerve blocks (1,781 subjects) followed by neuraxial (2,840 subjects) and general anesthesia (2,992 subjects).[17]

RA for the treatment of PLP and CSP was studied both as a single injection and as long-term PNCs from 6-30 days from the time of injection. McCormick et. al[13] found decreased PLP three months after administering a single injection PNB. A six-day catheter decreased PLP at one month, with median pain scores decreasing from 5.0 to 3.0 in the treatment group. At 12 months, the average pain scores remained reduced by a median of 2.0 for the treatment group and 0.0 for the control group.[12,16] Borghi et. al[14] reported a case study using a thirty-day continuous PNB that resulted in a patient with no recurrence of PLP at 6, 12, 24, and 36-month follow-ups.

Perioperative peripheral nerve catheter placement has mixed results for the prevention of PLP. Three reviews found inconclusive results or no appreciable effect on PLP and CSP with perioperative nerve catheter placement, mainly used short-term.[5,7,8] Others demonstrated effectiveness in reducing PLP with various techniques.[5,7,14,16,17] Successful strategies included long-term or prolonged catheter use of greater than 30 days, simultaneous use of two catheters at different locations, such as femoral and sciatic catheters for lower limb amputations, and utilization of continuous nerve catheters as a critical component of an ERAS protocol.[5,7,14,17] Peripheral nerve blocks reduced the incidence of PLP over general or neuraxial anesthesia.[17]

Various peripheral nerve blocks are also used to treat established chronic PLP and CSP following limb amputation surgery. Reducing established PLP and CSP after amputation surgery was effective with peripheral nerve catheters lasting six days, sympathetic plexus blocks, and peripheral nerve injections.[8,11,12,15]

A research gap exists in using peripheral nerve blocks and catheters to prevent and treat PLP. Randomized control studies that evaluate the effectiveness of PNBs related to PLP are limited, and existing research had small sample sizes making generalizations challenging. One study incidentally noted a six-fold reduction in PLP with dual PNC placement[18]; however, no other studies examine this technique. It remains unclear which techniques are effective in preventing PLP or treating established PLP. Further research is needed to determine the role of single-shot injections versus single or dual peripheral nerve catheters in preventing and treating PLP and CSP.

An unintended outcome resulted from a single study. Most studies evaluated single peripheral nerve catheters; however, Benedetti et al.[18] assessed the effectiveness of two concurrent peripheral nerve catheters. Lower limb amputation patients with a combination of femoral and sciatic catheters were found to be six times less likely to develop PLP than patients with one or no catheter. A significant six-fold decrease in chronic PLP is substantial and warrants further research.

The evidence is promising for using peripheral nerve blocks and catheters as effective pain management techniques for PLP in limb amputation surgeries.[8,11–18] Other studies were inconclusive or showed no effect on PLP and CSP.5,7 Long-term indwelling catheter infusions of six days to greater than 30 days effectively prevented PLP by 36.8-66% and reduced PLP by 29-94% based on VAS scores.[12–16,18] Incidence of PLP was shown to be 2.8% with PNB versus 4.3% with neuraxial and 6.4% with general anesthesia.[17] Perioperative continuous peripheral nerve blocks should be considered before surgery for limb amputation to reduce the incidence of PLP development. Peripheral nerve catheters and single-shot peripheral nerve blocks should also be considered when treating chronic PLP.

Discussion

Reducing the incidence or the intensity of PLP and CSP after amputation is a challenge, and though the literature is promising, more work is needed. Of the eleven studies in this review, all but two show that the use of RA helps to reduce the development of PLP and CSP or provide a means of treatment for existing PLP and CSP.[5,7] Both of these studies showed decreased pain scores and opioid consumption in the immediate postoperative period. One study only looked at amputations due to vascular disease.[7] We know that the development of PLP and CSP has many factors involving both central and peripheral nerves and differs among the different types of amputation patients. Vascular patients may have pain in their limb for an extended period before amputation, making it harder to treat post-amputation PLP and CSP compared to a patient with a traumatic injury requiring amputation. The wide variety of PNB, as well as placement by anesthesia providers or surgeons, further contributed to the mixed results of the studies. Most of the studies lacked a consistent local anesthetic concentration, volume, and dosing regimen.

Further research needs to be conducted to develop protocols that optimize treatment for this patient population.

This review included nine studies that provided evidence that RA, particularly PNCs, could help reduce PLP and CSP development and treat existing PLP and CSP. Only one study looked at PLP beyond one year, while the others covered shorter time frames of one year or less.[18] Designing research with long-term endpoints would enhance the prevention and treatment of chronic amputation pain.

Conclusion

PLP and CSP are complex chronic pain conditions highly prevalent among amputation patients. RA with or without catheters can potentially decrease PLP and CSP, but more research is needed to determine their clinical effectiveness. Though the literature demonstrates a decrease in the incidence of PLP with RA over neuraxial or general anesthesia[18], there is no consensus on the most effective regional anesthetic technique or the time frame in which it should be employed. Larger randomized control trials are needed to evaluate which techniques are most effective. Further studies evaluating the double catheter technique should be evaluated as these demonstrated the most promising results in decreasing the development of PLP in retrospective studies.

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