The Role of Peripheral Nerve Stimulation in Perioperative Analgesia

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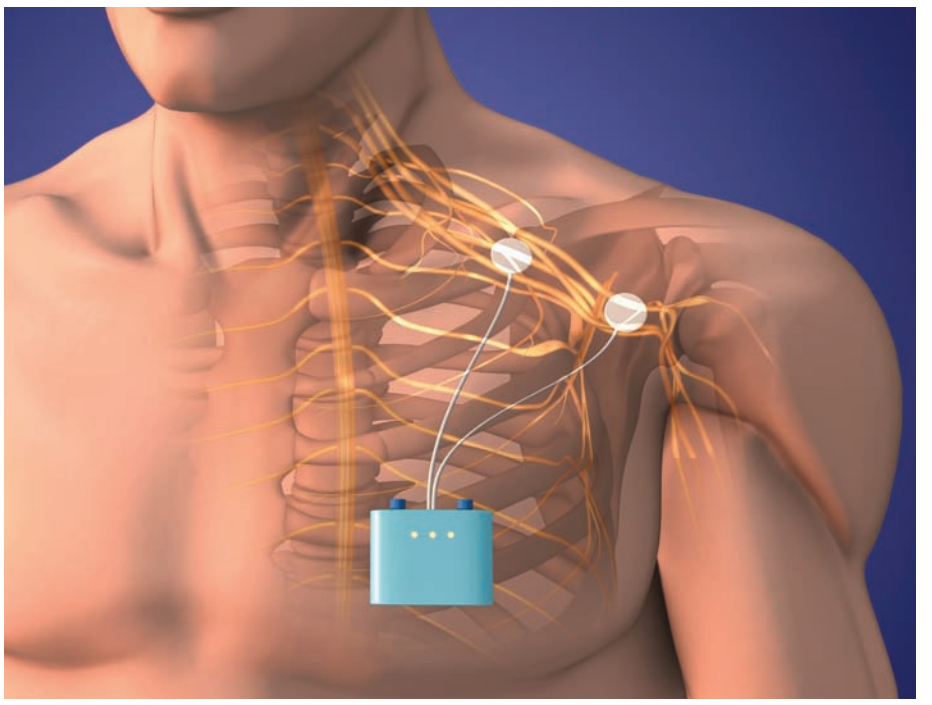
Peripheral nerve stimulation (PNS) is commonly used for chronic pain conditions involving specific nerve distributions or discrete regions of the trunk or limbs when symptoms are refractory to more conservative management (*Pain Physician* 2021;24:E131-E52). Common applications with level I and II evidence include chronic migraine, cluster headache, postamputation pain, chronic pelvic pain, chronic low back pain, and lower-extremity pain, with lower levels of evidence in peripheral neuropathic pain and postsurgical pain. Although efficacy and safety are well demonstrated for several chronic pain conditions, the use of PNS has not been well established in acute pain applications.

Peripheral nerve stimulation involves the delivery of electrical current via an external or internal pulse generator via a percutaneously implanted lead advanced through a needle adjacent to the target nerve. Temporary PNS systems using an external pulse generator (EPG) are cleared for use for up to 60 days, with newer systems capable of connecting two leads to a single EPG offering similar "trial" leads approved for use up to 30 days (*Anesthesiology* 2020;133:1127-49; *Pain Manag* 2022;12:795-04). The device cleared for up to 60 days has been analyzed in several pilot studies summarized here, and for the indication of analgesia delivers stimulation at a frequency of 100 Hz, with adjustable amplitude (0-30 mA) and pulse width (10-200 us) according to patient comfort and/or preference. It is thought to exert its affect by both central and peripheral mechanisms, with central inhibition of alpha-delta and C fibers to decrease pain signaling at the level of the cortex, and peripherally via the gate control theory with decreased nociceptive transmission (*Curr Pain Headache Rep* October 2023). Acutely, PNS may reduce expression of inflammatory proteins and activation of microglia with reduction of neuropathic hyperalgesia (*J Neuroinflammation* 2022;19:153).

Perioperative PNS has generated considerable interest, given that targets amenable to regional anesthetic blockade in the perioperative setting are often well-suited to feasible PNS lead placement (*Pain Manag* 2019;9:347-54). Several studies have explored such applications. A multicenter randomized controlled trial (RCT) investigated the use of PNS in foot/ankle surgery targeting the sciatic nerve, anterior cruciate ligament reconstruction targeting the femoral nerve, and rotator cuff repair targeting the brachial plexus (*Anesthesiology* 2021;135:95-10). A total of 32 subjects received 14 days of active electrical stimulation compared to sham control (n=34), with pain and opioid consumption significantly improved in the first seven days after surgery compared to sham (median opioid consumption 5 mg [0-30] versus 48 mg [25-90] oral morphine equivalents [ratio of geometric means 0.20, 97.5% CI 0.07 to 0.57, *P*<0.001]; mean average pain intensity according to the numeric rating scale 1.1 + 1.1 versus 3.1 + 1.7 [difference -1.8, 97.5% CI -2.6 to -0.9, *P*<0.001]). Notably, all patients received regional anesthetic blockade as well according to clinical standard of care. One



EPG stopped functioning during the treatment period and was replaced, one patient withdrew due to uncomfortable paresthesias, one subject developed erythema associated with the dressing, and two patients experienced lead fracture during removal (a fracture rate of 1/16, 6.25%). A single-center RCT randomized 16 Veterans 1:1 to receive 60 day PNS with standard therapy or standard therapy alone, with all subjects receiving an infusion of ropivacaine 0.2% at 10 ml/h through five-seven days post-surgery via peripheral catheter (*Pain Manag* 2022;12:357-69). Only participants who reported pain at least 4/10 in intensity were enrolled into the trial, with percutaneous PNS placed adjacent to the femoral and sciatic nerves for up to 60 days. The a priori responder rate of >50% pain relief compared to baseline was 100% in the treatment group and 50% in the control group at four weeks, which remained stable in the treatment group and increased to 86% in the control group at three months postoperatively. Only 20% of the subjects in the PNS group were using opioids at eight weeks, compared to 50% in the control group. Notably, the cohorts were very small, with only 5/8 subjects completing the 60 days of PNS treatment (one subject required revision surgery and withdrew, and two others withdrew due to unrelated medical issues). Notably, two subjects required lead-reimplantation due to accidental dislodgement of the lead. In terms of acute analgesia, PNS did not provide adequate pain relief in the immediate postoperative period in 16 subjects undergoing rotator cuff repair compared to anesthetic peripheral nerve blocks at the target of the brachial plexus, but it did seem to attenuate pain in the prolonged acute postoperative period (*Reg Anesth Pain Med* 2019;44:310-8). Again, among such a small cohort, the rate of device-related complications was significant, with two lead dislodgements and four lead fractures reported.

Temporary PNS in acute postoperative pain management has been touted as beneficial compared to peripheral nerve catheter placement due to its ability to provide analgesia without motor blockade, reduced bulk for patients because there is no medication bag for the anesthetic, and a significantly longer duration of treatment available (*Expert Rev Med Devices* 2021;18:145-50; *Anesthesiol Clin* 2022;40:469-79). However, the majority of the research has been conducted by a small cohort of authors, and there are significant numbers of reported device-related complications, including fractures during planned device removal. Cost is also a significant barrier to implementation, with the price of percutaneous PNS leads all but prohibitive for large-scale utilization outside of clinical trials.

Although PNS has been hailed as a promising tool in the arsenal of enhanced recovery after surgery, with the goal of improving pain and function and reducing opioid utilization, its benefit in terms of long-term outcomes for patients and cost effectiveness has not yet been demonstrated in acute pain and/or regional anesthesia applications. Additionally, the rate of device-related complications is significant, raising the question of the appropriateness of its utilization, particularly when employed for all patients in acute applications. PNS may be a highly useful and effective treatment in chronic pain applications, but with currently available technologies, its role in the perioperative setting probably remains limited to specific patient populations. Efforts to reduce the cost of such devices and study its effectiveness in larger populations are likely worthy of consideration. ■

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Editor's Note: This is the second of several articles that will share the perspective of ASRA Pain Medicine with the readership of the *ASA Monitor*.