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Percutaneous auricular nerve stimulation (neuromodulation) for the treatment of pain: A proof-of-concept case report using total joint arthroplasty as a surrogate for battlefield trauma

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BACKGROUND: There are few effective pain treatments following trauma on the battlefield other than opioids, which are limited by respiratory depression. Ultrasound-guided percutaneous peripheral nerve stimulation ("neuromodulation") has been proposed as an analgesic, but requires physician-level skills, advanced equipment, and an hour to administer. In contrast, percutaneous auricular neuromodulation may be placed by a medic in the field under nonsterile conditions in a few minutes, theoretically provides analgesia for any anatomic location, has no side effects, and no significant risks. It therefore offers the potential to be applied quickly on the battlefield without any of the limitations of opioids. We propose total joint replacement as a surrogate for battlefield trauma and here present a case report to demonstrate proof of concept.

METHODS: Following open total knee or hip arthroplasty under spinal anesthesia, two patients had an auricular neuromodulation device applied within the recovery room. Patients were discharged with the unit and contacted daily for 7 days.

RESULTS: The devices were each applied in under 3 minutes without difficulty, were well tolerated during use, and removed without complication at home on Day 5. During use, neither patient experienced pain while lying, sitting, or ambulating. Neither required analgesics other than scheduled celecoxib; and a single tablet (50 mg) of tramadol for one patient on postoperative Days 3 and 4 for pain while lowering herself to a seated position. On Days 6 and 7, both patients experienced an increase in pain, one of whom required around-the-clock tramadol.

CONCLUSION: Ambulatory postoperative percutaneous auricular neuromodulation is feasible. In these two cases, it appears to have markedly reduced pain scores and opioid requirements free of systemic side effects during the week following major orthopedic surgery. Considering the potential of this modality to treat trauma on the battlefield without systemic side effects, additional investigation appears warranted. (*J Trauma Acute Care Surg.* 2022;93: S165–S168. Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Therapeutic/care management; Level V.

KEY WORDS: Neuromodulation; percutaneous auricular nerve stimulation; percutaneous nerve stimulation; vagus nerve stimulation; battlefield trauma; case report.

There are few effective treatments for pain following trauma on the battlefield other than opioids. Unfortunately, the use of opioids is limited due to respiratory depression, which may result in aspiration or death. Peripheral nerve stimulation has been used to treat pain since the Ancient Greeks applied living torpedo fish—which produce up to 220 volts—directly to patients' bodies to treat various etiologies from labor pain to headaches.[1] Modern forms of peripheral nerve stimulation incorporate surgically implanted, percutaneously inserted, and transcutaneous leads/electrodes to treat primarily *chronic* pain. However, ultrasound-guided percutaneous peripheral nerve stimulation has been used to treat pain following total knee arthroplasty, with this procedure used as a surrogate for battlefield trauma.[2] Unfortunately, it requires application by physicians with advanced training in regional anesthesia, ultrasound devices, a sterile field due to the deep lead insertion, and approximately 1 hour to place two leads for lower extremity injuries.[3] It is, therefore, not viable to replace or supplement opioids as a temporizing measure from the battlefield to an advanced care facility.

In contrast, percutaneous *auricular* nerve stimulation is applied simply by pressing four electrodes into general areas *around the ear* and may be applied by a medic in the field under nonsterile conditions in a few minutes (Fig. 1). Auricular neuromodulation is theorized to function by stimulating various cranial and peripheral nerves that influence the limbic system, which is involved with many aspects of behavior including responses to stress.

A device that delivers low-frequency electric pulses is approved by the United States Food and Drug Administration for

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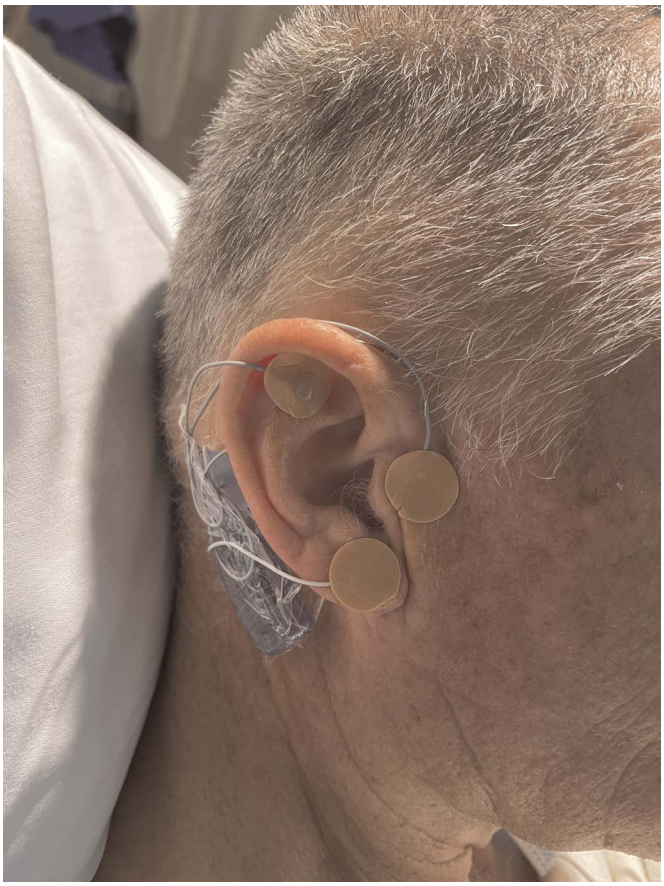

Figure 1. A percutaneous auricular nerve stimulation system (NSS-2 Bridge; Masimo, Irvine, CA) as seen administered to the right ear. The pulse generator is adhered directly to the patient behind the ear over the mastoid process. Leads are placed (1) at the most cephalad portion of the antihelix; (2) immediately cephaloanterior to the incisura and posterior to the superficial temporal arterial pulse; and (3) on the posterior ear opposite the antihelix at the level of the incisura. The ground electrode is inserted on the anterior side of the lobule. Used with permission from Brian M. Ilfeld, MD, MS.

use to reduce symptoms associated with opioid withdrawal for up to 5 days.[4–6] However, one prospective and two retrospective studies suggest that this form of neuromodulation also provides analgesia to hospitalized patients following abdominal and pelvic surgery.[7,8] The device itself is relatively simple to apply; has few contraindications, side effects, or associated adverse events; and has no potential for misuse, dependence, or diversion. This analgesic modality therefore offers the potential to be applied quickly on the battlefield immediately following trauma without any of the limitations of opioids. The stimulator uses an integrated 3-volt battery, has a load impedance range of 1 k to 10 k Ω with 3.2 volt maximum, and symmetrical, biphasic stimulation cycles occur at a frequency of 0.125 Hz with periodic rest. Each of the three electrodes and a ground has a 2-mm-long integrated needle(s) (Figs. 1 and 2) and is affixed with a small, round adhesive bandage.

It remains unknown whether percutaneous auricular nerve stimulation will provide analgesia following major orthopedic surgery, which itself can act as a surrogate for battlefield trauma; and if patients will accept the device outside of the hospital setting (including removal at home). We now report two off-label cases to[1] explore the possibility of treating pain following major joint arthroplasty with ambulatory percutaneous auricular neuromodulation,[2] help optimize a future study protocol, and[3] estimate the treatment effect in preparation for developing a subsequent controlled clinical trial.

PATIENTS AND METHODS

Two otherwise-healthy women with osteoarthritis undergoing open total hip (n = 1; age, 66 years) and knee (n = 1; age, 59 years) arthroplasty were offered, and consented for, postoperative administration of percutaneous auricular neuromodulation (Fig. 2, NSS-2 Bridge, Masimo, Irvine, CA). The university's institutional review board waives any review requirements for case reports or short series; but both patients provided both verbal and written consent to receive auricular neuromodulation for the off-label use of postoperative pain control and publish these deidentified case reports and nonidentifiable photos. When creating this case report, the (SDC CARE Checklist, http://links.lww.com/TA/C573) was utilized when creating this case report.

The patient having knee surgery received an ultrasound-guided single-injection adductor canal nerve block with ropivacaine 0.5% and epinephrine prior to surgery. Both patients underwent surgery with a single-injection bupivacaine spinal and sedation with intravenous propofol. Within the recovery room and in a semirecumbent position, each patient received intravenous fentanyl 25 μg, and the application locations were wiped with an alcohol pad and benzoin over the mastoid process for the pulse generator and at the four points of electrode placement (Fig. 1).

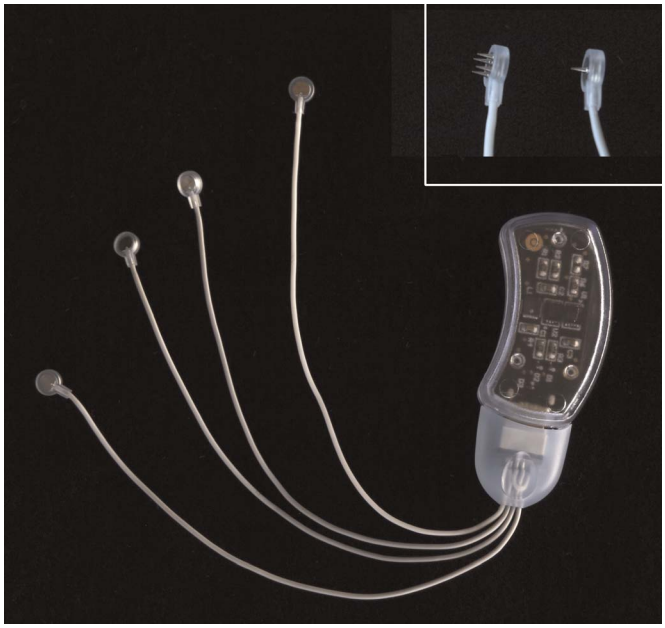

Figure 2. A percutaneous auricular nerve stimulation system (NSS-2 Bridge; Masimo, Irvine, CA). Each of the three electrodes has a 2-mm-long integrated needle/lead (inset) and the ground electrode has four 2-mm-long integrated needles/leads (inset). Used with permission from Brian M. Ilfeld, MD, MS.

The pulse generator was applied to the posterior aspect of the right ear with a double-sided adhesive pad which was further secured with a clear adhesive dressing. The first lead was placed at the most cephalad portion of the antihelix by simply pressing the electrode directly into the skin and affixed with an overlying dressing (Fig. 1). The second electrode was inserted immediately cephaloanterior to the incisura and posterior to the superficial temporal arterial pulse. The third electrode was inserted on the posterior ear opposite the antihelix at the level of the incisura. The ground electrode with four 2-mm-long integrated needles was inserted on the anterior side of the lobule (Fig. 2, inset), completing the circuit, and beginning the 5-day period of stimulation.

RESULTS

Total duration for application was under 3 minutes for each patient. Both patients described the discomfort of application as a 2 of 10 on the Numeric Rating Scale for pain. One patient described the postapplication sensation as a "soft thumping," while the other described the area of the ear as "warmer." The sensations did not trouble either patient, and both were discharged home within 12 hours with prescriptions for scheduled celecoxib 200 mg twice per day, as well as tramadol 50 mg and oxycodone 5-mg tablets if needed (same-day or 23-hour stays following joint arthroplasty are common at our institution). Patients were instructed to keep the pulse generators dry and provided with the contact phone numbers of the administering physician and acute pain service. Patients were contacted daily by telephone through postoperative Day 8.

In the first five postoperative days, neither patient experienced any pain while lying, sitting, or ambulating. Both reported pain of 2 to 5 on the 0 to 10 Numeric Rating Scale while lowering themselves onto the toilet, and the patient who underwent a knee arthroplasty took one tramadol tablet (50 mg) on each of postoperative Days 3 and 4. One patient experienced few pulsating sensations around her treated ear while the other continued to experience "warmth" which she did not find bothersome (but rather reassuring that the device was functioning). The pulse generators automatically ceased functioning after 120 hours (5 days) and caretakers for each patient removed the round bandage of the grounding electrode, which detached the electrode from the patient along with the bandage. Caretakers subsequently removed the remaining 3 electrodes in the same manner followed by the pulse generator and discarded the disposable devices. No device-related localized irritation, systemic side effects, or complications were identified.

Approximately 6 hours after removal of the stimulators, both patients experienced an increase in surgical pain that continued for at least the following 3 days. The day following removal the patient who had undergone hip arthroplasty reported pain up to a 5/10 during physical therapy, although no additional supplemental analgesics were required and no sleep disturbances due to pain occurred. Her resting pain increased the following day to a 2/10 at rest, which continued through postoperative Day 8. The patient who had undergone knee arthroplasty reported that for the 3 days following device removal, her average resting pain level increased to 2/10, increasing to 7/10 during physical therapy. In addition, this patient reported one to two awakenings/night due to pain and requiring tramadol every 4 hours to 6 hours to help control her pain. No oxycodone was required for either patient at any postoperative time point.

DISCUSSION

This case report demonstrates that percutaneous auricular neuromodulation is feasible on an outpatient basis following major orthopedic surgery. In the two described cases, this modality appears to have markedly reduced pain scores and opioid requirements free of systemic side effects during the week following major orthopedic surgery (patients undergoing these procedures at our institution usually require intravenous—or at least oral—opioids).[9,10] While percutaneous auricular nerve stimulation has been previously documented to provide analgesia following tonsil,[11] retroperitoneal,[12] and pelvic surgery,[13] its mechanism of action is multifactorial, complex, and only partially understood.[14]

Importantly, multiple studies demonstrate that neurologic effects of auricular stimulation outlast the stimulation itself, suggesting a mechanism for the prolonged analgesia reported in clinical use.[15] Indeed, the two patients of the current report experienced no increase pain until 6 hours following removal; and far less operative pain on postoperative days 6 to 8 than is commonly observed following open total hip and knee arthroplasty.[16] Although certainly not perfectly analogous to trauma (lacking the frequent hemorrhage, psychological shock, and chaotic tissue destruction), the predictably severe pain following these major orthopedic procedures makes them possible surrogates for battlefield trauma and evaluation of potential analgesic modalities.

It is notable that investigators at Womack Army Medical Center proposed treating battlefield injuries with traditional (*non*stimulating) acupuncture at five auricular points.[17] Using tonsillectomy as a surrogate for battlefield trauma, they found that 15–45 minutes of perioperative acupuncture decreased postoperative pain scores and opioid consumption, although not to a statistically significant degree.[17] However, *electrical* stimulation of auricular acupuncture points has been demonstrated more effective than traditional *manual* auricular acupuncture,[18] and so 5 days of auricular neuromodulation would theoretically improve analgesia compared with traditional acupuncture applied for less than 1 hours.[17] Relatedly, a full day of traditional perioperative three-point auricular acupuncture decreased opioid requirements by 15% ($p = 0.008$) following total hip arthroplasty.[19] Since electrical auriculotherapy has been demonstrated more effective than conventional auricular acupuncture, we anticipate that 5 days of auricular neuromodulation will result in a greater degree of opioid sparing.

The ideal battlefield analgesic would be applicable for any anatomic injury location and patient. The auricular neuromodulation device used for patients of the current report has few contraindications listed on its label: (1) use of cardiac pacemakers due to a lack of clinical data to demonstrate safety; (2) hemophilia; and (3) psoriasis vulgaris. In addition, the skin where the leads are applied should be intact. The only reported complications have been minor bleeding at the skin (0.91%) and dermatitis from the adhesive bandages (0.91%). We administered a minimal dose of fentanyl (25 μg) for our postoperative patients with intravenous lines *in situ*, but for the pivotal studies of outpatients (n = 1,207), no analgesic was administered for electrode

placement and only two participants complained of "significant" pain (0.17%).[6]

Once placed, the stimulator remains functional for 5 days without requiring any intervention—the unit could be applied on the battlefield and remain in situ during evacuation to a forward operating base, main in-country health care facility, transportation to a military treatment facility, and during an inpatient stay for a total of up to 120 hours. In addition to its low health care provider burden, the device's low patient burden is reflected in its low weight (5 g) and size (36 × 16 × 17 mm, Fig. 2). Further, numerous factors favor percutaneous neural stimulation over opioid analgesics. Neuromodulation avoids the systemic side effects related to opioid use such as nausea, sedation, and respiratory depression; and it has no potential for misuse, dependence, and diversion.

The cases reported here demonstrate that postoperative percutaneous auricular neuromodulation is feasible in outpatients following major orthopedic surgery. In these 2 off-label cases, it appears to have markedly reduced pain scores and opioid requirements free of systemic side effects during the week following hip and knee arthroplasty. Considering the potential of this modality to treat trauma on the battlefield without systemic side effects, additional investigation appears warranted.

AUTHORSHIP

Each of the authors has contributed significant to, and is willing to take public responsibility for, one or more aspects of the study as listed as follows: B.M.I. participated in the design, data acquisition, and article preparation. J.J.F. participated in the design, data acquisition, and article preparation. E.T.S. participated in the design and article preparation. K.R.C. participated in the design and article preparation. S.T.B. participated in the design, data acquisition, and article preparation.

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DISCLOSURE

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