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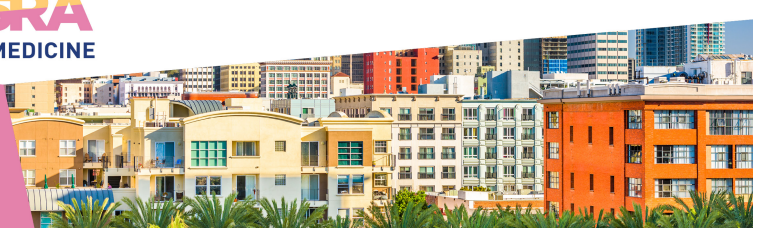

Abstract: 5068

Scientific Abstracts > Emerging Technology

Percutaneous Auricular Neuromodulation following Total Knee Arthroplasty: A Randomized, Double-Masked, Sham-Controlled Pilot Study

Brian Ilfeld, John Finneran, Brenton Alexander, Wendy Abramson, Jacklynn Sztain, Scott Ball, Francis Gonzales, Baharin Abdullah, Brannon Cha, Engy Said
University of California, San Diego

Introduction

Percutaneous auricular nerve stimulation (neuromodulation) is an analgesic technique involving the percutaneous implantation of multiple leads on/around the ear followed by the delivery of electric current using an external pulse generator. The mechanism of action is multifactorial, complex, and remains under investigation, but probably involves modulation of serotonergic, noradrenergic, and endorphinergic pathways with associated release of serotonin, norepinephrine, and endogenous opioids such as beta-endorphins.1 Auricular vagal nerve stimulation further chemically modulates nociceptive processing, anxiety, and depression.1

The device is relatively simple to apply—it necessitates neither advanced training nor physician application—requires no additional equipment, has few contraindications, and is not associated with serious complications. In contrast with opioids, auricular neuromodulation is medication-free, lacks systemic side effects, and has no potential for misuse, dependence, or diversion. Furthermore, it theoretically treats pain originating from any number and/or combination of peripheral nerves, is disposable, and is a fraction of the cost relative to ultrasound-guided percutaneous neuromodulation devices.

A percutaneous auricular neuromodulation device is currently cleared by the United States FDA to reduce symptoms associated with opioid withdrawal for up to 5 days (Fig. 1). The current randomized, controlled pilot study was undertaken to (1) determine the feasibility and optimize the protocol for a subsequent definitive clinical trial; and (2) estimate the treatment effect of auricular neuromodulation on postoperative pain and opioid consumption following total knee arthroplasty.

Materials and Methods

The study was prospectively registered (NCT05521516) and IRB approved. The IRB determined that the auricular stimulator is a non-significant risk device per the criteria outlined in 21 CFR 812.3(m), and therefore approved the off-label use of this device to investigate its potential to provide postoperative analgesia. Written, informed consent was obtained from all participants. Within the recovery room following primary, unilateral, total knee arthroplasty, an

auricular neuromodulation device was applied using 3 percutaneous leads and one ground electrode (NSS-2 Bridge, Masimo, Irvine, California; Fig. 1). Participants were randomized to 5 days of either electrical stimulation or sham stimulation using an external pulse generator in a double-masked fashion. Participants were discharged with the stimulator in situ and removed the disposable devices at home. The dual primary treatment effect outcome measures were the cumulative opioid use (oral oxycodone) and the mean of the "average" daily pain measured with the Numeric Rating Scale (NRS) for the first 5 postoperative days.

This investigation was designated a priori as a pilot study to assist in planning a subsequent definitive trial and we therefore used a convenience sample of 30 participants undergoing total knee arthroplasty. While there were two primary outcomes specified prior to enrollment, there was no specific data analysis plan defined prospectively. Comparisons of independent samples were performed using a two-tailed Mann-Whitney U test, Chi Square test, and/or Fisher's Exact test. $P<0.05$ was considered statistically significant. Adjustments were not made for multiple comparisons.

Results/Case Report

Participants (n=30) were randomized to either active stimulation (n=15) or sham (n=15) and had a neuromodulation device applied successfully (Table 1). Primary outcomes: during the first 5 postoperative days, oxycodone consumption in participants given active stimulation was a median [IQR] of 4 mg [2, 12] versus 13 mg [5, 23] in patients given sham treatment (P=0.039); during this same period the average pain intensity in patients given active stimulation was a median [IQR] of 2.5 [1.5, 3.3] versus 4.0 [3.6, 4.8] in those given sham (P=0.014).

Secondary outcomes: daily average pain between days 2 and 7 were lower in the active treatment than sham group (Fig. 2). Worst and least pain scores as well as opioid consumption was generally lower in the active treatment group, though only occasionally to a statistically significant degree (Fig. 2). Two (13%) participants who received active stimulation avoided opioids for the entire study period, versus none (0%) in those given sham (P=0.483). Regarding the highest "average" daily pain level over the first 8 postoperative days, no participants who received active stimulation experienced severe pain, versus 27% in those given sham (P<0.001; Fig. 1). Participants who received active treatment had less physical and emotional interference due to pain during both the treatment (postoperative days 2 and 4) and post-treatment (days 6 and 8) phases, although the differences did not reach statistical significance (Fig. 2). Awakenings due to pain over all 8 postoperative nights in participants given active stimulation was a median [IQR] of 5 [3, 8] versus 11 [4, 14] in those given sham (P<0.001).

Discussion

This pilot study provides evidence that percutaneous auricular neuromodulation reduces pain scores, opioid requirements, and sleep disturbances during the initial week after total knee arthroplasty. Auricular neuromodulation also decreased pain's interference with physical and emotional functioning as measured with the Brief Pain Inventory's interference scale both during and following active treatment, although the between-group differences did not reach statistical significance (Fig. 2). This is unsurprising given the limited power of the current pilot study. However, if a subsequent adequately powered trial found the observed improvements reached statistical significance, it would be notable since they are in the range of what the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) concluded "would be a reasonable benchmark for future studies designed to identify to minimally clinically important changes."2

Using the specific device of the current study, various small series and case-control studies have suggested its potential in providing postoperative analgesia.3 However, the only 2 published randomized, controlled studies—involving colorectal and Cesarean surgeries—were negative for their

primary endpoints and most secondary outcomes.4,5 The differing results relative to the current study may be due to the different types of surgery, anatomic surgical sites, or the study protocols themselves.

In conclusion, percutaneous auricular neuromodulation is feasible for knee arthroplasty and may be an effective analgesic enabling decreased opioid consumption. Considering the ease of application, few contraindications, applicability to any anatomic surgical location, low patient and provider burden, lack of systemic side effects and serious adverse events as well as no misuse, dependence, or diversion potential, further study with a larger, definitive trial appears warranted.

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Disclosures

No

Tables / Images