Original Article

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Transcutaneous electrical nerve stimulation for pain during propofol injection: a randomized clinical trial

Dongwoo Lee[1], Juhwa Jin[2], Ji Hyo Kim[2], Jinyoung Oh[2], Younghoon Jeon[1]

[1]Department of Oral and Maxillary surgery, School of Dentistry, Kyungpook National University, Daegu, Republic of Korea
[2]Department of Anesthesiology and Pain Medicine, School of Medicine, Kyungpook National University, Daegu, Republic of Korea

Background: Propofol is a short-acting intravenous sedative widely used for procedural sedation and general anesthesia. However, pain during propofol injection is a distressing adverse effect. This study was designed to investigate whether transcutaneous electrical nerve stimulation (TENS) could reduce pain during propofol injection compared to sham TENS.

Methods: In a randomized controlled trial, 80 patients were allocated to two groups: the active TENS group received electrical stimulation via two electrodes on the venous cannulation site, whereas the sham TENS group received no stimulus. After 20 min following TENS, propofol 0.5 mg/kg pain was injected intravenously and pain was evaluated using a four-point score (0 = none, 1 = mild, 2 = moderate, 3 = severe). Adverse effects associated with TENS were also recorded.

Results: The overall incidence of pain during propofol injection was 47.5% in the TENS group and 87.5% in the sham group ($P < 0.001$). The incidence of moderate pain was significantly lower in the TENS group (7.5%) than in the sham TENS group (42.5%) ($P < 0.001$). There were no complications associated with TENS.

Conclusion: Pre-treatment with TENS significantly reduced the incidence and intensity of pain during propofol injection.

Keywords: Intravenous Injections; Pain; Propofol; Transcutaneous Electric Nerve Stimulation.

INTRODUCTION

Propofol (2,6-diisopropylphenol) is a short-acting intravenous sedative widely used for procedural sedation and general anesthesia. However, about 80–90% of patients complain of pain when propofol is administered via a vein on the dorsal hand [1-3]. Pretreatment with several agents, such as lidocaine, opioids, and nitroglycerin, has been used to reduce this pain. However, despite these treatments, propofol injection pain still occurs and is a persisting problem [1-3].

Transcutaneous electrical nerve stimulation (TENS), segmentally applied to the pain site, has a rapid onset of analgesic effect and is widely used for the treatment of several types of pain, such as inflammatory and neuropathic pain [4-7]. Therefore, in the present study, we investigated whether pretreatment with TENS could reduce pain due to propofol injection compared to sham TENS.

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Corresponding Author: Younghoon Jeon, Department of Oral and Maxillary surgery, Department of Anesthesiology and Pain Medicine, School of Dentistry, Kyungpook National University, 130 Dongdeok-ro, Jung-gu, Daegu 41944, Republic of Korea
Tel: +82 53 200 5871 Fax: +82 53 426 2760 E-mail: jeon68@gmail.com

METHODS

This study was approved by the Ethics Committee of Kyungpook National University Hospital (2021-03-036-001), and written informed consent was obtained from all participants. This study was registered at ClinicalTrials.gov (NCT05046054). Exclusion criteria included patients with cardiac, neurologic, or psychiatric disorders and patients who had analgesic or sedative agents within 24 h before surgery. The study included 80 patients aged 19–70 years, with American Society of Anesthesiologists (ASA) physical status I and II, scheduled for elective dental surgery under general anesthesia.

No premedication with sedatives or analgesics was administered. On arrival at the operating room, a 20-gauge catheter was inserted into the dorsal vein of the patient's non-dominant hand 30 min prior to the injection of propofol. Noninvasive blood pressure, electrocardiography, and pulse oximetry were performed. TENS using a TENS YW-5000 (YoungWon Medical Co, Korea) was delivered through two electrodes (5 × 5 cm, YoungWon Medical Co, Korea). Electrodes were attached after cannulation. The cathode was placed 2 cm proximal to the catheter insertion site, while the anode was placed 4 cm apart more proximally (Fig. 1). A computer-generated table was used to randomly assign patients to the two groups. The active TENS group received electrical stimulation at 80 pulsed currents per second, with a pulse duration of 200 μs for 20 min. The current amplitude slowly increased until the patients reported a "strong but comfortable" intensity level, without noticeable muscle contraction. In the sham TENS group, the TENS device was on, but electrical stimulation was not provided. All participants were notified that they may or may not experience electrical stimulation during the TENS procedure. TENS was performed by the same anesthesiologist, who was aware of the group allocation. After application of TENS for 20 min, the electrodes were removed and propofol 0.5 mg/kg was administered at the rate of 0.5 ml/s using syringe pump. Propofol injection pain was evaluated by a blinded anesthesiologist using a four-point scale: 0 = no (negative response to questioning), 1 = mild pain (pain reported only in response to questioning without any behavioral signs), 2 = moderate pain (pain reported in response to questioning and accompanied by behavioral signs or pain reported spontaneously without questioning), and 3 = severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal, or tears). Next, propofol 1.5 mg/kg and rocuronium 0.8 mg/kg were administered for endotracheal intubation. Anesthesia was maintained using a mixture of air and oxygen supplemented with sevoflurane 2% to 2.5% and continuous infusion of 0.1–0.3 μg/kg/min of remifentanil. During the first 24 h after surgery, any complications associated with TENS were assessed by a blinded investigator. In this study, the primary outcome was the incidence of pain during propofol injection and the secondary outcome included the side effects of TENS.

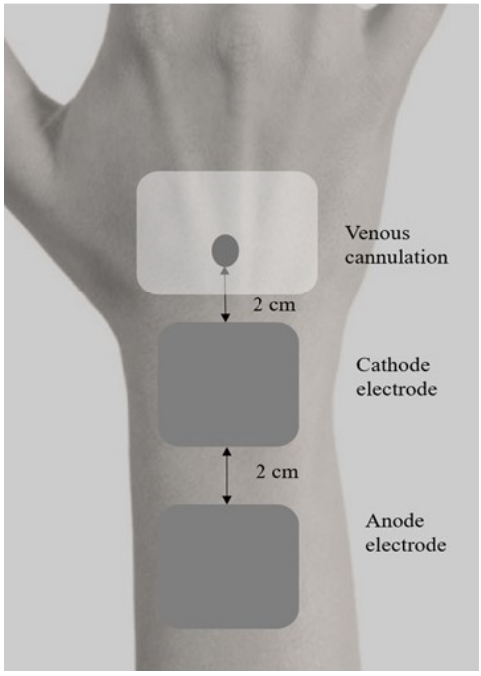

Fig. 1. Electrode placement for transcutaneous electrical nerve stimulation.

Statistical analysis

Based on previous studies, [2,3] the incidence of pain

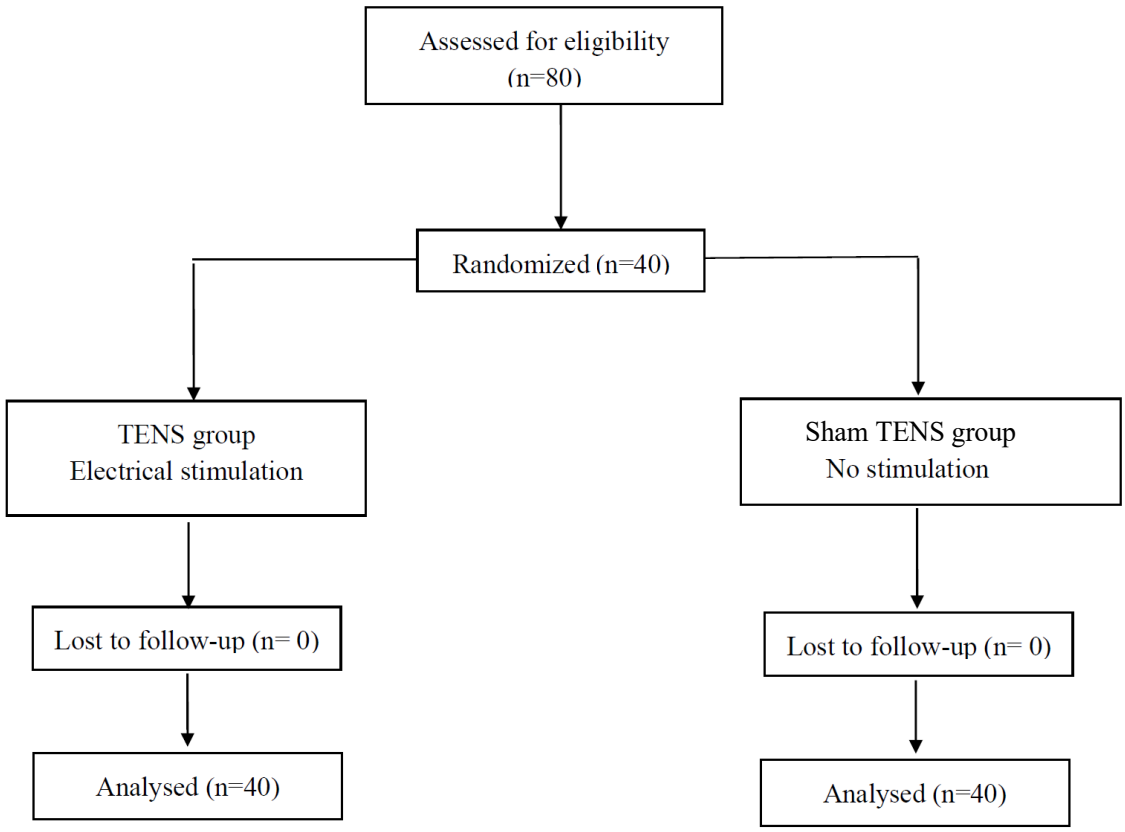

Fig. 2. Flow diagram of the study.

during propofol injection in the placebo group would be at least 80%. A 50% reduction in incidence (from 80% to 40%) between the sham TENS and TENS groups was considered clinically significant. A minimum sample size of 40 patients per group was required to detect such differences with a two-tailed test of the proportions with an α error of 0.05 and a β error of 0.8.

Data are presented as number (%), median, or mean ± standard deviation (SD).

The Student's t-test was used for the analysis of continuous data. Fisher's exact test or chi-square test was used for the analysis of categorical data. Statistical significance was set at $P < 0.05$. SPSS (version 16.0) was used for the statistical analysis.

RESULTS

Eighty patients completed the study (Fig. 2). There was no statistical difference in the demographic data between the groups (Table 1). The incidence and intensity of pain during propofol injection are shown in Table 2. The overall incidence of pain upon injection of propofol was 19 (47.5%) with TENS stimulation, compared to 35 (87.5%) in the sham TENS group ($P < 0.001$). The incidence of moderate pain was significantly lower in the TENS group (7.5%) than in the sham TENS group (42.5%) ($P < 0.001$). There were no complications associated with TENS.

Table 1. Patient demographics

	Active TENS (n = 40)	Sham TENS (n = 40)
Age (yr)	44 ± 15	39.9 ± 13.2
Sex (M/F)	30/10	28/12
Height (cm)	169 ± 9.4	169.7 ± 9.4
Weight (kg)	68.3 ± 14.1	69.5 ± 15.8
ASA physical status I/II	24/16	28/12

Values are mean ± SD or number. ASA, American Society of Anesthesiologists; TENS, transcutaneous electrical nerve stimulation.

Table 2. Pain on injection of propofol

	Active TENS (n = 40)	Sham TENS (n = 40)
Patients with pain (%)	19 (47.5%)	35 (87.5%)*
Pain score (median)	0	2*
None [0]	21 (52.5%)	5 (12.5%)*
Mild [1]	16 (40%)	15 (37.5%)
Moderate [2]	3 (7.5%)	17 (42.5%)*
Severe [3]	0	3 (7.5%)

Values are numbers (%). * $P < 0.001$ vs active TENS. TENS, transcutaneous electrical nerve stimulation.

DISCUSSION

Our findings demonstrated that pretreatment with active TENS significantly decreased the incidence and intensity of pain from propofol injection compared to sham TENS. No side effects were associated with TENS.

Propofol is a potent intravenous hypnotic agent commonly used for sedation and general anesthesia. However, pain during propofol injection is a common clinical issue and an unpleasant experience for both patients and anesthesiologists [3,8]. However, the exact mechanism of pain associated with propofol injection remains unclear. Pain may result from direct stimulation of nociceptive receptors or free nerve endings in vessels by free propofol molecules [9]. Pain during administration of propofol via the dorsal hand vein may occur in 80–90% of patients [1-3]. In the present study, the incidence of pain due to propofol was 87.5%, which is consistent with previous studies [1-3].

TENS is an acknowledged noninvasive peripheral nerve stimulation technique used to decrease pain. It delivers pulsed electrical currents across the intact surface of the skin to stimulate underlying nerves [6,7]. TENS generally has a rapid onset of analgesia, which is effective for the treatment of various painful conditions, including nociceptive and neuropathic origins, and is popular with patients and practitioners because it is inexpensive, easy to administer and safe [10,11].

There are several types of TENS techniques, including conventional and intense TENS [12]. Conventional TENS has high-frequency (50-100 Hz), low intensity (strong but comfortable paresthesia), and pulse width of 50-200 μs [12,13]. Theoretically, conventional TENS selectively stimulates large-diameter, low-threshold non-noxious afferents (Aβ fibers) in dermatomes associated with pain, which consequently reduces the activity in second-order nociceptive transmission neurons, similar to the gate control theory of pain [12-14]. Pain relief with conventional TENS is maximized when a patient experiences strong but comfortable paresthesia. Additionally, high-frequency TENS involves δ-opioid receptors and increases γ-aminobutyric acid levels in the spinal cord [10,15]. In a previous study, pretreatment with conventional TENS was effective in decreasing the pain intensity of venous cannulation [16]. In the present study, TENS with 80 pulsed currents per second and a pulse duration of 200 μs was delivered to patients prior to propofol injection. The incidence and intensity of pain after propofol injection were significantly lower in the active TENS group than in the sham TENS group.

Injection pain occurs in 80%–90% of patients when propofol is injected into the dorsal hand vein [1-3]. The inclusion of a sham TENS group was considered unethical for the present study. Even though the adverse effects of TENS are rare [12], it may cause muscle aches, nausea, and dizziness [17,18]. Therefore, we included a sham TENS group to investigate the complications of TENS, and no side effects were observed in the active TENS group.

The present study has several limitations. Premedication was not administered in this study. Premedication with sedatives affects the incidence of postoperative recall of pain during propofol injection, which increases patient discomfort during anesthetic care [19]. Further studies are required to assess the incidence of pain recall after propofol injection.

In conclusion, pretreatment with conventional TENS significantly reduced the incidence and intensity of pain during propofol injection compared with sham TENS.

AUTHOR ORCIDs

Dongwoo Lee: https://orcid.org/0000-0001-7280-5973
Juhwa Jin: https://orcid.org/0000-0001-7596-411X
Ji Hyo Kim: https://orcid.org/0000-0003-2313-1217
Jinyoung Oh: https://orcid.org/0000-0003-3562-908X
Younghoon Jeon: https://orcid.org/0000-0002-7168-4214

AUTHOR CONTRIBUTIONS

Dongwoo Lee: Writing - original draft
Juhwa Jin: Data curationNew, Formal analysis
Ji Hyo Kim: Investigation
Jinyoung Oh: Formal analysisNew
Younghoon Jeon: Conceptualization, Writing - review & editing

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