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Preemptive Analgesic Effects of Transcutaneous Electrical Nerve Stimulation (TENS) on Postoperative Pain: A Randomized, Double-Blind, Placebo-Controlled Trial

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Abstract

Background: Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological analgesic method used to control different types of pain.
Objectives: The aim of this study was to evaluate the effects of preoperative TENS on post inguinal hernia repair pain.
Patients and Methods: This randomized, double-blind, placebo-controlled clinical trial was performed on 66 male patients with unilateral inguinal hernias who were admitted to the Shahid Beheshti hospital in Kashan, Iran, from April to October 2014. Participants were selected using a convenience sampling method and were assigned to intervention (n = 33) and control (n = 33) groups using permuted-block randomization. Patients in the intervention group were treated with TENS 1 hour before surgery, while the placebo was administered to patients in the control group. All of the patients underwent inguinal hernia repair by the Lichtenstein method, and pain intensity was evaluated at 2, 4, 6, and 12 hours after surgery using a visual analogue scale. Additionally, the amounts of analgesic administered by pump were calculated and compared between the two groups.
Results: The mean estimated postoperative pain intensity was 6.21 $\pm$ 1.63 in the intervention group and 5.45 $\pm$ 1.82 in the control group (P = 0.08). In the intervention group pain intensity at 2 and 4 hours after surgery were 3.54 $\pm$ 1.48 and 5.12 $\pm$ 1.41 (P < 0.001), respectively. In the control group these values were 4.0$\pm$1.5 and 4.76 $\pm$ 1.39 (P = 0.04), respectively. No significant differences were observed in mean pain intensities at 6 and 12 hours.
Conclusions: TENS can reduce postoperative pain in the early hours after inguinal hernia repair surgery.

Keywords: Transcutaneous Electric Nerve Stimulation, Analgesia, Inguinal Hernia, Postoperative Pain

1. Background

Inguinal hernia is one of the most common surgical conditions and is estimated to affect approximately 50% of men during their lives. It accounts for more than 800000 surgeries being performed in the united states annually (1, 2). Spontaneous healing of inguinal hernia is nearly impossible and surgery is the only way to repair it. The surgery should be done in a timely manner to avoid the life threatening consequences (3). Despite the development of various surgical techniques for repair of inguinal hernias, pain is a common problem in patients due to manipulation and the mesh hernioplasty, which can cause local nerve damage (4).

Since postoperative pain can affect many physical, cognitive, and emotional characteristics of the patients, it is important to find an appropriate way to control postoperative pain (5). Preemptive analgesia is an effective strategy that involves all attempts for reduction of pain and analgesic use (6). The methods of preemptive analgesia (e.g. local nerve blockage, epidural injections of opioids, and systemic steroids) are based on prescription drugs (7). Although there are few studies regarding non-pharmacological methods of preemptive analgesia (such as acupuncture and electroacupuncture), the results indicate an obvious pain reduction in the patients (8, 9).

Transcutaneous electrical nerve stimulation (TENS) is a non-pharmacological method of analgesia. It is approved by the food and drug administration (FDA) and is a fast, safe, non-invasive, and inexpensive form of physical therapy. Compared to other analgesic methods, it also has the least side-effects (10-12) and is used to control postoperative pain after inguinal hernia repair. Although the method has been proven to have effectiveness in previous studies (13), it has not been used for preemptive analgesia.

2. Objectives

The aim of the present study was to evaluate the effect of preoperative TENS on postoperative pain in patients undergoing inguinal hernia repair.

3. Patients and Methods

3.1. Study Participants

This randomized, double-blind, placebo-controlled clinical trial was performed on 66 male patients with unilateral inguinal hernias who were admitted to the Shahid Beheshti hospital in Kashan, Iran, from April to October 2014. Shahid Beheshti hospital is a public hospital with 400 beds and 16 specialty and subspecialty wards and functions as a regional referral hospital.

In this study, we examined male patients with ages ranging from 20 to 50 years who had been admitted to the Shahid Beheshti hospital for unilateral inguinal hernia repair. Samples were selected using a convenience sampling method. To this end, we studied all patients aged 20 - 50 years who were candidates for unilateral inguinal hernia surgery using the Lichtenstein technique and had a physical status class I or II, based on the American society of anesthesiologists (ASA) classification. This selection continued until we attained of the required number of subjects (n = 66).

Patients were excluded from the study for the following reasons: infection or wound at the contact points of the electrodes, incarcerated or recurrent hernia, use of a heart pacemaker, and having a risk of any malignancy or neurological problems. Further exclusion criteria were having liver or kidney disorders, a body mass index (BMI) > 27 kg/m^2, undergoing treatment with antidepressants, addiction to drugs or alcohol, and having cognitive and sensory disorders.

Since no previous studies had been done on the effects of preemptive TENS on the level of postoperative pain, a pilot study was performed on 20 patients in the intervention and control groups (10 patients per group) to determine the sample size before the main study. The average pain was measured at 2 hours after surgery. Given that the average pain at 2 hours after surgery was 1.32 $\pm$ 4.1 in the intervention group and 1.55 $\pm$ 5.21 in the control group, the sample size in each group was calculated as being equal to 27 by taking a power of 80% and Z1-α/2 = 1.96. However, 33 people were examined in each group by taking into account the possible loss of 20% for the patients in this study.

All of the patients were visited by an anesthesiologist who examined their conditions for participation in the study. Demographic and clinical data of the patients were also recorded in a pre-designed questionnaire.

The patients were randomly assigned to either an intervention or control group using permuted-block randomization and 11 blocks of six patients, which had been classified by number and were used for this purpose (Figure 1). All stages of designing and implementing the study were verified and approved by the ethical committee of the Shahid Beheshti hospital (No. P/3145/1/5/29). All ethical considerations were carefully observed during the study. Written consent was obtained from all participants after they received comprehensive information on the study implementation. The present study was registered in the Iranian Registry of Clinical Trials (IRCT ID: IRCT2012102311228N1).

3.2. Interventions

An hour before the surgical incision, TENS was used for patients in the intervention group and dermal irritation continued until the induction of anesthesia in this way, that we used a TENS system (Model EV-906, Taiwan) that was set at a range of 0 - 18 milliamps after the relevant disposable electrodes were placed on the incision site for the intervention group. The frequency and wavelength of each channel were increased until the patient felt tingling, but no discomfort. Similarly, one hour before surgery, the electrodes of the system were placed on the incision site for the control group. The system indicator showed that it was active, but no electrical stimulation was applied.

After arrival in the operating room, a venous catheter was inserted in the cubital area and the patients were hydrated with 2 mL/kg Ringer's. Heart rate, blood pressure, and arterial oxygen pressure were automatically monitored after the patient was placed on the operating tabulation. About 2 μg/kg fentanyl was administered intravenously as a prodrug to all patients and anesthesia was induced using 6 mg/kg Nesdonal. In addition, 0.5 mg/kg atracurium was used to facilitate tubing. The patients were intubated with an appropriate cuffed tracheal tube and supported using a ventilator with 100% oxygen. Anesthesia was continued with isoflurane, and atracurium was used as a muscle relaxant. Fentanyl (2 μg/kg/hour) was also infused for analgesia. The technique used for hernia repair was the Lichtenstein technique using a mesh through a 10-cm incision made in the inguinal region in the least possible time. At the end of the operation, 40 μg/kg neostigmine and 20 μg/kg atropine were used to reverse the anesthesia, and the patients were extubated and monitored for 2 hours in the recovery unit. If any pain was felt during recovery, pethidine was administered intravenously at a dose of 25 mg, which was then recorded in the questionnaire.

During the patient's transfer from the recovery unit, a patient-controlled analgesia (PCA) pump containing 100 mL of pethidine and normal saline with a concentration of 2 mg/mL was used for each patient. The PCA infused a

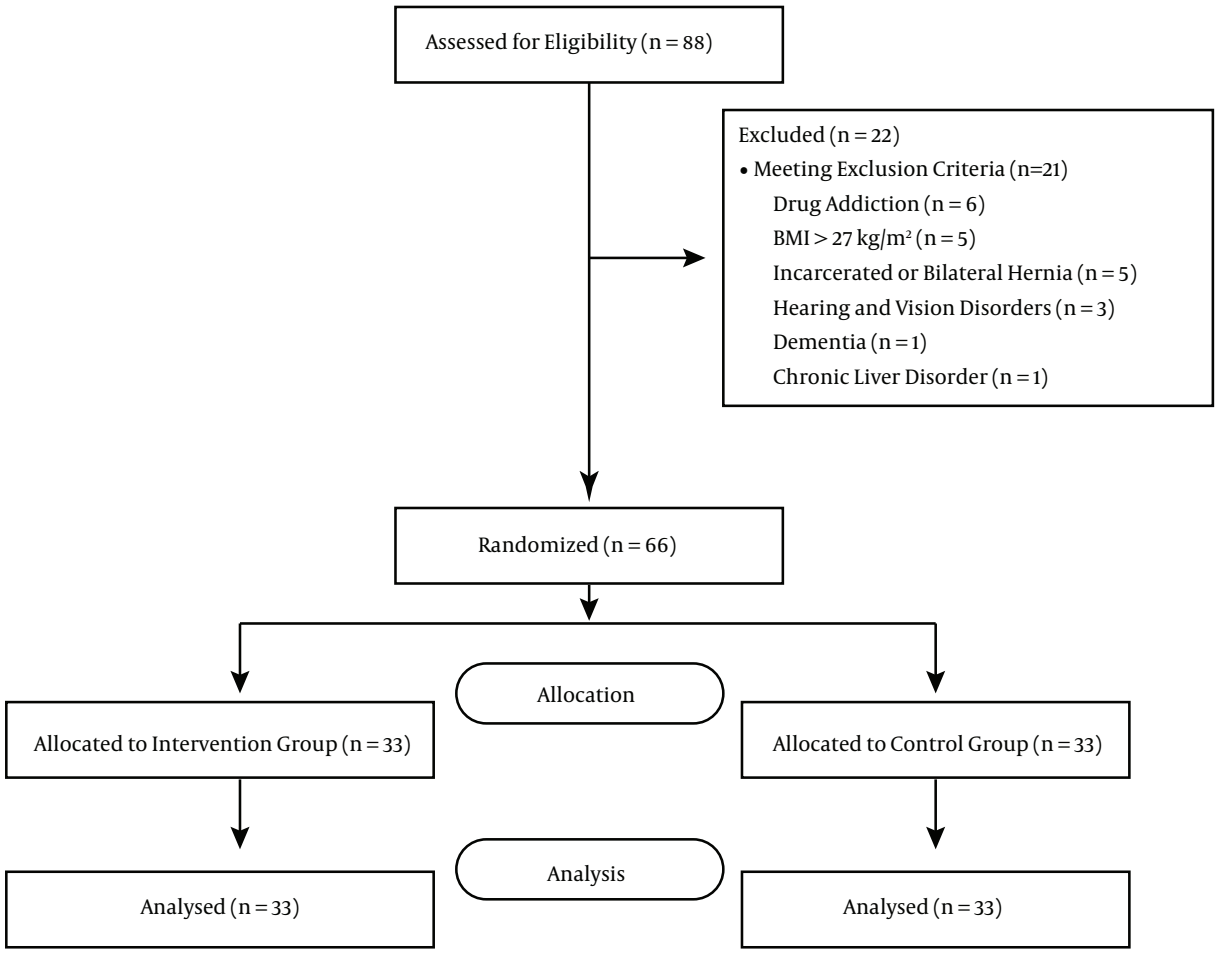

Figure 1. Study Flow Chart

pethidine solution through the venous catheter at a rate of 4 mL/hour. In case of any pain, the patient could press the button on the pump to receive 1 mL of solution in a bolus form. In this way, the patient was allowed to receive only four bolus doses at intervals of 15 minutes per hour, and pressing the key more than four times an hour would not lead to the administration of more drug. If, despite the bolus doses that were received, the patient still complained of pain, a 100 mg diclofenac suppository was administered at intervals of 6 hours, while nausea and vomiting were controlled by the administration of 4 mg of venous ondansetron. The amounts of drug, diclofenac suppository, and ondansetron, which were used for each patient at 12 hours after surgery, were extracted from the medical records and registered in the checklist.

3.3. Instruments

Two checklists were used to collect data for the study. The first checklist contained questions concerning demographic characteristics including age, height, weight, BMI, history of the disease, surgical history, smoking, and drug abuse. The second checklist was related to clinical data including systolic and diastolic blood pressures; ASA classification; the surgery duration; the pain intensity at 2, 4, 6, and 12 hours after surgery; the amount of opioid analgesics used; the number of diclofenac suppositories; and ondansetron injections used after surgery.

Content validity of the clinic checklist was examined and verified by five anesthesiologists and surgeons, and the reliability of the checklist was evaluated by an inter-observer method. For this purpose, in the initial pilot study, a questionnaire was completed by three researchers for five patients in each group, and the agreement between the three researchers was calculated (r = 0.93).

The pain intensity was measured using a visual analogue scale (VAS) that had a horizontal line with 10 equally spaced markers ranging from 0 (least amount of pain) to 10 (highest amount) (14). The pain intensity was determined at 2, 4, 6, and 12 hours after surgery.

The consumption level of analgesic (such as morphine) was verified by the PCA pump and the number of diclofenac suppositories was evaluated as another indicator of pain intensity. Additionally, nausea requiring medical intervention was examined by measuring the amount of the prescribed anti-nausea medicine (intramuscular ondansetron).

3.4. Statistical Analysis

The data collected in the present study were analyzed by SPSS software, version 18. The qualitative results were reported as absolute frequency and relative frequency, while the quantitative results were expressed as mean ± standard deviation. The distribution of data was tested using the Kolmogorov-Smirnov test, and the data analysis was performed using the chi-square test, independent t-test, Mann-Whitney U test, and repeated measures analysis of variance (ANOVA), all of which were two tailed. The level of significance was set at $P < 0.05$.

4. Results

A total of 88 patients were examined for inclusion in the study, but 21 patients were excluded for the following reasons: drug addiction (6 patients), BMI > 27 kg/m^2 (5 patients), incarcerated or bilateral hernia (5 patients), hearing and vision disorders (3 patients), dementia (1 patient), and chronic liver disorder (1 patient).

We ultimately examined 66 patients who were assigned to the control and intervention groups. All patients were males with ages ranging from 20 to 50 years (mean age: 33.73 ± 7.16 years). Table 1 shows the demographic and clinical characteristics of the patients in each group.

The estimated mean pain score was 6.21 ± 1.63 for the intervention group and 5.45 ± 1.82 for the control group (P = 0.08). The average duration of the operation was 57.87 ± 91 minutes and 58.94 ± 12.42 minutes for the intervention and control groups, respectively (P = 0.69). The mean amount of the pethidine used by PCA at 12 hours after surgery was 136.48 ± 28.44 mg for the intervention group and 154.79 ± 30.58 mg for the control group (P = 0.01). Table 2 shows the mean pain intensity at different times of the examination as well as the amounts of prescribed rectal and anti-nausea drugs. The use of repeated measures ANOVA along with the modification of confounding effects showed that the group receiving TENS before surgery reported significantly less pain than the control group in all stages of the study (P = 0.02) (Figure 2).

Table 1. Baseline Characteristics

Characteristics	Groups[a]		P Value
	Intervention	Control	
Age			0.63
Mean ± SD	34.15 ± 7.34	33.3 ± 7.06	
Range	22 - 48	22 - 49	
Weight			0.9
Mean ± SD	72.45 ± 8.26	72.24 ± 5.86	
Range	62 - 106	60 - 83	
Height			0.13
Mean ± SD	1.77 ± 0.08	1.8 ± 0.08	
Range	1.62 - 2	1.64 - 2	
BMI			0.06
Mean ± SD	23.11 ± 1.74	22.3 ± 1.76	
Range	19.39 - 26.5	19.5 - 26.2	
Systolic blood pressure			0.31
Mean ± SD	120.42 ± 6.79	122.3 ± 8.02	
Range	109 - 135	109 - 136	
Diastolic blood pressure			0.68
Mean ± SD	79.79 ± 6.02	80.36 ± 5.3	
Range	65 - 90	71 - 90	
ASA Class[b]			0.38
I	27 (81.8)	24 (72.7)	
II	6 (18.2)	9 (27.3)	
Surgery History[b]			0.11
No	20 (60.6)	26 (78.8)	
Yes	13 (39.4)	7 (21.2)	
Smoking[b]			0.4
No	26 (78.8)	23 (69.7)	
Yes	7 (21.2)	10 (30.3)	

[a] N = 33.
[b] Values are expressed as No. (%).

5. Discussion

In this study, we examined the preemptive analgesic effects of TENS on post-inguinal hernia repair pain. The results showed that the use of TENS before inguinal hernia surgery can significantly reduce pain at 2 and 4 hours after surgery. Compared to the control group, the TENS

Table 2. Clinical Outcomes

Characteristics	Groups[a]		P Value
	Intervention	Control	
2nd hour post-surgery pain			< 0.001
Mean ± SD	3.54 ± 1.48	5.12 ± 1.41	
Range	1 - 7	1 - 8	
4th hour post-surgery pain			0.04
Mean ± SD	4.0 ± 1.5	4.76 ± 1.39	
Range	1 - 7	2 - 8	
6th hour post-surgery pain			0.71
Mean ± SD	4.15 ± 1.25	4.27 ± 1.35	
Range	1 - 7	1 - 7	
12th hour post-surgery pain			0.85
Mean ± SD	3.51 ± 1.5	3.57 ± 1.5	
Range	1 - 6	1 - 7	
Median (IQR)	4 (2.5)	4 (2.5)	
Diclofenac Use[b]			0.03
No	28 (84.8)	20 (60.6)	
Yes	5 (15.2)	13 (39.4)	
Ondansetron Use[b]			0.55
No	27 (81.8)	25 (75.8)	
Yes	6 (18.2)	8 (24.2)	

[a] N = 33.
[b] Values are expressed as No. (%).

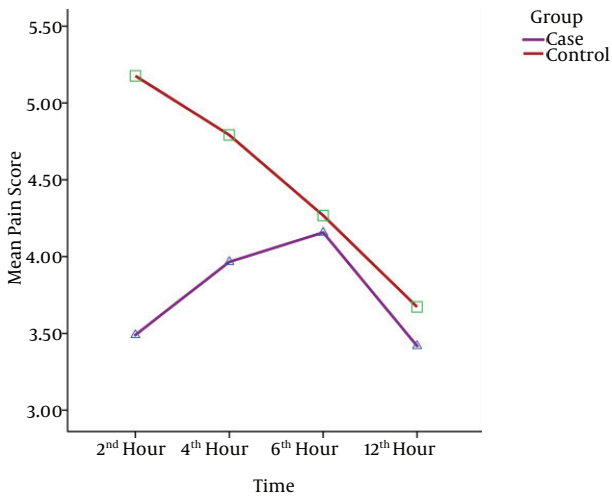

Figure 2. Mean Pain Score Changes in the Studied Groups

group was also observed to use fewer analgesic drugs after surgery.

No studies have been performed to evaluate just the effect of TENS preemptive analgesia in patients undergoing inguinal herniorrhaphy, thus, this study is the first one in this area. A study by Dalamagka et al. examined the effect of TENS in controlling the post-surgical pain of patients undergoing inguinal herniorrhaphy in three groups. These authors found that, although the patients receiving TENS experienced less pain than the control group, no differences were observed between the group treated with TENS before, during, and after surgery, and the group receiving only TENS before and after surgery (4).

A study similar to ours compared the effect of electroacupuncture before cardiac surgery and found that the patients treated with preoperative electroacupuncture needed smaller amounts of fentanyl to control pain than the control group (9).

The hypoalgesic effect of postoperative TENS on postoperative pain has also been demonstrated in previous studies that presented the hypothesis of stimulation of delta opioid receptors with a high frequency (13). Wang et al. showed that the use of high- and low-frequency TENS after surgery can reduce the dose of hydro-morphine in patients by 65% and 34%, respectively. Moreover, the postoperative consequences including nausea and vomiting were also significantly decreased (15). Several studies have shown the effects of TENS in relieving orofacial pain, toothache, chronic pain, labor pain, rheumatoid arthritis, neck pain, lower back pain, and chronic recurrent headache (16-23). TENS is widely used as a complementary or even an alternative to painkiller medicines (24).

There are many theories on how to protect the effectiveness of TENS, the most common of which is the gate control theory of pain. According to this theory, the stimulation of large diameter afferent nerves by TENS inhibits the nerve fibers that transmit pain signals in the dorsal horn of the spine (24). The gate control theory describes the possibility of segmental inhibition of intermediate substantia gelatinosa neurons that are located in the spinal dorsal horn. However, the main body of the theory explains the presence of descending pathways that affect the spinal neurons (24, 25). Currently, the mechanisms underlying the effect of TENS (e.g. anatomical pathways, neurotransmitters, receptors, and type of neurons related to pain inhibition) have been discussed in more detail.

Campbell and Taub (1973) suggested another mechanism by which a pain signal can be transmitted through the blockage or exhaustion of Aδ fibers by TENS (26). Janko and Trontelj argued that the bombardment of pain signals is intact during and after using TENS (27). Furthermore, the anti-hyperalgesic effects of TENS are maintained for 8

- 24 hours after stimulation, indicating a mechanism other than the blocking of the incoming impulse (25).

Ren et al. described the role of adenosine in the inhibition of pain produced by the vibratory stimulation of large diameter fibers (28). If, before the process, the person receiving TENS consumes caffeine, which acts as an antagonist of adenosine receptors, the analgesic effect of TENS can be significantly decreased compared to a placebo (29).

The role of endogenous opioids was analyzed to explain the mechanism underpinning the effect of TENS, particularly the high-frequency type. Studies have shown that such mechanisms can be generalized for both high- and low-frequency TENS (30-32). There are three types of opioid receptors, namely μ, δ, and κ, which are located in the spine and the regions involved in descending inhibition (e.g. the nucleus raphe magnus in the rostral ventral medulla [RVM] and the periaqueductal gray [PAG]). The PAG sends information toward the spinal cord. Stimulation of the PAG and RVM leads to the inhibition of the spinal dorsal horn and spinothalamic pathway (33, 34).

Beta-endorphin levels are increased in the blood and cerebrospinal fluid (CSF) after the use of TENS, under either high or low frequency (35). Additionally, the concentrations of met-enkephalin (agonist for δ-opioid receptors) and dynorphin A (agonist for κ-opioid receptors) are increased in the CSF of the lumbar region after TENS treatments (36). A study by Leonard et al. which was performed to reduce the effect of high-frequency TENS, found that the injection of naloxone (14 mg/kg) can neutralize the analgesic effects of TENS completely (37). Endogenous opioids have varying ranges of half-lives (e.g. 93 minutes for beta-endorphin in the CSF and about 105 minutes to 8.5 hours for dynorphins) (38, 39). If TENS is used before surgery, the role of endogenous opioids will likely be more important than other mentioned mechanisms. In our study, the intervention and control groups had the same levels of pain at 4 hours after surgery, which may be due to the vanishing of the secreted endogenous opioids. Both groups also received morphine via PCA pumps. The synergistic effects of endogenous opioids and the infused morphine are possible reasons why pain relief was observed in the intervention group. Further studies are needed because there are currently not enough studies to reach a definitive conclusion.

The results of this study, which is the first to examine the effect of preemptive TENS on pain following an inguinal herniorrhaphy, will be effective in improving the methods of pain control after surgery. The strength of this study was the measurement of pain levels using objective (the amount of opioid analgesics) and subjective (based on VAS) criteria, which reduced the risk of error. As a limitation of this study, the levels of endogenous endorphins in the blood and CSF could not be measured at various stages of the study. Due to ethical constraints and the requirement of the ethics committee to use the minimum number of samples, it was impossible to implement the study with a larger population. Another limitation of this study was the lack of similar studies, which limited the comparison of our results to those found in other studies.

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Footnotes

Author's Contribution: Development of the original idea, Mohammad Eidy and Mohammad Reza Fazel; study concept and design, Mohammad Eidy and Mohammad Reza Fazel; data collection, Monir Janzamini and Mostafa Haji Rezaei; analysis and interpretation of data, Ali Reza Moravveji; preparation of the manuscript, Monir Janzamini; revision of the manuscript, Mostafa Haji Rezaei.

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