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# **Treatment of migraine attacks by transcutaneous electrical nerve stimulation in emergency department; a randomized controlled trial**

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# Treatment of migraine attacks by transcutaneous electrical nerve stimulation in emergency department; a randomized controlled trial

## Abstract

**Purpose:** The primary purpose of this trial is to evaluate the effectiveness of Transcutaneous Electrical Nerve Stimulation (TENS) therapy application in the emergency department.

**Methods:** The patients were divided into 2 groups: a sham group, and a verum group. Patients in the Verum group include those who use the device for the first time. Both groups were connected to visually indistinguishable devices. Both groups underwent therapy for a total of 20 minutes. Using the Visual Analog Scale (VAS), the patients' perceived changes in pain intensity were recorded at the 20<sup>th</sup> and 120<sup>th</sup> minutes after initiation therapy. After the 120<sup>th</sup> minute, patients' individual needs for additional treatment were assessed. Additionally, their self-reported well-being was assessed using a Likert-type verbal scale.

## Results:

In total 151 patients that were admitted to the emergency ward were assessed, with the sham and verum group being assigned 39 patients each from this pool. For the verum group the VAS change from 0 to 120 minutes was  $-65.46 \pm 25.44$  and for the sham group it was  $-9.46 \pm 2.61$  ( $p < 0.001$ ). Verbal scores in the 120th min. were found to be 1.2 for sham group and 4.5 in the verum group ( $p < 0.001$ ). Thirty patients (76.92%) in the sham group and 1 (2%) in the verum group had additional analgesic requirement after 120 minutes.

## Conclusion:

TENS therapy is a fast-acting, effective therapy for the treatment of acute migraine in the emergency department.

## 1. Introduction

### 1.1. Background

Migraine is a type of primary headache that can be a major impairment to quality of life [1]. This disease has been found to be the 3rd most common globally, and the 7th most common

debilitating disease [2]. Migraine typically presents as a middling or severe, unilateral, pulsatile headache that last between 4 to 72 hours. This condition may be accompanied by nausea and / or photophobia and phonophobia [1]. Treatments for migraine conventionally aim to alleviate symptoms. There are two main groups of migraine treatments: preventative treatments and symptomatic treatments. Available treatment options generally have unwanted side effects and are not effective in some patients [3]. The most effective treatment options have success rates under 50%, and for chronic forms of migraine this proportion is even lower [4]. The incidence of suicide in migraine patients has been found to be higher than in the general population [5]. Migraine patients are often admitted to the emergency ward. For this reason, the development or discovery of an effective and cheap treatment option for use in the emergency department can be of great value in the management of this disease.

Transcutaneous Electrical Nerve Stimulation (TENS) is a non-invasive analgesic technique used in the treatment of nociceptive, neuropathic, and musculo-skeletal pain [6]. This therapy uses a non-invasive, self-administered device. This device delivers electrical current that causes peripheral nerve activation and consequently provides an analgesic effect. The electrical current is supplied through a portable device during therapy, and the current is delivered to the skin via electrodes. Rigorous neurophysiological evidence shows that this device inhibits the central nervous system's nociceptive signal transmission [7,8]. In fact, TENS therapy has been shown in the literature to have a sedative effect on healthy individuals [9]. Studies which evaluate TENS' effectiveness in treating acute migraine attacks suggest that this therapy may be beneficial.

The purpose of this study was to evaluate the TENS protocol's effectiveness in treating acute migraine in the emergency department.

## **2. Methods**

### **2.1. Study Design**

This was a prospective, double-blinded, randomized controlled trial (RCT) conducted at the Emergency Department of Kartal Dr.Lütfi Kırdar Training and Research Hospital in İstanbul, Turkey.

The study was approved by the ethics committee at Kartal Dr.Lütfi Kırdar Training and Research Hospital in İstanbul, Turkey (Ethics Committee Ruling number: 2019/514/156/3). All participating patients signed an informed consent form. All authors had full access to all study data.

## 2.2. Study Population

Patients admitted to the emergency ward with complaints of migraine with or without aura were admitted to the study. Inclusion criteria for patients were defined according to their conformation to the International Headache Society classification-3 and on the condition that they hadn't received any medication prior to being admitted to the emergency department. Inclusion and exclusion criteria are shown in detail in Table 1. To be included patients had to adhere exactly to all inclusion and exclusion criteria. The Guidelines of the International Headache Society for controlled trials of acute treatment of migraine attacks in adults Fourth edition was utilized during development of the criteria.

## 2.3. Study Interventions

The primary aim of this of this study is to evaluate the value of TENS therapy for patients admitted to the emergency department presenting with acute migraine through evaluating the palliative effectiveness at the 20th and 120th minute after initiation of therapy.

Patients were treated as per the following steps. Patients first underwent 20 minutes of TENS therapy using a Headaterm TENS device. Both groups were treated for 20 minutes after connecting the TENS device. At the end of this interval, the devices were disconnected. After attaching the adhesive and conductive band and pressing the central button (Figure 1), the device works automatically. The device's standard setting delivers 20 minutes of current before shutting down.

The device's current is delivered through the electrodes and conducts low frequency electricity over the supraorbital nerve. All headache-causing signals passing through biological and physical channels can be mediated through the use of electrical current. The device harnesses this capability to prevent or slow the transmission of pain signals from the cerebral cortex's pain centers passing through through the supraorbital nerve.

Name of the product which used in the study is "TENS device- Headaterm". It's specification and model is YF-HT-W1. Technical features of the device include 27K $\Omega$  resistance and 47nF capacitance connected in parallel to the load, a pulse repetition frequency of 50 Hz ( $\pm$ 1Hz), a pulse width of 125 $\mu$ s ( $\pm$ 10 $\mu$ s), an impulse amplitude of 60V ( $\pm$ 3V), and a pulse energy of 18.4  $\mu$ J ( $\pm$ 10%) on an oscilloscope.

Figure 1: The device is attached to the forehead as shown in the figure. (Image courtesy of WAT-MED, displayed with special permission.)

In order to evaluate patients' pain, the Visual Analog Scale (VAS) was used to design a form [10]. Patients' scores were graphically represented on 100mm long linear scales. Patients filled in their perceived pain as a point on the linear scales where 0mm corresponded to "no pain" and 100mm corresponded to "most severe pain you've ever felt". Patients were evaluated three times: once at baseline, once at the 20th minute past baseline, and once at the 120th minute past baseline. To analyze patients' scores, measurements were taken in millimeters using a ruler.

At the 120th minute after initiation of treatment, patients' response to therapy was evaluated using a 1 to 5 point scoring system according to the Likert-type verbal scale. In this scale, 1 corresponds to "in severe pain", 2 to "in pain", 3 to "moderate pain", 4 to "fine", and 5 to "more than fine". After this scale was explained to patients, they were asked to choose a number corresponding to their level of pain. These numbers were recorded on their forms. At the end of the treatment and observation interval, patients were asked if they required additional treatment. Patients who requested additional treatment were provided with alternative analgesic therapies. Every patient that requested additional treatment had this noted on their forms.

On the forms that were provided, patients also filled in their age, how many years they had suffered from migraine, how often they experienced migraine episodes, and the medications they preferred to use to treat their migraine.

For patients whose complaints increased in severity and requested to discontinue treatment, meperidine (0.75 mg/kg) rescue therapy was planned.

No changes were made to the methodology after the start of the trial.

#### **2.4. Randomization**

Seventy-eight eligible patients were included in the trial and were randomly divided into a verum TENS group and a sham TENS group in a 1:1 allocation ratio.

Patients were informed of the trial in a separate emergency department room with a bed. The verum group underwent therapy using a standard Headaterm TENS device that was battery-powered and charged. The sham group underwent therapy using a device that was visually indistinguishable. However, these sham devices had an empty battery and were not electrically active. The devices were then labelled as either '1' or '2'. An opaque envelope was used for allocation concealment. To carry out the trial in a double-blind manner,

measurements were conducted with neither the researcher nor the patient knowing which group the devices belonged to. The researcher tasked with processing of the results was also unaware of which device was assigned to which patients.

## 2.5. Study Outcomes

The primary outcome of the trial was to measure the TENS treatment's effect at the 20th minute and 120th minute after initiation of treatment. Patients' post-treatment Likert-type verbal scale scores, medicine usage, duration since the start of their illness in months, frequency of migraine episodes in days, whether they suffered from migraine with or without auras, and whether TENS therapy had an effect on their migraine symptoms was also evaluated.

## 2.6. Sample Size and Statistical Analysis

In order to determine a sample size, the G\*Power (v3.1.9) software application was utilized to carry out power analysis. Using a similar study's baseline to 1 hour VAS value changes (verum group average: 3.46, sham group average: 1.78) we aimed to determine a sample size [11]. Using these differences between group values as a reference and thresholds of  $\alpha=0.05$  and  $\beta=0.20$ , we determined that each group needed at least 24 patients in order to demonstrate statistically significant differences between the two. From the start to the end of the trial, 39 patients were assigned to each group.

For statistical analysis, NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) software application was utilized. Descriptive statistical methods were used to evaluate the trial data (average, standard deviation, median, first quartile, third quartile, frequency, percentage, minimum, maximum). Quantitative data was tested for conformation to normal distribution using the Shapiro-Wilk test and graphical analysis. For normally distributed quantitative variables, independent t-tests were utilized, while for non-normally distributed quantitative variables the Mann-Whitney U test was applied. For comparison of quantitative data, both the Pearson chi-squared test and the Fisher-Freeman-Halton exact test were applied. To determine the relationship between quantitative variables the Spearman correlation coefficient was used. To analyse the effects of the groups and time on VAS, the Generalized Linear Mixed Model was used. Age, gender, history of migraine, frequency of migraine episodes, medication usage and aura presence / absence was also subjected to covariate analysis.

### 3. Results

#### 3.1. Characteristics of study subjects

During the planned 5 month study period between June 2019 and October 2019, a total of 151 patients were deemed eligible for the trial based on inclusion/exclusion criteria. Of these patients, 33 ceased to meet the inclusion criteria, 23 patients declined to participate, and 12 patients were excluded due to other reasons (e.g. consumption of alcohol/cannabinoids in the 24 hours preceding admission). The remaining 83 patients were assigned to groups. Of the patients assigned to groups, 3 subjects from the verum group withdrew due to paresthesia caused by TENS application and 2 subjects from the sham group withdrew due to severe pain. For these patients, rescue therapy was utilized. The study was carried out with 39 randomized subjects in each group (Figure 2). The patients in the treatment and control groups were similar with respect to known prognostic factors.

*Figure 2* Flow diagram of the study [12]

#### 3.2.1. Main results

No statistically significant differences between the groups were found in terms of age, sex, frequency of migraine episodes, history of migraine, or presence/absence of aura ( $p > 0.05$ ). Patients were compared in three different subgroups according to medications they used regularly: non-steroidal anti-inflammatory drug users, selective serotonin reuptake inhibitor users, and other. No significant differences between these groups were found ( $p > 0.05$ ). When compared in terms of additional analgesic therapy requirements at the 120th minute after initiation of therapy, 30 subjects assigned to the sham group (76.9%) and 1 subject assigned to the verum group (2.6%) required additional analgesic medication (Difference = 74.3%, 95% CI: 59.9% to 87.6%).

When groups were compared in terms of their Likert-type verbal scale scores, the sham group's average score was found to be 1.2 while the verum group's score was found to be 4.5, a statistically significant difference ( $p < 0.001$ ). The tests carried out using the results of the study groups and variables are displayed in table 2.

#### 3.2.2. Relation between VAS results and groups

The relationship between VAS pain score and other variables was investigated. The generalized linear mixed model was used in order to determine the factors influencing

changes in VAS scores. Each variable was also analyzed individually. Analysed in accordance with the time-group interaction model, the changes in VAS scores over time were significantly different between groups ( $F=91.742$ ,  $p<0.001$ ).

The groups' difference in time to VAS values were compared using a post-hoc comparison model (Table 3). According to this, VAS values from both groups' baseline, 20th minute after initiation of treatment and 120th minute after initiation of treatment were analyzed for changes. In the verum group, baseline to 20, baseline to 120, and 20 to 120 were found to be statistically significant ( $p<0.001$ ,  $p<0.001$ ,  $p<0.001$ , respectively). For this group the baseline to 20 interval the change was found to be  $-51.13\pm 2.94$  mm, while the 20 to 120 interval change was found to be  $14 \pm 2$  mm. This suggests that the TENS therapy was more effective in the first 20 minutes post treatment. In the sham group, the baseline to 20 change was not statistically significant ( $p>0.05$ ) while the 20 to 120 and baseline to 120 intervals were found to be statistically significant ( $p<0.001$ ,  $p<0.001$ , respectively). The groups' baseline values were not significantly different ( $p>0.05$ ). However, the sham group's 20 and 120 values were found to be higher than the verum group's ( $p<0.001$ ,  $p<0.001$ , respectively).

#### **4. Limitations**

Despite adequate provision of information, our trial was extended due to emergency department patients' agitation at time of admission, addiction to frequently used injectable treatments, and a general avoidance of electrical treatments. Better public education about these treatment modalities may lead to a reduction in prejudice and allow these treatment options to be used more frequently. Also we did not use an intention to treat analysis as there were only a few patients that dropped out after randomization. The one of the most difficult factor to blind patients was that the active ones probably felt the TENS unit.

#### **5. Discussion**

This prospective, randomized, controlled, double blinded trial investigates the effectiveness of TENS therapy in treating acute migraine in the emergency department. The trial aims to evaluate the results of treatment of acute migraine in the emergency department at the 20th and 120th minute after initiation of treatment. No treatment-related skin reactions or unwanted effects were encountered during the trial. Of the verum group, 3 patients declined

continuation of treatment due to intolerance to paresthesia, and 2 patients in the sham group declined to continue treatment due to intolerable pain. These patients opted to instead receive 0.75mg/kg meperidine rescue therapy and were excluded from the trial.

Migraine is the 3rd most common cause of disability of people under 50 [13]. This illness has negative socioeconomic, personal, and societal consequences. Migraine has multiple subtypes, and patients may experience different types simultaneously. In our study, patients classified as having migraine with or without aura were included. Migraine with aura is characterized as unilateral, slowly progressing, presenting with recurrent episodes, and possessing reversible visual, sensory, or other central nervous system symptoms. Migraine without aura lasts 4 to 72 hours, is distinctively pulsatile, unilateral, intense, and may cause nausea with exposure to light, exercise, or noise [1].

Pharmacological agents are predominantly used as a first line treatment for acute migraine episodes in the emergency department [14]. Triptans, ergotamine derivatives, NSAIDs, opioids, and combined preperates may be used as proven treatments for migraine [14-16]. These treatments, however, may prove insufficiently effective or produce unwanted side effects [17-19]. Oral, intravenous, or intramuscular utilization of these treatments may each produce these effects. The development of cheap and effective methods for treatment of migraine episodes may reduce the incidence of migraine as well as having other positive effects such as reduced patient expenses and reduced incidence of unemployment. For this reason, studies evaluating TENS treatment are valuable.

Transcutaneous Electrical Nerve Stimulation is an electrical nerve stimulation therapy applied to the skin. The spinal cord and rostral ventral medulla opioid receptors are especially affected and activated, providing an analgesic effect.

TENS is primarily used for the treatment of pain. Different frequencies are utilized for treating different types of pain. TENS can be used for the treatment of a multitude of conditions, including postoperative analgesia, fibromyalgia, and childbirth.

In our study, we analysed whether the device would be appropriate to use in the emergency department.

We demonstrated that these devices, utilized in the emergency department, can significantly decrease patients' VAS scores, and that these devices are effective within the first 20 minutes of treatment ( $p < 0.001$ ). Significant statistical and clinical differences were observed between the verum and sham groups in our trial.

The patients' perceived changes in pain were evaluated at the 0-20, 20-120 and 0-120 intervals. The greatest reduction in pain was observed in the first 20 minutes, followed by a decelerating but continuous reduction in pain after the conclusion of treatment.

Acetaminophen, aspirin, diclofenac, ibuprofen, and naproxen sodium/sumatriptan are commonly used medications in the treatment of acute migraine. Accepted as medications with a Strength of Evidence Level A, these are proven and effective [16]. At the second hour after administration, these pharmacological treatments have been shown through placebo controlled trials to decrease pain by 57.8%, 48%, 45.8%, 41.7%, and 34% respectively [20-24]. Also prochlorperazine is an effective treatment method for acute migraine attacks which has found better than iv hydromorphone [25]. In our trial, we found that treatment with the Headatorm TENS device provided 69.66% pain relief for the verum group. This result suggests that TENS devices, like NSAID drugs, may be used in acute migraine episodes and may relieve pain more rapidly than many commonly used medications.

In our trial, we observed that patients experienced a statistically significant decrease in VAS score in the baseline to 20 minute interval, followed by another decrease in the 20 - 120 minute interval. Our results suggest that, while pain relief starts from the initiation of electrical therapy, this analgesic effect continues after the treatment is concluded, albeit at a slower rate.

In a study analyzing the costs of treatment of migraine sufferers, TENS devices were shown to be cheaper than treatment in emergency departments across 5 European countries [26]. In terms of cost-effectiveness, using the TENS device may prove a superior option to than being admitted to the emergency department and receiving medication. Due to this result, more studies may be carried out in order to assess any financial advantages of TENS treatments.

The conventional drugs used for treatment of migraine possess a much broader array of side effects compared to TENS devices. These side effects may cause patients to discontinue treatment, experience chronic medical issues, or otherwise render the treatment ineffective [27-29]. In particular, NSAIDs have been shown to have frequent unwanted gastrointestinal side effects [30]. Similarly, it is prudent to note that narcotic analgesics may cause dangerous side effects like hallucinations [16,17]. TENS treatment does not commonly cause side effects, but these may still occur due to incorrect usage or allergic interactions [31,32]. Consequently, no side effects were reported in our study.

## 6. Conclusion

TENS therapy is an effective and economical treatment with few side effects and may be used in the emergency department for treatment of acute migraine episodes.

## Source of support

This study was supported by Kartal Dr. Lütfi Kırdar Training and Research Hospital. The research did not receive any financial support from any public or private organization. During the conduct of the study, written permission was obtained from WAT-MED company for the use of HeadTerm TENS device and its documentation.

## Meetings

The study was not published anywhere or presented as an oral paper.

## Authors' contributions

**NMH:** Conceptualization, Methodology, Software, Writing- Reviewing and Editing, **MOE:** Writing- Original draft preparation, Supervision, **UDH:** Supervision, Writing- Reviewing and Editing, **AA:** Investigation, Data curation **DT:** Software, Validation. **AUS:** Investigation, Validation. All authors had access to the manuscript at every stage of the preparation. They approved the upload of the manuscript all together.

## Consent for publication

Written consent forms have taken from each patient. Also for using or publishing data about HeadTerm TENS device written permission letter taken from WAT-MED.

## Availability of data and material

The datasets used and/or analyzed during the current study are open from the corresponding author on reasonable request.

## Competing interests

The author(s) declare(s) that they have no competing interests.

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## References

- [1] Ettl DA. The international classification of headache disorders, (beta version). *Cephalalgia*. 2013;33:629-808. <https://doi.org/10.1177/0333102413485658>
- [2] Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012;380(9859):2095-128. [https://doi.org/10.1016/S0140-6736\(12\)61728-0](https://doi.org/10.1016/S0140-6736(12)61728-0)
- [3] Mulleners W, Chronicle E. Anticonvulsants in migraine prophylaxis: a Cochrane review. *Cephalalgia*. 2008;28(6):585-97. <https://doi.org/10.1111/j.1468-2982.2008.01571.x>
- [4] Fumal A, Schoenen J. Current migraine management—patient acceptability and future approaches. *Neuropsychiatr Dis Treat*. 2008;4(6):1043. <https://doi.org/10.2147/NDT.S3045>
- [5] Fuller-Thomson E, Hodgins GA. Suicide Attempts among Those with Migraine: Findings from a Nationally Representative Canadian Study. *Arch Suicide Res* 2019:1-20. <https://doi.org/10.1080/13811118.2019.1578710>
- [6] Watson T. *Electrotherapy E-Book: evidence-based practice*: Elsevier Health Sciences; 2008.
- [7] Johnson MI, Bjordal JM. Transcutaneous electrical nerve stimulation for the management of painful conditions: focus on neuropathic pain. *Expert Rev. Neurother* 2011;11(5):735-53. <https://doi.org/10.1586/ern.11.48>
- [8] Vance CGT, Rakel BA, Blodgett NP, DeSantana JM, Amendola A, Zimmerman MB, et al. Effects of transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: a randomized controlled trial. *Phys. Ther*. 2012;92(7):898-910. <https://doi.org/10.2522/ptj.20110183>
- [9] Piquet M, Balestra C, Sava SL, Schoenen JE. Supraorbital transcutaneous neurostimulation has sedative effects in healthy subjects. *BMC Neurol*. 2011;11(1):135. <https://doi.org/10.1186/1471-2377-11-135>

- [10] Huskisson EC. Measurement of pain. *The lancet*. 1974;304(7889):1127-31.
- [11] Chou DE, Shnayderman Y, Yurakh M, Winegarner D, Rowe V, Kuruvilla D, Schoenen J. Acute migraine therapy with external trigeminal neurostimulation (ACME): a randomized controlled trial. *Cephalalgia*. 2019;39(1):3-14. <https://doi.org/10.1177/0333102418811573>
- [12] CONSORT BT. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med*. 2010:152.
- [13] Steiner TJ, Stovner LJ, Vos T. GBD 2015: migraine is the third cause of disability in under 50s. 2016. <https://doi.org/10.1186/s10194-016-0699-5>
- [14] Steiner T, Paemeleire K, Jensen R, Valade D, Savi L, Lainez M, et al. European principles of management of common headache disorders in primary care. *J. Headache Pain* 2007;8:S3-47.
- [15] Lipton RB, Silberstein SD. Episodic and chronic migraine headache: breaking down barriers to optimal treatment and prevention. *Headache*. 2015;55:103-22. [https://doi.org/10.1111/head.12505\\_2](https://doi.org/10.1111/head.12505_2)
- [16] Marmura MJ, Silberstein SD, Schwedt TJ. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. *Headache*. 2015;55(1):3-20. <https://doi.org/10.1111/head.12499>
- [17] Colak S, Erdogan MO, Afacan MA, Kosargelir M, Aktas S, Tayfur İ, et al. Neuropsychiatric side effects due to a transdermal fentanyl patch: hallucinations. *Am J Emerg Med* 2015;33(3):477. e1-. e2. <https://doi.org/10.1016/j.ajem.2014.08.051>
- [18] Schoenen J. Migraine treatment with external trigeminal nerve stimulation: current knowledge on mechanisms. *Int Med Rev* 2017.
- [19] Colak S, Erdogan MO, Sekban H, Afacan MA, Uras AR, Ibrahim A, et al. Emergency diagnosis of upper gastrointestinal bleeding by detection of haemoglobin in nasogastric aspirate. *J Int Med Res*. 2013;41(6):1825-9. <https://doi.org/10.1177/0300060513505516>
- [20] Lipton RB, Baggish JS, Stewart WF, Codispoti JR, Fu M. Efficacy and safety of acetaminophen in the treatment of migraine: results of a randomized, double-blind, placebo-controlled, population-based study. *Arch Intern Med*. 2000;160(22):3486-92. <http://doi.org/10.1001/archinte.160.22.3486>
- [21] MacGregor EA, Dowson A, Davies PT. Mouth- dispersible aspirin in the treatment of migraine: a placebo- controlled study. *Headache*. 2002;42(4):249-55. <https://doi.org/10.1046/j.1526-4610.2002.02076.x>
- [22] Vecsei L, Gallacchi G, Sagi I, Semjen J, Tajti J, Szok D, et al. Diclofenac epolamine is effective in the treatment of acute migraine attacks. A randomized, crossover, double blind, placebo-controlled, clinical study. *Cephalalgia*. 2007;27(1):29-34. <https://doi.org/10.1111/j.1468-2982.2007.01236.x>

- [23] Codispoti JR, Prior MJ, Fu M, Harte CM, Nelson EB. Efficacy of nonprescription doses of ibuprofen for treating migraine headache. A randomized controlled trial. *Headache*. 2001;41(7):665-79. <https://doi.org/10.1046/j.1526-4610.2001.041007665.x>
- [24] Brandes JL, Kudrow D, Stark SR, O'Carroll CP, Adelman JU, O'Donnell FJ, et al. Sumatriptan-naproxen for acute treatment of migraine: a randomized trial. *Jama*. 2007;297(13):1443-54. <http://doi.org/10.1001/jama.297.13.1443>
- [25] Friedman BW, Irizarry E, Solorzano C, Latev A, Rosa K, Zias E, et al. Randomized study of IV prochlorperazine plus diphenhydramine vs IV hydromorphone for migraine. *Neurology*. 2017;89(20):2075-82. <http://doi.org/10.1212/WNL.0000000000004642>
- [26] Bloudek L, Stokes M, Buse D, Wilcox T, Lipton RB, Goadsby P, et al. Cost of healthcare for patients with migraine in five European countries: results from the International Burden of Migraine Study (IBMS). *J Headache Pain* 2012;13(5):361. <http://doi.org/10.1007/s10194-012-0460-7>
- [27] Schoenen J, Vandersmissen B, Jeanette S, Herroelen L, Vandenheede M, Gérard P, et al. Migraine prevention with a supraorbital transcutaneous stimulator: a randomized controlled trial. *Neurology*. 2013;80(8):697-704. <https://doi.org/10.1212/WNL.0b013e3182825055>
- [28] Magis D, Sava S, d'Elia TS, Baschi R, Schoenen J. Safety and patients' satisfaction of transcutaneous supraorbital neurostimulation (tSNS) with the Cefaly® device in headache treatment: a survey of 2,313 headache sufferers in the general population. *J Headache Pain* 2013;14(1):95. <https://doi.org/10.1186/1129-2377-14-95>
- [29] Lipton RB, Buse DC, Serrano D, Holland S, Reed ML. Examination of Unmet Treatment Needs Among Persons With Episodic Migraine: Results of the American Migraine Prevalence and Prevention (AMPP) Study. *Headache*. 2013;53(8):1300-11. <https://doi.org/10.1111/head.12154>
- [30] Singh G, Triadafilopoulos G. Epidemiology of NSAID induced gastrointestinal complications. *The J Rheumatol Suppl* 1999;56:18-24.
- [31] Llamas M, Santiago D, Navarro R, Sánchez- Pérez J, García- Díez A. Unusual allergic contact dermatitis produced by a transcutaneous electrical nerve stimulator. *Contact dermatitis*. 2010;62(3):189-90.
- [32] Ford KS, Shrader MW, Smith J, Mclean TJ, Dahm DL. Full-thickness burn formation after the use of electrical stimulation for rehabilitation of unicompartmental knee arthroplasty. *J Arthroplasty*. 2005;20(7):950-3. <https://doi.org/10.1016/j.arth.2004.10.018>

## Tables

**Table 1: Inclusion / Exclusion Criteria**

***Inclusion Criteria***

- *Patients' conformation to the International Headache Society(IHS CLASSIFICATION ICHD-3) migraine criteria*
- *No medication taken prior to admission to the emergency department*
- *Over 18 years old*
- *Below 50 years of age*
- *History of diagnosed migraine*
- *Frequency of migraine episodes between 2 and 8 per month*
- *Interval of at least 48 hours without headache between migraine episodes*
- *Diagnosis of migraine at least 1 year prior to admission*
- *All preventative migraine treatments ceased at least 1 month before admission*

***Exclusion Criteria***

- *Pregnancy*
- *History of epilepsy or arrhythmia*
- *Cranial implants, cardiac pacemakers, metal foreign objects inside patients*
- *Brain tumors or acute cerebrovascular event patients*
- *Patients with history of head trauma*
- *Patients with history of psychiatric disease*
- *Patients with a fever of more than 38 degrees or suspected meningitis*
- *Patients with any altered consciousness or meningeal irritation*
- *Hypertension*
- *Secondary headaches e.g. medication-overuse headache*
  - *15 headache days per month.*

**Table 2. Comparison of descriptive characteristics between groups**

	Total (n=78)	Sham (n=39)	Verum (n=39)
<b>Age</b>	34.61±9.50	33.62±10.20	35.62±8.77
<b>Gender (1); n (%)</b>	30 (38.5)	15 (38.5)	15 (38.5)
<b>Migraine history (months)</b>	72 (36, 120)	84 (48, 120)	60 (36, 120)
<b>Migraine frequency (months)</b>	4 (3, 6)	4 (3, 7)	5 (4, 6)
<b>Medication</b>			
NSAID	48 (61.5)	24 (61.5)	24 (61.5)
SSRI	21 (26.9)	11 (28.2)	10 (25.6)
Other	9 (11.5)	4 (10.3)	5 (12.8)
<b>Aura (+)</b>	20 (25.6)	12 (30.8)	8 (20.5)
<b>Additional therapy requirement</b>	31 (39.7)	30 (76.9)	1 (2.6)
<b>Likert-type verbal scale</b>	3 (1, 5)	1 (1, 2)	5 (4, 5)

**Table 3. Post-hoc comparisons regarding group \* time interaction**

	Sham (n=39)	Verum (n=39)	<sup>a</sup> p
	mean±se	mean±se	
<b>Baseline</b>	73±3	73±3	
<b>20</b>	72±2	22±2	<0.001**
<b>120</b>	63±2	7±2	<0.001**

<sup>a</sup>Inter-group comparisons

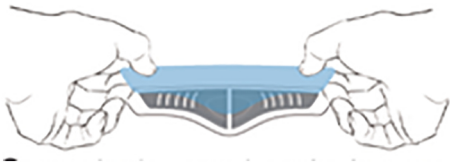


Figure 1

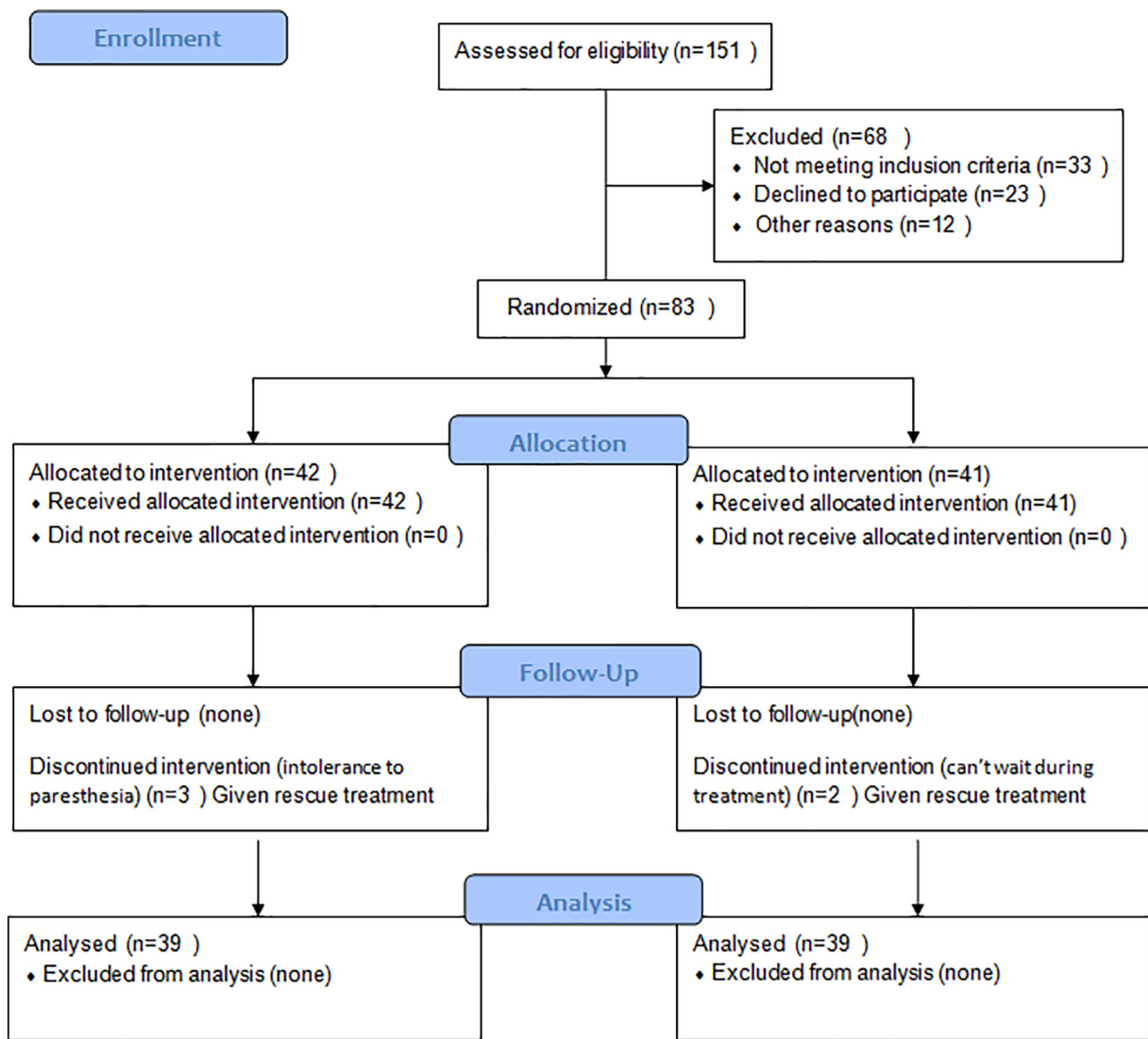


Figure 2