

# Effects of preemptive intravenous paracetamol and ibuprofen on headache and myalgia in patients after electroconvulsive therapy

## A placebo-controlled, double-blind, randomized clinical trial

Erol Karaaslan<sup>a,\*</sup>, Sedat Akbas<sup>a</sup>, Ahmet Selim Ozkan<sup>a</sup>, Esra Porgalı Zayman<sup>b</sup>

### Abstract

**Background:** The aim of this study is to determine the efficacy of preemptive analgesia with paracetamol and ibuprofen to reduce the intensity and incidence of headache and myalgia after electroconvulsive therapy (ECT).

**Methods:** Sixty patients with major depression who were treated with ECT were randomized to receive ECT 3 times a week. The first 3 sessions were included in the study. The patients were divided into 3 groups; Group C (Control, Saline, n=20), Group P (Paracetamol, n=20), and Group I (Ibuprofen, n=20). Demographics, duration of seizure, visual analog scale (VAS) for headache and myalgia and nausea, vomiting and pruritus were evaluated at postoperative 24 hours period.

**Results:** Duration of seizure after ECT was similar in all groups ( $P=.148$ ). In the study, heart rate and mean arterial pressure were found to be some changes in some of the sessions. There were no significant differences in any comparison for all groups in all sessions regarding VAS scores for headache and myalgia. Incidence of headache and myalgia in Group I was lower than the other groups ( $P=.233$ ,  $P=.011$ , respectively). But, there was no significant difference between the other groups. There was no significant difference in vomiting, intergroups, and intragroup.

**Conclusions:** The findings of our study indicate that pain intensity of headache and myalgia did not show a significant change between groups and within groups. While pain intensity of myalgia between the groups reached no statistical significance, ibuprofen was significantly lowered the incidence of myalgia at postoperative 24 hours period.

**Abbreviations:** ASA = American Society of Anesthesiologists, Control = group C, ECT = electroconvulsive therapy, HR = heart rate, Ibuprofen = group I, MAP = mean arterial pressure, NSAID = nonsteroidal anti-inflammatory drug, Paracetamol = group P, VAS = visual analog scale.

**Keywords:** electroconvulsive therapy, headache, ibuprofen, myalgia, paracetamol

Editor: Somchai Amorniyotin.

This study was approved by the LECIU Medical Faculty, Malatya, Turkey (Protocol no: 2018/01).

ECT trial is registered at the US NIH (ClinicalTrials.gov) #NCT03783312.

This study was supported by the Inonu University Coordination Unit of Scientific research projects (Project no: TSA-2018-1067).

The authors have no conflicts of interest to disclose.

<sup>a</sup> Department of Anesthesiology, <sup>b</sup> Department of Psychiatry, Inonu University Medical Faculty, Malatya, Turkey.

\* Correspondence: Erol Karaaslan, Department of Anesthesiology and Reanimation, Inonu University Medical Faculty, Malatya, Turkey (e-mail: erkara44@hotmail.com).

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How to cite this article: Karaaslan E, Akbas S, Ozkan AS, Zayman EP. Effects of preemptive intravenous paracetamol and ibuprofen on headache and myalgia in patients after electroconvulsive therapy: A placebo-controlled, double-blind, randomized clinical trial. *Medicine* 2019;98:51(e18473).

Received: 29 March 2019 / Received in final form: 28 September 2019 /

Accepted: 21 November 2019

<http://dx.doi.org/10.1097/MD.0000000000018473>

## 1. Introduction

Electroconvulsive therapy (ECT) is considered to be the most effective and rapid treatment in patients with major depression.<sup>[1]</sup> Treatment response to ECT in patients with mania and major depression was reported as 78% and 83%, respectively ECT is performed under general anesthesia and the electric current causes tonic clonic seizures for approximately 20 to 60 seconds.<sup>[2]</sup> Treatments are typically performed 3 times a week for a total of 6 to 12 sessions.<sup>[3]</sup> The mechanism of action of ECT is unclear, but recent studies suggest that it leads to an increase in nerve cell growth factor and hippocampus volume.<sup>[4]</sup>

Headache is one of the most common side effects of ECT and seen in 48% to 85% of patients who undergo the treatment.<sup>[2,5]</sup> Headaches begin immediately after patients regain consciousness or after a short time interval. There are several theories such as vascular changes, stimulating 5-hydroxytryptamine<sub>2</sub> receptors and succinylcholine inducing contractions, increased cerebral blood flow, and blood pressure concerning the etiology of headache after ECT.<sup>[5]</sup>

Another known side effect after ECT is myalgia. Although the mechanism of myalgia is not fully known, it has been suggested to be caused by the use of muscle relaxant agents such as succinylcholine, as well as muscle injury due to fasciculation and seizures during the procedure.<sup>[6]</sup>

Preemptive analgesia has been described as an effective method for the prevention of headache after ECT.<sup>[2]</sup> Patients with severe and untreated myalgia and headache cannot tolerate the pain and may discontinue treatment.<sup>[7]</sup> Effective analgesic treatment is important for continued treatment and patient comfort.

To our knowledge, this is one of the few studies to evaluate both paracetamol and ibuprofen in terms of headache and myalgia. The primary aim of this double-blind, placebo-controlled, randomized study is to evaluate the efficacy of preemptive analgesia with paracetamol and ibuprofen to reduce the incidence and intensity of headache and myalgia after ECT. Also, secondary aim is to analyze the effects on hemodynamics, duration of seizure, and postoperative side effects (nausea, vomiting, and pruritus) in patients who underwent ECT.

## 2. Methods

### 2.1. Protocol

This trial was approved by the Local Ethic Committee of Inonu University (Protocol no: 2018/01) and registered at the US National Institutes of Health (Clinical Trials.gov) #NCT03783312. We conducted a prospective, randomized, double-blind, placebo-controlled clinical trial with 60 patients scheduled for ECT under general anesthesia from December 2018 to February 2019 at a university hospital. This study was prepared in accordance with the consolidated standards of reporting trials guidelines.<sup>[8]</sup>

### 2.2. Study participants

Patients, who were treated with ECT for a diagnosis of major depression, with American Society of Anesthesiologists (ASA) scores I-II and 18 to 65 years old were included in this study.

Patients were randomized to receive ECT 3 times a week to complete an average of 6 to 12 ECT sessions. The first 3 sessions of each patient were included in the current study.

Patients with ASA score III-IV, under the age of 18, over the age of 65 and with pregnancy, myocardial infarction or stroke within the last 3 months, congestive heart failure, lung disease, liver and kidney dysfunction, bleeding disorders, migraine, neuromuscular disease, peptic ulcer, intracranial hypertension, glaucoma, allergic history to paracetamol, succinylcholine, propofol or any type of nonsteroidal anti-inflammatory drug (NSAID), and refused informed consent form were excluded from the study.

### 2.3. Randomization

This study was planned as a randomized prospective trial. Randomization was conducted by an independent researcher with the MedCalc for Windows (medcalc.com.tr.), version 16 statistical software to receive either normal saline placebo, 1 g of intravenous (IV) paracetamol or 800 mg of IV ibuprofen.

### 2.4. Study design

Written informed consent was obtained from patients who agreed to participate in the study. The study was performed in accordance with the Helsinki Declaration. On the day of ECT procedure, all patients were informed about the undergoing study and all drugs including opioids, paracetamol, NSAIDs, and possible related side effects. The patients were divided double-blinded into 3 groups (Group C: control, saline, n=20, Group P: paracetamol, n=20 and Group I: ibuprofen, n=20) using sealed in opaque envelopes by a research coordinator without involvement of further study (Fig. 1. Flow diagram). The anesthesia nurse got 1 envelope and prepared all the study

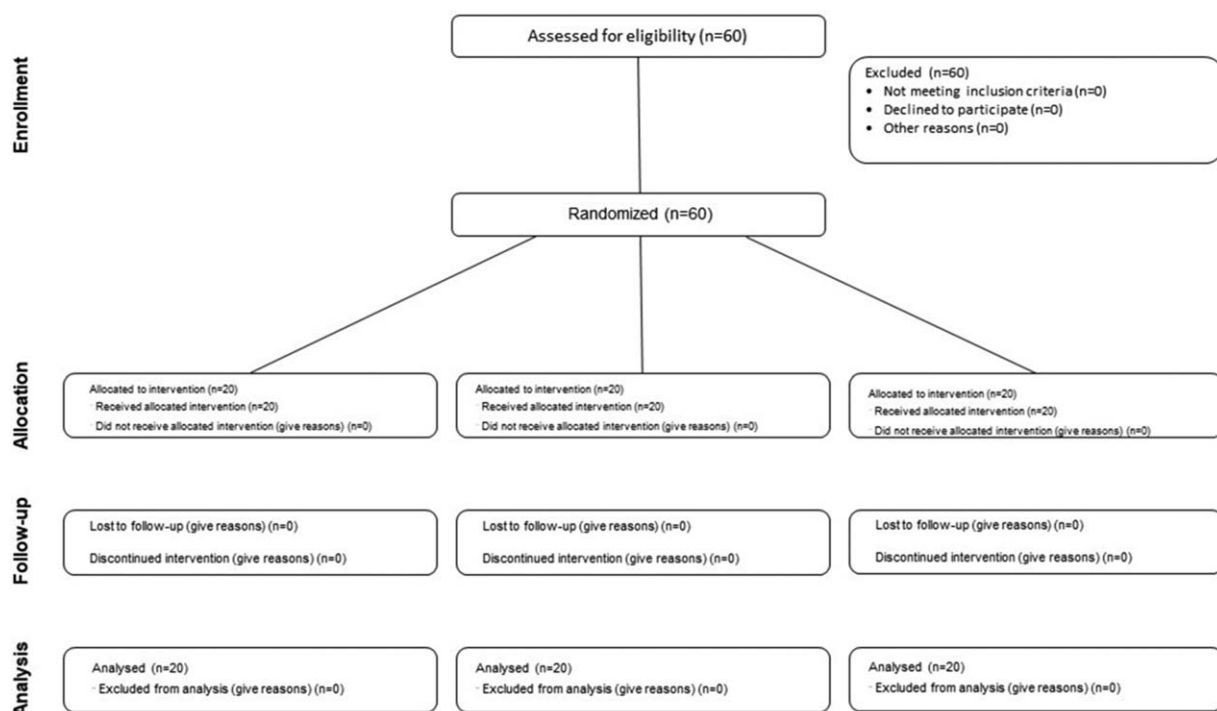


Figure 1. Flow diagram. Group C = control, saline n=20, Group I = ibuprofen n=20, Group P = paracetamol n=20.

solutions. Analgesic drugs were prepared before preemptive administration with 250 mL of saline for Group C, 1g of paracetamol for Group P and 800 mg of ibuprofen (diluted with 250 mL of saline) for Group I. The anesthesia nurse was not involved in the further study; patients and anesthesiologists performing anesthesia were blinded to the allocation.

### 2.5. Preoperative procedures

Premedication of midazolam was not performed to any patient. Preemptive normal saline, 1 g of IV paracetamol or 800 mg of IV ibuprofen were administered 60 minutes before ECT procedure. Patients were then taken to the operating room. Standard monitoring procedures were used, including heart rate (HR), mean arterial pressure (MAP), electrocardiogram, and peripheral oxygen saturation.

### 2.6. General anesthesia and ECT procedure

A standardized general anesthesia protocol was performed to all patients by an experienced anesthesiologist. After preoxygenation (100% 4L/min O<sub>2</sub> for 3 minutes), propofol (2–2.5 mg/kg) and succinylcholine (1 mg/kg) were administered during the induction of anesthesia via IV route. Assisted mask ventilation was initiated with 100% oxygen and continued during the clonic phase to avoid oxygen desaturation, and was maintained until adequate spontaneous ventilation resumed. The bite block was removed when seizure activity had stopped. Before the treatment, a bite block was placed in the patient's mouth to prevent tongue biting and to protect teeth. Atropine (0.015 mg/kg) was administered to patients if they had severe bradycardia during and after ECT. Esmolol (0.5 mg/kg, bolus) was administered to patients with severe hypertension and tachycardia.

Thymatron system IV (Somatics, LLC, Lake Bluff, IL, Class 1, type BF) ECT machine was used in the treatment of all patients and electrical stimuli were delivered via bitemporal electrodes. All the study participants received bilateral ECT and the energy level was calculated according to the stimulus dosing method.<sup>[9]</sup> Energy levels used in administering ECTs were decided according to the individual seizure thresholds which varied from person to person with age, gender, and current medication.<sup>[10]</sup> Electroencephalogram (EEG) tracings were recorded continuously from 2 frontal electrodes. The duration of the EEG seizure was recorded from the EEG trace.

### 2.7. Outcome measures

Primary outcome measures were the pain intensity of headache and myalgia after ECT. Patients were evaluated for pain intensity using a visual analog scale (VAS) score<sup>[11]</sup> (from 0–10, 0=no pain and 10=the worst pain imaginable). VAS (myalgia) and VAS (headache) were postoperatively recorded by trained nurses who were blinded to the patient group at T4 (postop 2nd hour), T5 (postop 4th hour), T6 (postop 6th hour), T7 (postop 12th hour), T9 (postop 24th hour). On the other hand, presence of headache and myalgia at postoperative period is defined by a scale with 0=absent or 1=present.

The hemodynamics, duration and severity of seizure, and postoperative side effects were evaluated for all groups as secondary outcome measures. The hemodynamics including HR and MAP were perioperatively recorded at T0 (5 minutes before the procedure), T1 (3 minutes after the anesthesia induction), T2 (post-seizure), T3 (5 minutes after the procedure). The duration

of seizure was defined as the time from start of the motor seizure to the cessation of tonic-clonic movements in the isolated arm. The duration of seizure was monitored during each ECT session and was used as a reference for dose adjustment, as motor seizures lasting less than 15 seconds without a tonic-clonic phase are ineffective in treatment<sup>[12,13]</sup> while seizures lasting more than 120 seconds are defined as prolonged seizure. The presence of long-term seizures is not a contraindication for ECT; however, the use of concomitant medications that reduce the seizure threshold, the presence of electrolyte imbalance, and the presence of inadequate hydration are important parameters to be considered. In case of prolonged seizure, patients were treated with oxygen and anticonvulsive drugs.<sup>[14]</sup> Postoperative side effects (presence of nausea, vomiting, and pruritus) were also recorded by trained nurses at postoperative period and also is defined by a scale with 0=absent or 1=present.

### 2.8. Postoperative management

Patients, who had no complications during or after the ECT procedure, were then transferred to the post-anesthesia care unit. Patients with stable hemodynamics and adequate spontaneous breathing (saturation >97%) were kept for approximately 1 hour in the post-anesthesia care unit. Patients scored 9 and higher in the modified Aldrete score were transferred to the psychiatry ward.<sup>[15]</sup>

In patients with tonic-clonic seizures lasting more than 1 minute, IV midazolam (3 mg) was administered, and if the patient complained of a headache and myalgia (in case of the pain score  $\geq 4/10$  on VAS during 1–24 hours), the patient was treated with IV ketorolac (30 mg).

### 2.9. Statistical analysis

All analyses were performed in SPSS v21 for Windows. Power analysis was performed to determine the number of patients required to complete the study with the following parameters: effect size: 0.5, alpha error: 0.05, 90% power. The result showed that a total of 54 patients (18 in each group) had to be enrolled into the study. For the normality check, the Shapiro Wilk test was used. Analysis of HR and MAP was performed by using multivariate repeated measurements analysis variances. For pairwise comparisons, Fisher least significant difference method was used. Analysis of VAS scores were made by using Friedman test for repeated measurements. For the between groups comparison of VAS scores, differences between measurements were calculated, then these differences were compared by the Kruskal-Wallis test. Analysis of categorical variables were made by using generalized estimating equations models and Cochran Q Test.  $P < .05$  values were accepted to show statistical significance.

## 3. Results

We included a total of 60 patients (30 males and 30 females) into this study and mean age was  $36.62 \pm 12.64$  years. There were no significant differences between the groups regarding age, sex, height, weight, and body mass index, ideal body weight and ASA scores. Duration of anesthesia and operation were similar between groups and also between sessions. Between-group comparisons showed that duration of seizure was similar between groups ( $P = .148$ ). On the other hand, in the controls, duration of seizure in the second session of ECT was significantly lower than session 1 ( $P = .008$ ). In the Group P, seizure duration

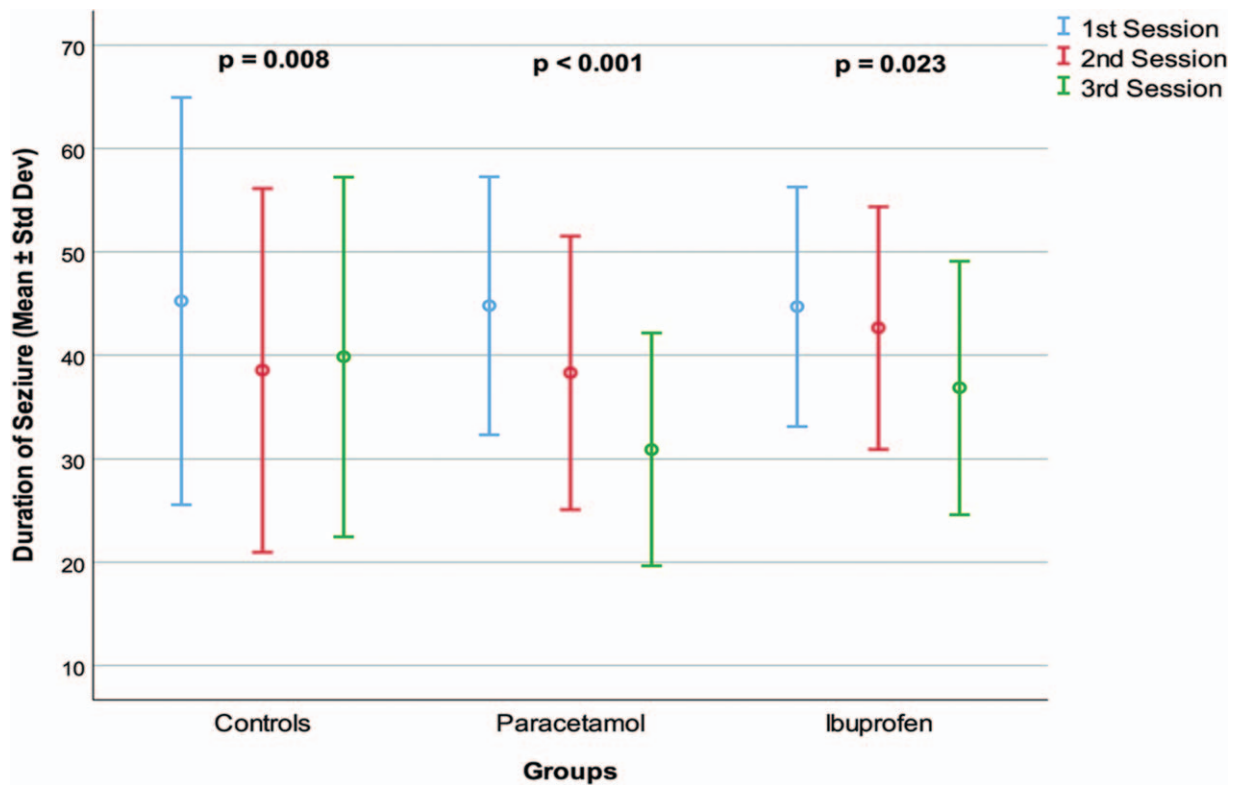


Figure 2. Duration of seizure. \* $P < .05$ , statistically significant. Group C = control, Group I = ibuprofen, Group P = paracetamol.

showed a significant reduction from session 1 to session 2 and session 3 ( $P < .001$ ). In the Group I, session 3 seizure duration was significantly lower than session 1 ( $P = .023$ ; Fig. 2). Summary of patients' characteristics and intervention durations are presented in Table 1.

There were no significant differences in any comparison (neither between group nor repeated measurements) for all groups in all sessions regarding VAS scores for headache. Headache VAS scores of the patients after sessions and analysis results are presented in Table 2. When we evaluated VAS scores for myalgia we found no significant differences between our groups and repeated measurements for all groups in all sessions. Myalgia VAS scores of the patients after sessions and analysis results are presented in Table 3.

During postoperative 24 hours period, incidence of headache in Group I was lower than the other groups, while there were no significant differences between the groups ( $P_{i\frac{1}{2}} = i\frac{1}{2}.233$ ). While myalgia VAS scores between the groups reached no statistical significance, we evaluated the presence of myalgia at postoperative 24 hours period, we found that myalgia was less common in the Group I than the other groups ( $P = .011$ ). Presence of headache and myalgia at the patients after sessions are presented in Table 4.

And, 12th and 24th hours HR (after operation) were significantly lower than the HR values after induction, at 4th and 6th hours ( $P = .036$ ). In the Group I, HR values after induction and seizure were significantly lower than 2nd hour and all of the following HR measurements ( $P = .001$ ). In the third session, 2nd, 4th, and 6th hours HR values were significantly higher than before induction, after induction and after seizure HR values in the Group C ( $P = .001$ ; Fig. 3). We observed that

atropine was administered to 1 patient in Group C and 1 patients in Group P.

In the first session; before induction, after induction, after seizure and after 5 minutes MAP values were significantly higher than 2nd hour values and all of the following measurements in the Group C ( $P < .001$ ). In the Group P, before induction, after induction, after seizure, and after 5 minutes MAP were significantly higher than 4th hour and the following measurements ( $P < .001$ ). In the Group I, before induction, after induction, after seizure and, after 5 minutes MAP were significantly higher than 6th hour and all following measurements ( $P = .001$ ). In the second session; in the Group C, before induction, after induction, after seizure, and after 5 minutes MAP values were significantly higher than 2nd hour and all following measurements ( $P < .001$ ). In the Group P, after seizure MAP value was significantly higher than 2nd hour and all following measurements ( $P = .001$ ). In the Group I, after seizure and after 5 minutes MAP values were significantly higher than 12th hour and 24th hour MAP values ( $P = .007$ ). Finally in the third session; in the Group C, before induction MAP was found to be significantly higher than all other measurements ( $P = .017$ ). In the Group P, before induction, after seizure, and after 5 minutes MAP values were significantly higher than 4th hour and all following measurements ( $P < .001$ ). In the Group I, after seizure and after 5 minutes MAP values were significantly higher than 6th hour, 12th hour, and 24th hour values ( $P < .001$ ). Additionally, we found that third session MAP was significantly higher than the first session in the Group I ( $P = .014$ ; Fig. 4). We observed that esmolol was administered to 2 patients in Group C and 1 patients in Group P

We observed that 6 patients in Group C, 4 patients in each Group P and I had nausea. Also 4, patients in Group C, 2 patients in each Group P and I groups had vomiting. We observed that 1

**Table 1**  
Summary of patient's characteristics and intervention durations.

	Control (n=20)	Paracetamol (n=20)	Ibuprofen (n=20)	P (between groups)
Age, yr	36.15 ± 15.41	37.00 ± 12.32	36.70 ± 10.31	.978
Sex				
Male, n (%)	9 (45.00)	10 (50.00)	11 (55.00)	.819
Female, n (%)	11 (55.00)	10 (50.00)	9 (45.00)	
Height, cm	170.10 ± 11.06	166.05 ± 8.00	165.00 ± 6.77	.163
Weight, kg	69.95 ± 9.25	70.60 ± 10.66	69.30 ± 11.12	.925
BMI, kg	23.65 ± 2.89	25.05 ± 2.63	25.15 ± 3.28	.206
IBW, kg	61.80 ± 10.57	57.60 ± 7.23	57.05 ± 5.75	.137
ASA				
I, n (%)	9 (45)	8 (40)	6 (30)	.610
II, n (%)	11 (55)	12 (60)	14 (70)	
Duration of anesthesia, s				
1st Session	367.90 ± 73.26	354.75 ± 63.54	365.50 ± 75.96	.666
2nd Session	345.55 ± 60.69	361.40 ± 52.49	365.00 ± 65.31	
3rd Session	342.55 ± 84.50	350.15 ± 45.64	365.20 ± 77.98	
P (within groups)	.121	.474	.972	
Duration of operation, s				
1st Session	58.65 ± 11.87	55.40 ± 8.96	54.25 ± 9.01	.161
2nd Session	54.70 ± 14.39	52.05 ± 10.08	55.50 ± 10.31	
3rd Session	61.90 ± 11.29	53.20 ± 11.77	56.00 ± 11.34	
P (within groups)	.104	.201	.421	
Duration of seizure, s				
1st Session	45.25 ± 19.69	44.80 ± 12.46	44.70 ± 11.57	.148
2nd Session	38.55 ± 17.59	38.30 ± 13.21	42.65 ± 11.72	
3rd Session	39.85 ± 17.39	30.90 ± 11.24	36.85 ± 12.24	
P (within groups)	.008*	<.001*	.023*	

Data given as mean ± standard deviation or frequency (percentage).

ASA = American Society of Anesthesiologist, BMI = body mass index, IBW = ideal body weight.

\* P < .05, statistically significant, duration of anesthesia was defined as the time from the patient is taken to the operating room until transfer to the post anesthesia care unit, duration of operation was defined as the time from placing the electrodes bitemporally in the respective regions until removal after the process was completed, duration of seizure was defined as the time from start of the motor seizure to the cessation of tonic clonic movements in the isolated arm.

**Table 2**  
Headache VAS scores of the patients after sessions and analysis results.

	Control	Paracetamol	Ibuprofen	P value (between groups)
VAS scores (headache)				
Session 1				
After 2 h	0 (0–6)	0 (0–6)	0 (0–4)	.432
After 4 h	0 (0–8)	0 (0–6)	0 (0–6)	
After 6 h	0 (0–2)	0 (0–6)	0 (0–6)	
After 12 h	0 (0–0)	0 (0–2)	0 (0–0)	
After 24 h	0 (0–0)	0 (0–0)	0 (0–2)	
P-value (within groups)	.051	.121	.294	
Session 2				
After 2 h	0 (0–6)	0 (0–6)	0 (0–4)	.352
After 4 h	0 (0–2)	0 (0–6)	0 (0–2)	
After 6 h	0 (0–2)	0 (0–6)	0 (0–4)	
After 12 h	0 (0–2)	0 (0–0)	0 (0–2)	
After 24 h	0 (0–0)	0 (0–2)	0 (0–0)	
P-value (within groups)	.121	.177	.688	
Session 3				
After 2 h	0 (0–8)	0 (0–6)	0 (0–4)	.183
After 4 h	0 (0–4)	0 (0–2)	0 (0–2)	
After 6 h	0 (0–0)	0 (0–2)	0 (0–0)	
After 12 h	0 (0–0)	0 (0–0)	0 (0–0)	
After 24 h	0 (0–0)	0 (0–2)	0 (0–2)	
P-value (within groups)	.110	.119	.406	

Data given as median (minimum–maximum).

VAS = visual analog scale.

**Table 3**  
Myalgia VAS scores of the patients after sessions and analysis results.

	Control	Paracetamol	Ibuprofen	P-value (between groups)
VAS Scores (Myalgia)				
Session 1				
After 2 h	0 (0–6)	0 (0–6)	0 (0–6)	.765
After 4 h	0 (0–8)	0 (0–6)	0 (0–2)	
After 6 h	0 (0–6)	0 (0–2)	0 (0–6)	
After 12 h	0 (0–4)	0 (0–6)	0 (0–0)	
After 24 h	0 (0–4)	0 (0–2)	0 (0–0)	
P-value (within groups)	.189	.053	.210	
Session 2				
After 2 h	0 (0–6)	0 (0–4)	0 (0–6)	.394
After 4 h	0 (0–6)	0 (0–2)	0 (0–4)	
After 6 h	0 (0–2)	0 (0–2)	0 (0–0)	
After 12 h	0 (0–0)	0 (0–0)	0 (0–0)	
After 24 h	0 (0–0)	0 (0–0)	0 (0–0)	
P-value (within groups)	.250	.162	.236	
Session 3				
After 2 h	0 (0–8)	0 (0–6)	0 (0–4)	.639
After 4 h	0 (0–4)	0 (0–4)	0 (0–2)	
After 6 h	0 (0–4)	0 (0–2)	0 (0–0)	
After 12 h	0 (0–4)	0 (0–2)	0 (0–0)	
After 24 h	0 (0–6)	0 (0–6)	0 (0–0)	
P-value (within groups)	.211	.369	.424	

Data given as median (minimum–maximum).

VAS = visual analog scale.

	Control	Paracetamol	Ibuprofen	P-value
Headache, n (%)	13 (65%)	14 (70%)	9 (45%)	.233
Myalgia, n (%)	15 (75%)	15 (75%)	7 (35%)	.011*

Data given as frequency (percentage).

\*  $P < .05$ , statistically significant.

patient in Group C and 2 patients in Group I had pruritus. On the other hand, none of the patients had pruritus in the Group P in all sessions. Also, there were no significant differences between the groups regarding postoperative side effects. Presence of postoperative side effects are presented in Table 5.

#### 4. Discussion

ECT has been used safely in the treatment of various psychiatric diseases for more than 70 years. It is known that ECT has many side effects such as headache, myalgia, and nausea and vomiting; making the management of these side effects crucial for patient quality of life and also continuation of treatment.<sup>[16]</sup>

The seizure duration is considered the standard for determining therapeutic efficacy and a motor seizure (typically lasting for a minimum of 20–25 seconds) is recommended. The dose of treatment, age, sex, number of treatments, and the use of psychotropic drugs may affect seizure duration. It has been shown that age and number of treatments are usually inversely proportional to seizure duration.<sup>[17]</sup> In the current study, as expected, seizure durations reduced after the first session in all groups; however, the reduction in duration was more pronounced in the Group P.

Headache is one of the most common side effects of ECT. The American Psychiatric Association recommends symptomatic prophylactic use of paracetamol and NSAID drugs for the treatment of headache after ECT. It has been reported that

preemptive analgesia is effective in pain management, and paracetamol and ibuprofen have been shown to have significant efficacy in preemptive analgesia.<sup>[9,18]</sup> However, in the present study, no differences were found in inter and intragroup comparisons in terms of headache VAS scores. In a study conducted by Isuru et al,<sup>[2]</sup> it was reported that the frequency of headache was significantly lower in those who received acetaminophen (paracetamol) compared to placebo (36% vs 71%, respectively,  $P < .001$ ). Similarly, paracetamol has also been shown to significantly decrease headache VAS scores after ECT.<sup>[19]</sup> Ibuprofen has also been shown to have significant effects in preventing headaches after ECT (vs placebo,  $P = .022$ ) in a study by Leung et al.<sup>[18]</sup>

Various other studies have shown that naproxen sodium,<sup>[20]</sup> topiramate and methylsalicylate<sup>[21–23]</sup> are also effective in reducing headache frequency or severity after ECT. Although studies with contrasting results also exist; for instance, it was reported that headache frequency after ECT was similar in recipients of ketorolac and placebo the majority of studies reported significant efficacy with NSAIDs in the prevention of post-ECT headaches.<sup>[3]</sup> Our results were largely in contrast with these studies; this may have been caused by the relatively low number of patients included in our study (even though we included a higher number of patients than the values obtained with power analysis). We believe the differences observed in various studies may be attributed to the number of patients included in studies, as well as other environmental factors and the differences in the use of analgesics in each study.

Another common side effect after ECT is myalgia, which is sometimes very severe. Myalgia may also lead to patient dissatisfaction, sometimes causing rejection of effective treatment. It is still unclear whether myalgia after ECT is associated with insufficient muscle relaxation, succinylcholine-induced fasciculations, succinylcholine itself, or a combination of these and perhaps other factors.<sup>[24]</sup> Because of its rapid onset, short duration of action and rapid recovery time, we have chosen the

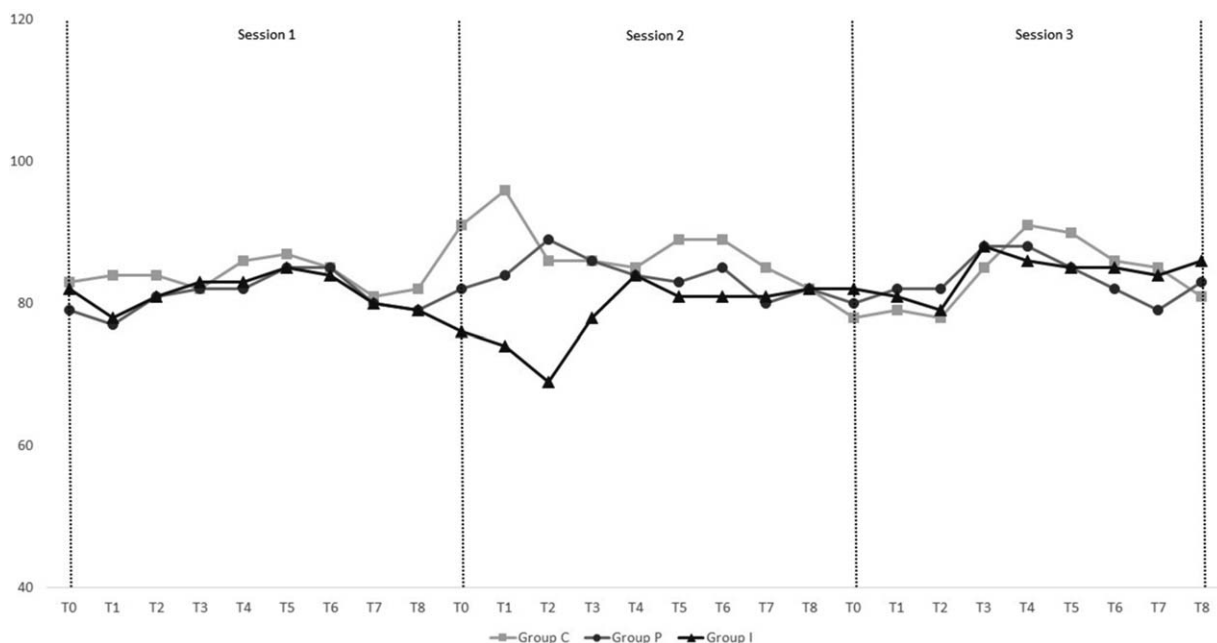


Figure 3. Heart rate. Group C = control, Group I = ibuprofen, Group P = paracetamol.

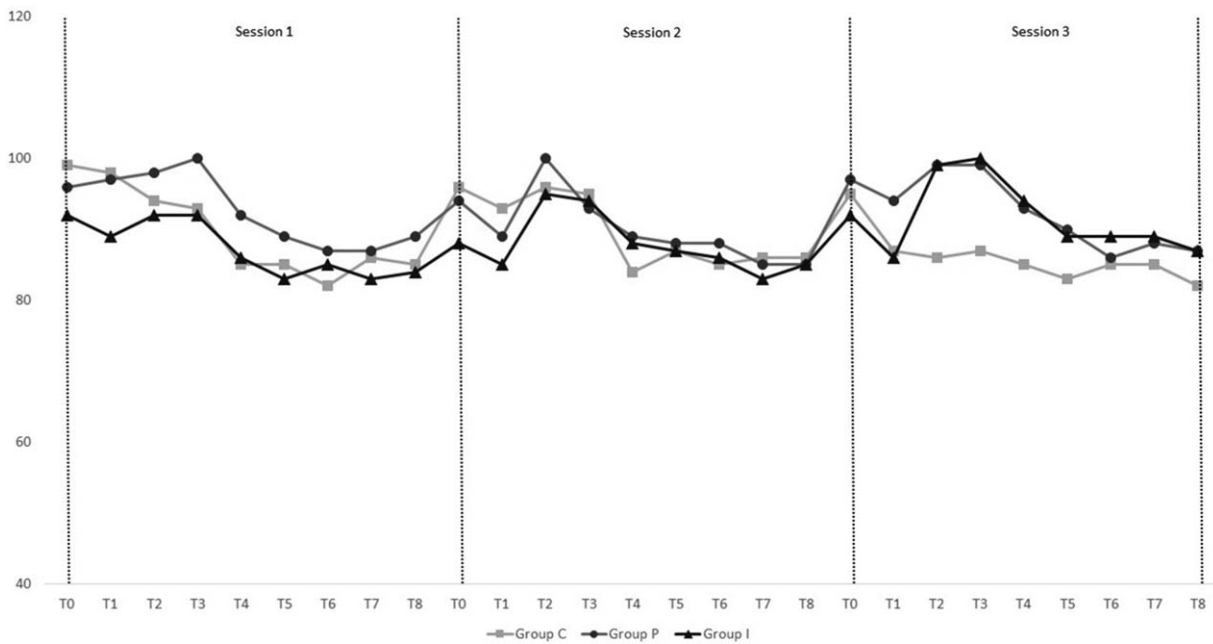


Figure 4. Mean arterial pressure. Group C = control, Group I = ibuprofen, Group P = paracetamol.

succinylcholine for ECT; however, a nondepolarizing neuromuscular blocking agents need to be considered in some patients with metabolic, neuromuscular, or neurologic comorbidities or other contraindications to succinylcholine (eg, immobilization or pseudocholinesterase deficiency). To complete all scheduled ECT sessions in a safe manner, minimizing the frequency and severity of myalgia after ECT is of utmost importance. In the present study, VAS scores for myalgia were not found to be different between the groups. Similarly, Rasmussen et al<sup>[6]</sup> reported no significant difference between ketorolac recipients and controls in terms of post ECT myalgia. Furthermore, Nasser et al<sup>[25]</sup> reported that the addition of ketamine to anesthesia induction had no effect on myalgia after ECT. On the other hand, while myalgia VAS scores between the groups reached no statistical significance, we evaluated the presence of myalgia at postoperative 24 hours period, we found that myalgia was less common in the Group I than the other groups ( $P = .011$ ). We may; therefore, concluded that ibuprofen had positive effects on the frequency of myalgia at postoperative 24 hours period, although it had no statistically significant effect on pain intensity.

Hemodynamic alterations following electroconvulsive stimulus are usually in the form of bradycardia or short asystole and a period of increase in HR following the stimulant.<sup>[26]</sup> As a result, a consistent increase in HR and blood pressure may develop during and immediately after ECT.<sup>[27]</sup> In the current study, various changes in HR and MAP were observed following ECT sessions,

which were similar to the changes reported in a previous study.<sup>[26]</sup>

The frequency of nausea after ECT has been reported to vary between 1% and 23%.<sup>[22]</sup> Nausea can occur at any time during ECT and is usually independent of headache. Vomiting occurs more rarely than nausea, but preventive treatments are required for both. For this purpose, drugs such as metoclopramide and ondansetron are preferred.<sup>[14]</sup> In the present study, it was observed that nausea in the Group P only developed after the first session at post-procedure 2nd hour, and this complaint had disappeared by the 4th hour, resulting in a significant intragroup difference ( $P = .017$ ). However, there was no significant difference when groups were compared with each other. Finally, there were also no significant differences in intra and intergroup comparisons in terms of vomiting. In a study conducted by Li et al<sup>[9]</sup> it was reported that post-ECT nausea decreased with the use of Mirtazapine, while Kramer et al<sup>[22]</sup> reported that post-ECT nausea and vomiting decreased with electrical stimulation to subcutaneous acupuncture points. The latter study is interesting because it may suggest an association between muscle spasms and vomiting after ECT; however, this is only an assumption and further studies are definitely required.

#### 4.1. Limitations

The low number of patients in each group and the fact that females were at a significantly higher frequency in the Group C, are the major limitations of the study. Also, the fact that pain perception was evaluated according to the patients' own perceptions (as is the case with VAS scores), it is very difficult to conclude that pain levels were objectively measured as it is a subjective test by nature. In addition, patients' perception of the VAS scoring system may be different from each other. Since all patients have major depression, they may have intentionally or unintentionally misdiagnosed the VAS. However, patients were given detailed information before measurement with VAS and

	Control	Paracetamol	Ibuprofen	P
Nausea, n (%)	6 (30)	4 (20)	4 (20)	.689
Vomiting, n (%)	4 (20)	2 (10)	2 (10)	.562
Pruritus, n (%)	1 (5)	0 (0)	2 (10)	.349

Data given as frequency (percentage).

were asked to score their pain only after fully understanding the test. Another limitation is associated with each individual's pain threshold, therefore limiting the efficacy of comparisons among groups. However, intragroup comparisons would not be effected by this problem. Finally, patients' experience of the ECT procedure may have also caused important differences, as the stress caused by being treated with such an invasive procedure in the operating room may result in significant alterations in patients' perceptions regarding the treatment.

## 5. Conclusions

The findings of our study indicate that pain intensity of headache and myalgia did not show a significant change between groups and within groups (Groups C, P, and I). There was no statistically significant difference between the groups in terms of myalgia VAS scores after ECT (2, 4, 6, 12, and 24 hours). However, at 24 hours postoperatively, the incidence of myalgia was lower in the ibuprofen group. Also, nausea, vomiting, and pruritus were similar in all groups. The results of this study will provide effective management of side effect.

## Author contributions

**Conceptualization:** Esra Porgali Zayman.

**Data curation:** Erol Karaaslan.

**Investigation:** Sedat Akbas, Ahmet Selim Ozkan, Esra Porgali Zayman.

**Methodology:** Erol Karaaslan, Sedat Akbas, Ahmet Selim Ozkan.

**Project administration:** Erol Karaaslan.

**Supervision:** Ahmet Selim Ozkan.

**Validation:** Esra Porgali Zayman.

**Visualization:** Esra Porgali Zayman.

**Writing original draft:** Erol Karaaslan.

Erol Karaaslan orcid: 0000-0002-8534-3680.

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