Pretreatment With Ibuprofen to Prevent Electroconvulsive Therapy–Induced Headache

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Background: Although electroconvulsive therapy (ECT) has been widely recognized as an effective treatment for severe depression and various other psychiatric illnesses, adverse effects have been frequently reported, especially a high incidence of headache. Analgesics, such as acetaminophen, narcotics, or nonsteroidal anti-inflammatory drugs (NSAIDs), are commonly used to treat ECT-induced headache. The objective of this study was to determine whether pretreatment with ibuprofen would prevent the onset or decrease the severity of headache that occurs after ECT.

Method: All inpatients on the psychiatric units who required ECT treatment were asked to participate in the study. Thirty-four patients were randomly assigned to receive either ibuprofen, 600 mg, or placebo orally 90 minutes prior to the initial ECT session, with the alternate treatment given for the second ECT treatment. Patients were asked to complete a questionnaire prior to and after the first 2 ECT treatments regarding the pattern, severity, and onset of headache. Severity of the headache was measured on a visual analogue scale (VAS).

Results: Ten patients experienced headache in neither treatment arm, while 7 patients experienced headache in both treatment arms. Eleven patients experienced headache with placebo but not with ibuprofen, while 2 patients experienced headache with ibuprofen but not with placebo. Ibuprofen was significantly more effective than placebo in preventing the onset of headache post-ECT ($p = .022$). The mean ± SD VAS headache scores were 1.49 ± 1.54 and 0.54 ± 0.91 in the placebo and ibuprofen arms, respectively. Ibuprofen was significantly more effective than placebo in reducing the severity of ECT-induced headache ($p = .007$).

Conclusion: Ibuprofen premedication reduced the frequency and severity of headache post-ECT and should be considered for appropriate patients who suffer from ECT-induced headache.

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Although electroconvulsive therapy (ECT) has been widely recognized as an effective treatment for severe depression and various other psychiatric illnesses, many adverse effects have been described, such as disorientation, cognitive impairment, and headache.[1–2] While the incidence of headache has been reported to be as high as 48%,[3] little has been written on its etiology or treatment. In clinical practice, various options have been tried as prophylaxis or treatment, including acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and narcotics. However, analgesics are commonly given after the patients have returned to the nursing unit when they are already suffering from a headache. Preemptive use of NSAIDs has been shown to reduce postoperative pain after various surgeries or procedures.[4–6] The potential for NSAIDs to be useful analgesics for treatment and prophylaxis of ECT headache is based on anecdotal experience. The combination of naproxen and propranolol was found effective in a single case report for a 32-year-old woman with post-ECT headache that was not prevented or relieved by naproxen or acetaminophen alone.[7]

The primary purpose of this study was to investigate if giving ibuprofen prior to ECT would prevent the onset of headache. The second purpose was to determine if the premedication would reduce the severity of headache post-ECT.

METHOD

All inpatients on the psychiatric units undergoing ECT treatments were asked to participate in this prospective, randomized, double-blind, placebo-controlled study. Patients were excluded if they had known hypersensitivity to acetylsalicylic acid or NSAIDs, active gastrointestinal ulceration or inflammatory diseases, previous nonresponse or adverse reactions to NSAIDs, or if they were mentally incompetent to give informed consent. Patients gave written informed consent to participate in the study at the time of consent to ECT. The study was approved by the institutional research and ethics review process.

The random assignment process was performed by the Department of Pharmacy of St. Paul's Hospital using a random number table and was blinded to the patient,

Table 1. Comparisons Between Placebo and Ibuprofen Arms (N = 30)

Variable	Placebo	Ibuprofen	p Value
Seizure duration, mean ± SD, sec	33.6 ± 12.0	38.2 ± 17.4	.16
Well-modified seizure,[a] N	26	27	1.00
Succinylcholine dose, mean ± SD, mg	47.1 ± 9.0	48.1 ± 11.5	.48
Thiopental dose, mean ± SD, mg	240.5 ± 40.3	244.8 ± 47.0	.36
Patients with headache, N	18	9	.022
VAS headache scores (0–5), mean ± SD	1.49 ± 1.54	0.54 ± 0.91	.007

[a]A well-modified seizure is one in which only slight flickering of the eyelids, fingers, or toes is observed.
Abbreviation: VAS = visual analogue scale.

physician, and treatment team. On the initial ECT treatment, 34 patients were randomly assigned to receive either ibuprofen, 600 mg, or placebo orally 90 minutes before the first ECT session, with the alternate treatment given for the second ECT treatment. Both ibuprofen and placebo (glucose powder) were dispensed in identical gelatin capsules. Only anesthetic agent, neuromuscular blocking agent, and atropine were allowed as part of the ECT treatment. The protocol did not specify or control the dosages of any of these medications. ECT was provided via a Thymatron DGx (Somatics, Inc., Lake Bluff, Illinois).

Data Collection

Patient demographics were collected via chart review and patient questionnaire prior to ECT, including age, sex, diagnosis, and history of headache (frequency, type, quality, location, associated symptoms, severity, duration, and previous treatment). Other confounding variables were also recorded, including ECT parameters (placement of electrodes, stimulus intensity, and seizure duration), caffeine dose (if applicable), dose or type of neuromuscular blocking agent, dose or type of anesthetic agent, and whether tonic seizure was poorly or well modified as rated by the psychiatrists.

Prior to and after the first 2 ECT sessions, patients were interviewed within 2 hours to assess any headache (time to onset, type, frequency, quality, location, associated symptoms, and severity) and adverse effects. The severity of a headache was measured using a visual analogue scale (VAS) with 0 labeled as "no pain" and 5 labeled as "excruciating pain." The dose of analgesics used post-ECT was also noted.

Statistical Analysis

For nonparametric analysis, the McNemar test was used to compare the occurrence of a headache following ECT with ibuprofen versus that with placebo. The 2-tailed Student t test was used to compare the mean VAS headache scores for all patients between the 2 arms. Statistical significance was set at 0.05 a priori. Episode-specific confounding factors were compared to ensure no statistically significant differences between the 2 treatment arms.

RESULTS

Thirty-four patients who met the inclusion criteria were enrolled into the study. Four patients were excluded due to violation of the protocol: only 1 ECT treatment was given (N = 1), nonstudy ibuprofen supply was given (N = 1), or additional analgesics were given prior to or immediately after ECT treatment in anticipation of a headache (N = 2). Thirty patients were included in the analysis: 13 men and 17 women. The mean age was 47 years (range, 32–88 years). DSM-IV diagnoses were major depressive disorder (N = 15), major depressive disorder with psychotic features (N = 7), postpartum depression (N = 2), bipolar depression (N = 4), and bipolar mania/mixed episode (N = 2).

Confounding variables were considered comparable in the ibuprofen and placebo arms (Table 1). All patients received succinylcholine as the neuromuscular blocking agent and thiopental as the anesthetic agent, and no caffeine or other premedications were given. All patients received right unilateral ECT.

Eighteen patients experienced a headache with placebo, while 9 patients had a headache with ibuprofen. Ten patients experienced no headache with either ibuprofen or placebo, while 7 patients experienced a headache with both. Eleven patients experienced a headache with placebo but not with ibuprofen, while 2 patients experienced a headache with ibuprofen but not with placebo. Ibuprofen was more effective in preventing the onset of headache as compared with placebo (p = .022). Most patients noticed the headache almost immediately upon awakening from treatment. Duration of the headache varied from less than 1 hour to more than 14 hours in both treatment arms, while 1 patient in the placebo treatment arm had the headache for more than 24 hours.

Sixteen patients had a previous history of headache symptoms (migraine N = 4, tension N = 12). Of these, 3 patients experienced no headache with either ibuprofen or placebo, while 5 experienced a headache with both. Six patients had a headache with placebo but not with ibuprofen, while 2 had a headache with ibuprofen but not with placebo.

The mean ± SD VAS headache scores for all included patients were 1.49 ± 1.54 and 0.54 ± 0.91 with placebo

and ibuprofen, respectively. The mean difference in the severity of headache with placebo as compared with that in the ibuprofen group was 0.95 ± 1.78 (95% confidence interval = 0.28 to 1.61, p = .007).

Additional analgesics were required to treat the headaches in 15 patients who received placebo (1 dose, N = 6; 2 doses, N = 5; 3 doses, N = 2; 4 doses, N = 2) and 8 patients who received ibuprofen (1 dose, N = 2; 2 doses, N = 4; 4 doses, N = 2). Acetaminophen, ibuprofen, and acetaminophen with codeine, 30 mg, were used in both treatment arms. There were no differences between the amount and type of additional analgesics used in either treatment arm. No adverse effects were noted from either treatment arm.

DISCUSSION

Although ECT is widely regarded as being both safe and efficacious for the treatment of depression and other psychiatric illnesses, headache is a well-documented side effect, with its incidence estimated to be up to 48%.[2,3] Similarly, 18 (60%) of 30 patients taking placebo experienced headache after ECT in this study. Some data have suggested that ECT not only can induce headache in previously unaffected patients, but also can exacerbate the problem in patients with preexisting headache symptoms.[3] Moreover, the headache pattern may change from tension to migrainous type. Some patients may suffer from the headaches for months after a series of ECT treatments.[3]

Despite the high incidence of headaches after ECT, there are no controlled, blinded studies using premedication in an attempt to prevent the onset or reduce the severity of the headache. An early single case report found sumatriptan prophylaxis useful in preventing post-ECT migraine headaches.[8] In an open, unblinded study of only 8 patients with moderate-to-severe post-ECT headache, the use of intranasal sumatriptan (20-mg single dose) was found to reduce the headache over the subsequent 2 hours.[9] No evaluation of prophylaxis with sumatriptan was conducted in this study. A single patient with severe headache following an initial ECT treatment benefitted from sumatriptan, 6 mg, subcutaneously administered immediately following ECT during each of 12 subsequent sessions.[10]

Other potential therapies have been only lightly explored. In a double-blind study of 5 patients with post-ECT headaches, percutaneous electrical nerve stimulation administered prior to or immediately after the ECT was found beneficial in reducing headache.[11] Comparisons of NSAIDs with other preemptive therapy have not been published.

This study shows that ibuprofen prophylaxis is effective in preventing the onset and reducing the severity of headache post-ECT. Due to the small number of subjects, no attempts were made to determine whether ibuprofen prophylaxis would be effective in reducing the risk of headaches in the subgroup of patients with preexisting headache symptoms. We cannot theorize on the specific mechanism of action of NSAIDs for this indication above the known anti-inflammatory, analgesic action of this class of drugs. Psychiatric patients usually have many somatic complaints, which could contribute to their depressive symptoms. Also, patients are generally ambivalent about ECT treatments[2]; therefore, any adverse effects or discomfort endured from the procedure will impede the patients' progress. By proactively minimizing any adverse effects, effective analgesic therapy would potentially promote compliance with ECT treatments.

Limitations to this study include the small sample size and the reliability of information obtained from patients with cognitive impairment secondary to their ECT treatments. However, all questionnaires were completed with the patients by the treatment team and all ambiguous answers were clarified where feasible.

CONCLUSION

Pretreatment with ibuprofen appears safe and effective in reducing the frequency and severity of ECT-induced headache. Ibuprofen prophylaxis should be considered in appropriate patients who suffer headaches from ECT treatments.

Drug names: acetaminophen with codeine (Tylenol w/codeine No. 3, Phenaphen w/codeine, and others), atropine (Atropen and others), ibuprofen (Ibu-tab, Motrin, and others), naproxen (Naprosyn and others), propranolol (Inderal and others), succinylcholine (Anectine, Quelicin, and others), sumatriptan (Imitrex).

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