ROLE OF PERIOPERATIVE ANALGESIA WITH ACETAMINOPHEN IN REDUCING PAIN FOLLOWING ELECTROCONVULSIVE THERAPY

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ABSTRACT

Objective: To assess the efficacy of perioperative analgesia with acetaminophen in reducing the occurrence and severity of post-ECT pain.

Study Design: Quasi experimental study.

Study Place and Duration: Tertiary care mental health facility at Rawalpindi, Jun to Nov 2018.

Methodology: Patients of all age groups and either gender for whom elective ECT was recommended during the study time period were included in the study. Acetaminophen (1g/100ml) and placebo (100ml) infusions were infused according to randomized sequence during ECT session. Study participants were assessed for presence and severity of pain i.e. headache and/or myalgia, two hours before and after ECT by using visual analog scale (VAS).

Results: A sum of 146 study participants were randomized to either receive intervention (Group A) or placebo (Group B), both the groups comprised of 73 participants each. The frequency of post-ECT headache and myalgia in group A, who received acetaminophen infusion, was 8.2% and 2.7% respectively as compared to placebo group B where incidence of post-ECT headache and myalgia was reported to be 24.7% and 10.9% respectively (8.2% vs 24.7%, *p* 0.013 and 2.7% vs 10.9%, *p* 0.03 respectively). Uni-variate analysis showed that participants in group A were 72.6% less likely to develop post-ECT headache (OR 0.27, 95% CI 0.11-0.73, *p* 0.007), and 55% less likely to develop post-ECT myalgia (OR 0.45, 95% CI 0.21-0.80, *p* 0.01) than participants in group B.

Conclusion: Acetaminophen has been found effective in reducing the incidence and severity of headache and myalgia following electroconvulsive therapy.

Keywords: Electroconvulsive therapy, Headache, Myalgia, Perioperative analgesia, Quasi experimental study.

INTRODUCTION

Since 1930's, electroconvulsive therapy (ECT) has been reported to be a safe and effective mode of treatment in a variety of psychiatric disorders. It is commonly utilized in treatment resistant cases of severe depression, bipolar mania, schizophrenia and schizoaffective disorders and for prevention of relapse during maintenance therapies[1]. ECT is cost effective and relatively low-risk medical procedure with higher response rate as compared to pharmacological treatments[2]. Though considered as a well-tolerated treatment; still side effects like headache, myalgias, cognitive impairment and craniofacial pain may affect the quality of life of patients for few days to weeks and may compel them to deny for the next session for this procedure. Despite its effectiveness, established safety and rapid response as compared to pharmacological treatment ECT remains underutilized treatment. Controversial depiction of ECT in press, film, coalitions lobbying for anti-ECT legislation, and the internet resulted in misinformation among general public about its use[3]. Moreover, fear and stigma linked to it and side effect profile including headache and body aches alsocontribute to underuse of this potentially life-saving treatment[4].

Among side-effects, headache and myalgia are the most commonly reported postoperative pain, which can be mild, moderate or severe in nature. The exact cause of post ECT headache is not clearly known but it may occur as a result of

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seizures during the procedure, anesthesia, and contracture of the temporalis & masseter muscles, vascular changes and alteration of serotonergic neurotransmission in the brain. Incidence of post ECT headache has been reported to occur in 20-45% of the patients[3,5,6], which is usually mild to moderate in intensity but affects the quality of life of patients already suffering from a psychiatric illness adversely[7]. Whereas, myalgia is the second most common side effect of ECT, prevalence of which has been reported to range from 7-9%[5,8]. Myalgia occurs mainly due to excessive muscle fasciculation associated with the administration of depolarizing muscle relaxants such as succinylcholine during the procedure[5].

Management of headache and myalgia is of high importance because it significantly reduces patient suffering and also plays an important role in enhancing positive patient attitude towards ECT[9,10]. Not a lot of work has been done in this regard especially in our part of the world. Few studies done in west have shown that pre ECT analgesia or analgesia during this procedure has been superior in pain relief as compared to post ECT analgesia[11]. Although most of the studies had established effectiveness of pre-emptive analgesia in reducing occurrence and severity of post-ECT headache and body pain, still it has not been adopted as a standard practice, may be because quite a small number of randomized controlled trials had been conducted on matter under discussion[12,13].

Patients in our part of the world usually report late to the psychiatric facility when the disease has undergone a long process and usually has become resistant to the routine treatment. Moreover in many cases long term follow up has not been possible. Therefore ECT has been treatment of choice in many patients who report to tertiary care psychiatric facility. Limited work has so far been conducted on our own population regarding the pain management after this procedure. This study was planned to look for the efficacy of perioperative analgesia with acetaminophen in reducing the occurrence and severity of post-ECT pain in comparison with the placebo.

METHODOLOGY

This quasi experimental study was carried out at tertiary care mental health facility, Rawalpindi from June to November 2018. Sample size was calculated at 1:1 ratio in intervention and control group to detect an odds ratio of 0.23[11], considering 60% incidence of headache in unexposed group with 95% confidence interval and 80% study power. Online sample size calculator developed by "UCSF Clinical & Translational Science Institute" (http://www.sample-size. net) was used and a sample size of 146 was calculated, after adding 15% contingency margin, with 73 study subjects in each group. Non probability consecutive sampling technique was used to gather the sample. After permission from hospital ethical review committee, patients of all age groups of either gender for whom elective ECT was recommended during the study time period were included in the study. Patients with reported allergies to acetaminophen, who had pain or headache or were on analgesics 24 hours prior to ECT, those who developed complications after electroconvulsive therapy that is delirium or trauma and those who lacked the capacity to give an informed consent were excluded from the study.

ECT sessions were conducted in specialized ECT theatres under supervision of consultant psychiatrist and consultant anesthetist. All study subjects underwent bilateral ECT. Duration of stimulus was kept constant however energy levels were adjusted depending on individual seizure threshold, severity of illness, age, gender and current medication[14]. Propofol and suxamethonium was used for anesthesia and muscle relaxation respectively.

Study intervention comprised of Acetaminophen infusion (1g/100ml), whereas placebo, as defined by Finniss *et al*[15] as an inert substance, containing no active drug, was prepared and packaged by Bosch Pharmaceuticals in identical infusion bottles labeled as A and B respectively.

Patients for ECT who gave informed written consent were randomized to either receive

intervention or placebo via sealed-envelope method. There were 146 envelops, randomly numbered from 1 to 146 containing 73 A's and 73 B's, and were kept at ECT theatre. The patients and nurses who were responsible for administering the placebo or intervention to patients were blinded. Patients were randomized prior to ECT, where nurse on-duty at ECT room drew a numbered envelope and administered either A or B infusion to the patients prior to ECT. The code was opened by statistician at the end of study.

Acetaminophen (1g/100ml) and placebo (100 ml) infusions were infused according to randomized sequence during ECT session. Demographic and clinical characteristics were noted for all patients prior to ECT. Study participants were also assessed for presence and severity of headache and myalgia two hours before and two

Table: Comparison of demographic and clinical characteristics among two study groups.

Characteristics	Acetaminophen Group A (n=73)	Placebo Group B (n=73)	*p*-value
Age (years) (mean ± SD)	37.1 ± 12.4	38.8 ± 12.5	0.4108
Age Range (years) (n,%)			
18-40	54 (74.0%)	50 (48.1%)	0.73
41-59	14 (19.2%)	16 (53.3%)	
60 and above	5 (6.8%)	7 (9.6%)	
Gender n (%)			
Male	48 (65.8%)	55 (75.3%	0.20
Female	25 (34.2%)	18 (24.7%)	
Educational Status (n,%)			
Uneducated	10 (13.7%)	5 (6.8%)	0.26
<10 years of education	14 (19.2%)	11 (15.1%)	
>10 years of education	49 (67.1%)	57 (78.1%)	
Employment Status (n,%)			
Student	8 (11.0%)	7 (9.6%)	0.68
Unemployed	24 (32.9%)	18 (24.7%)	
Employed	33 (45.2%)	33 (45.2%)	
Marital Status (n,%)			
Unmarried	33 (45.2%)	27 (37.0%)	0.57
Married	38 (52.1%)	43 (58.9%)	
Divorced/Separated	2 (2.7%)	3 (4.1%)	
Substance Abuse (n,%)			
Smoking	15 (20.5%)	11 (15.1%)	0.54
Alcohol	3 (4.10%)	-	0.71
Cannabis	2 (2.7%)	2 (2.7%)	0.21
Niswaar	3 (4.1%)	5 (6.8%)	0.76
Co-morbidities (n,%)			
Hypertension	1 (1.4%)	5 (6.8%)	0.20
Diabetes	5 (6.8%)	3 (4.1%)	
Seizure Duration (mean ± SD)	22.5 ± 21.0	18.7 ± 8.8	0.22
Post-ECT pain (n,%)			
No pain	65 (89.0%)	53 (72.6%)	
Headache	6 (8.2%)	18 (24.7%)	0.013
Myalgia	2 (2.7%)	8 (10.9%)	0.03
Post-ECT pain score (mean ± SD)	2.0 ± 0.89	4.1 ± 1.30	0.001

A: Independent samples T-test, B: Chi-square Test, C: Mann-Whitney U Test, * Significant *p*-values

hours after ECT. Consultant psychiatrist and anesthetist were responsible for independent assessment of pain both kept blinded for intervention and placebo. Visual analogue scale (0-10) was used to assess the presence and severity of headache and/or myalgia, where 0 indicated no pain and 10 indicated worst pain.

Statistical analysis was performed by using SPSS (version 23.0). Data was presented as means and standard deviation for quantitative variables while frequencies and percentages were calculated for qualitative variables. For categorical group comparisons Pearson's Chi-square test was applied; while for comparison of continuous data Student's t-test was used for normally distributed data and Mann-Whitney U-test otherwise. The *p*-value of less than or equal to 0.05 was considered to be significant.

RESULTS

A sum of 146 study participants were randomized to either receive intervention (group A) or placebo (group B) in this study, with in allocation ratio of 1:1. Both the groups comprised of 73 participants each. Overall, there were 103 (70.5%) males and 42 (29.5%) females in the study, with a mean age of 37.9 ± 12.5 years. Majority of the study participants belonged to age range of 18-40 years 104 (71.2%) and 41-59 years 30 (20.5%). Eighty (54.8%) study participants were married, 61 (41.8%) unmarried and 5 (3.4%) were divorced at the time of enrollment. There were 15 (10.27%) uneducated participants, while 25 (17.1%) and 106 (72.6%) had less and more than ten years of education respectively. Out of 146, 42 (28.8%) participants were unemployed, 61 (41.7%) employed, 28 (19.2%) house-wives, and 15 (10.2%) were students. There were 26 (17.8%) regular smokers while 4 (2.7%) reported to be using cannabis and 8 (5.5%) participants were niswaar addicts.

In group A, there were 48 (65.8%) males and 25 (34.2%) females, with mean age of 37.1 ± 12.4 years. Similarly, Group B (Placebo) comprised of 55 (75.3%) and 18 (24.7%) males and females with 38.8 ± 12.5 years of age. Depression 65 (44.5%) was the most common diagnosis among study participants, followed by schizophrenia 39 (26.7%), bipolar affective disorder 31 (21.2%), obsessive compulsive disorder 7 (4.8%) and personality disorder 4 (2.7%). Demographics, clinical characteristics and ECT-parameters of both groups A and B are compared (table), along with *p*-values.

The frequency of post-ECT headache and myalgia in group A, who received acetaminophen infusion, was 8.2% and 2.7% as compared to placebo group B where frequency of post-ECT

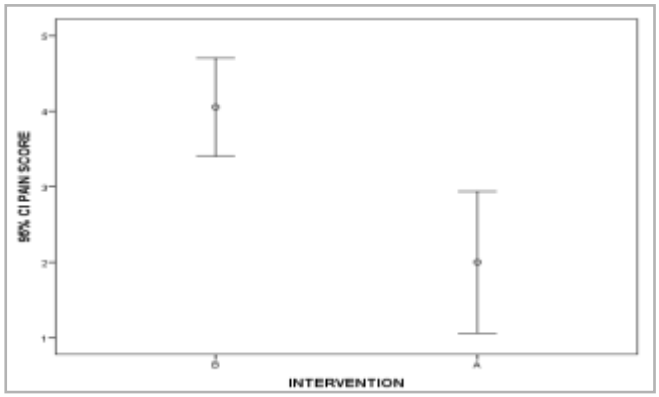

Figure: Error-bar plot of post-ECT pain score in acetaminophen and placebo group.

headache and myalgia was reported to be 24.7% and 10.9% (8.2% vs 24.7%, *p* 0.013 and 2.7% vs 10.9%, *p* 0.03). A statistically significant difference was found between cumulative mean post-ECT pain score for both headache and myalgia, in group A as compared to group B (figure).

DISCUSSION

In this study, the interventional group, to whom acetaminophen infusion was administered perioperative, showed a reduced frequency and severity of most commonly reported side effect of ECT therapy, i.e. pain in terms of headache and myalgia. It was found that only 8.2% and 2.7% of participants in the intervention group developed headache and myalgia respectively, two hours after ECT, as compared to 24.7% and 10.9% of participants in placebo group who developed post-ECT headache and myalgia respectively. Similar sort of results have been reported by Leung *et al*[13] in a randomized controlled trial where thirty four patients were randomized to

either receive placebo or ibuprofen prior to ECT, and significantly lower number of patients in the intervention group were reported to develop post-ECT headache and myalgia, which were of relatively milder severity assessed via visual analogue pain scale. Another randomized controlled trial, conducted by Kertesz *et al*[16], reported that 28% (20/72) patients who underwent ECT therapy developed post-ECT headache, similarly, in this present study 24.7% participants in placebo group were reported to develop post-ECT headache.

A prospective analytical descriptive study conducted by Haghighi *et al*[5], including 621 psychiatric patients who underwent ECT, out of which 21.9% (126/621) were reported to develop post-ECT headache assessed six hours after procedure, while 9% (56/621) developed post-ECT myalgia. The incidence of both post-ECT headache and myalgia are similar to what we have found in present study, but in our study, we have assessed post-ECT headache after two hours of procedure while Haghighi *et al*[5] assessed in six hours after ECT procedure. After two hours patient might have been under the effect of pre-anesthetic drug medication so even placebo group may show less number of post ECT symptoms. More research is required in this regard to establish the fact regarding the time at which post ECT headache is maximum and require intervention in most of the cases.

In present study, a statistically significant association has been established between perioperative administration of acetaminophen and a lower frequency of developing post-ECT headache, and post-ECT myalgia which means that participants in group A were 72.6% and 55% less likely to develop post-ECT headache and myalgia respectively, as compared to group B. Our results were very similar to another randomized controlled trial, conducted by Isuru *et al*[12], in which 126 patients were randomized to either receive placebo or 1 g oral acetaminophen tablet prior to ECT therapy, and patients in acetaminophen group were reported to have low incidence of headache, with an odds ratio of 0.23, 95% CI: 0.11–0.48, $p<0.001$). Our study has yet another similar finding with Isuru *et al*[12], who failed to show significant associations between post-ECT pain and other possible covariates including age, gender, marital status, educational status, employment status, co-morbidities, history of migraine by applying multiple logistic regression. Haghighi *et al*[5], also reported that gender, age, duration of seizure, and treatment sessions were not predictors of headache and myalgia 6 hours after ECT.

In summary, the results of our study are quite similar to other randomized controlled trials and descriptive studies[13,16-18] done on frequency of post-ECT pain in terms of headache and myalgia, and effect of perioperative analgesia on lowering the frequency and severity of post-ECT pain. There were a few limitations of the study that we need to highlight, including; pain measurement using visual analogue is a very subjective finding which might be perceived differently by different individuals, therefore the margin of error is high; we followed up the patient for not more than 2 hours to assess incidence and severity of headache and myalgia which might have compromised the incidence rate. Therefore it is recommended to conduct more sophisticated, well controlled randomized controlled trials in order to justify and generalize the results.

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CONCLUSION

Perioperative analgesia, using acetaminophen, has been found effective in reducing the frequency and severity of post ECT pain that is headache and myalgia among psychiatric patients.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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