Original Research Article

A prospective study to compare the effect of ketamine and sodium thiopental in drug resistant major depression

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Abstract

Background: Major depression or major depressive order is characterized by persistent feeling of sadness or lack of interest in any outside stimulus. Electroconvulsive therapy (ECT) is one of the most successful options for treatment. It was observed that Ketamine and sodium thiopental both increased the seizure duration. The aim of present study was to compare the effects of ketamine and sodium thiopental in drug resistant. **Methods:** This study was double blind study and we included 100 patients who were diagnosed of drug resistant major depression according to Diagnostic and Statistical manual of Mental Disorders. Patients were divided into Group A and Group B where patients in Group A received ketamine 0.8 mg and patients in group B received sodium thiopental 1-21.5 mg/kg as the anestheic agent for induction. All the patients received 8 sessions of ECT divided as 3 times per week each lasting for 30-90 seconds. At the end of 2nd, 4th, 6th, 8th session patient's recovery time and post anesthesia complications were recorded in 1st hour. Hamilton Depression Rating Scale (HDRS) was used to analyse the effect of these drugs on depression. The scoring on HDRS was done before the 1st ECT and at the end of 2nd, 4th, 6th and 8th session of ECT. **Results:** The side effects such as headache, nausea and fear of awakening illusions were significantly more in ketamine group in all the sessions (p value <0.05). The rise in both systolic and diastolic blood pressure was also significantly more in Ketamine group than in sodium thiopental group (p<0.05). Repeated measures of seizure duration showed a significant reduction of seizure duration with each successive session of ECT in both the groups. (p=0.02). The scoring of HDRS showed the decreasing trend in the scores with successive sessions of ECT more so in the ketamine group than in sodium thiopental group by the end of last session. **Conclusion:** Ketamine with premedication is a promising agent which can be used as induction agent of choice for ECT in patients with drug resistant major depression as there is clear improvement in the depression scores with repeated infusions of ketamine.

Key Word: major depression, ketamine, sodium thiopental, Hamilton depression rating scale

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Received Date: 20/12/2018 Revised Date: 13/01/2019 Accepted Date: 02/02/2019

DOI: https://doi.org/10.26611/1015924

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 06 February 2019

INTRODUCTION

Major depression or major depressive order is characterized by persistent feeling of sadness or lack of interest in any outside stimulus. It is well recognized psychological disorder worldwide.[1] As per the statistics world health organisation has predicted that by 2020 depression will be among the top major diseases affecting 20-30% of the population.[2] The incidence is higher in females than in males. There have been many behavioural and pharmacological therapies for its treatment and most of them are successful but there are still group of patients who do not respond to these therapies. In such patients electroconvulsive therapy (ECT) is one of the most successful options for treatment.[3] ECT is given under anesthesia and various agents such as methohexital, propofol, midazolam, remifentanil, sodium thiopental, ketamine etc have been used. The most important parameter to be looked upon for a therapeutic response is the seizure duration. It was observed that Ketamine and sodium thiopental both increased the seizure duration.[4, 5] The aim of present study was to compare the effects of

How to site this article: Mohammed Mukarram Iqbal, Ajay Dhage, Kaja Sriram Murthy. A prospective study to compare the effect of ketamine and sodium thiopental in drug resistant major depression. *MedPulse International Journal of Anesthesiology.* February 2019; 9(2): 104-108. http://medpulse.in/Anesthsiology/index.php

ketamine and sodium thiopental in drug resistant major depression patients.

METHODS

This study was double blind study and we included 100 patients who were diagnosed of drug resistant major depression according to Diagnostic and Statistical manual of Mental Disorders. The other important inclusion criteria were age between 18-65 years, both male and female patients and who did not receive ECT in last three months. Patients who had any contraindications for ECT, untreated cardiovascular disease, Increased intracranial pressure, respiratory tract infection, previous unhealed fractures, glaucoma, uncontrolled hypertension and diabetes mellitus, previous history of epilepsy, allergy to anesthetic drugs used in the study, alcohol, drug abuse, other psychiatric disorders, and pregnant females were excluded from the study. A separate diary for all the patients was maintained which recorded their demographic data and all the parameters and events occurring before, during and after each session of ECT. Written informed consent was obtained from all the patients before the start of study. Patients who eventually entered the study were given two different anesthetic agents on alternate basis and later they were assigned as Group A and Group B where patients in Group A received ketamine 0.8 mg and patients in group B received sodium thiopental 1-21.5 mg/kg as the anestheic agent. All the patients received 8 sessions of ECT divided as 3 times per week each lasting for 30-90 seconds. At the end of 2nd, 4th, 6th, 8th session patient's recovery time and post anesthesia complications were recorded in 1st hour if any. To analyse the effect of these drugs on depression as such, Hamilton Depression Rating Scale (HDRS) was used. The scale ranges from 0-52.[6, 7] This scale has validity between 0.91-0.94 and reliability of 0.74.[8, 9] The scoring on HDRS was done before the 1st ECT and at the end of 2nd, 4th, 6th and 8th session of ECT. The study was approved by the institutional ethics committee of Mahadevappa Rampure Medical College, Kalaburagi, Karnataka, India. Continuous data with normal distribution were presented as mean (standard deviation [SD]) and analyzed with Student's *t*-test; Categorical data were analyzed with the Chi-square test, ANOVA was used to analyse repeated measures. A *p* value of <0.05 was considered as statistically significant. All the data was analysed in the latest version of SPSS (IBM Corp. NY)

RESULTS

Table 1 shows the demographic profile of the study subjects. Both the groups were comparable in their characteristics. No significant difference was found between both groups in the distribution characteristics such as age group, gender, smoking habits, urban/rural population, age at the time when major depression was first diagnosed, duration of current episode of major depression, ECT naïve patients, systolic and diastolic BP before commencement of ECT. The readings of blood pressure are presented as mean ± SD

Table 1: Demographic profile and baseline characteristics of two study groups

Variables	Group A (Ketamine)	Group B (ST)	*P* value
Age group (years)			
18-29	30	29	
30-39	36	24	0.42
40-49	18	25	
50-65	16	24	
Females	55	52	0.56
Rural patients	24	20	0.47
Cigarette smoking	27	35	0.28
Age at first diagnosis of MD (years)			
<20	22	20	
20-29	37	40	0.96
30-39	26	24	
≥40	15	16	
Duration of current episode of MD (years)			
<2	29	31	0.88
2-2.9	19	23	
3-3.9	22	20	
≥4	30	26	
ECT naïve	78	65	0.12
Systolic BP (mmHg)	122.1± 14.8	121.6±13.1	0.41
Diastolic BP (mmHg)	74.9±9.2	75.1±8.6	0.35

ST= sodium thiopental, MD=major depression, BP= blood pressure

Patients in both the groups suffered the adverse effects. However these were more in ketamine group than in sodium thiopental group. The most common recurring side effects were headache, nausea and fear of awakening illusions and they were significantly more in ketamine group in all the sessions (p value <0.05). Pain at injection site, short term and long term delirium episodes were also more in ketamine group but this difference was not statistically significant. **Table 2** shows the changes in systolic and diastolic blood pressure along with seizure duration in both the groups after 1st, 2nd, 4th, 6th and 8th session of ECT. The rise in both systolic and diastolic blood pressure was observed in both the groups but it was significantly more in Ketamine group than in sodium thiopental group (p<0.05). However there was no difference of statistical significance between the repeated measures of BP in each group. Seizure durarion was seen to be reduced with both anesthetics with each successive session of ECT. The difference among both the groups was not statistically significant, however the repeated measures showed a significant reduction of seizure duration with each successive session of ECT in both the groups. (p=0.02)

Table 2: Comparison of systolic and diastolic BP, seizure duration after ECT in both groups

Session	Group A (Ketamine)	Group B (ST)	*p*-value
Systolic BP (mmHg)			
1	185.1±25.9	169.1±18.9	<0.001*
2	188.9±26.1	171.4±18.9	
4	186.2±20.6	168.9±22.4	
6	189.5±22.4	169.9±21.1	
8	188.1±20.8	170.8±17.9	
Repeated measure *p* value	0.42	0.84	
Diastolic BP (mmHg)			
1	98.1±16.3	90.9±16.4	<0.001*
2	100.0±13.2	91.7±14.0	
4	100.3±12.4	92.2±15.8	
6	100.4±13.4	90.5±14.2	
8	100.3±13.5	93.1±16.2	
Repeated measure *p* value	0.85	0.80	
Duration of seizure (seconds)			
1	37.8±10.1	35.5 ±12.5	>0.05
2	35.9±10.7	35.1±8.7	
4	36.1±8.8	34.1±7.3	
6	35.5±10.5	32.9±9.8	
8	35.1±7.8	30.1±7.2	
Repeated measure *p* value	0.02*	0.02*	

*ST= Sodium thiopental, BP= blood pressure, ECT= electroconvulsive therapy, * statistically significant:* **Table 3** shows the scoring of HDRS presented as mean ± SD. It shows the decreasing trend in the scores with successive sessions of ECT in both the groups. At the end of 8th session it was also observed that the scores in ketamine group were less than the sodium thiopental group and this difference was statistically significant (p=0.04). However this difference in the scores of HDRS was significantly different at the end of each session before the final 8th session.

Table 3: HDRS scores as mean ± SD in both groups

Session	Group A (Ketamine)	Group B (ST)	*p-value*
1 (pre ECT)	30.1 ± 7.4	28.9 ± 7.5	0.45
2	29.5 ±7.1	22.1± 6.9	0.28
4	14.9±6.2	16.1±8.4	0.06
6	11.9± 6.5	13.2±8.5	0.28
8	8.4±5.2	10.6±7.9	0.04*

HDRS= Hamilton Depression Rating Scale, SD=standard deviation, ST= Sodium thiopental, ECT= Electroconvulsive therapy, * statistically significant:

DISCUSSION

Our study was a single blinded study where patients were unaware of inducing agent used. The results of our study clearly showed that the rise in blood pressure was seen in both the groups but it was significantly more with ketamine than sodium thiopental. The side effects such as headache, nausea and fear with awakening illusions were more with ketamine group. Another study done by Jung HJ *et al*, showed that the incidence of emergence delirium was similar with ketamine and sodium thiopental.[10] Both the anesthetic drugs showed reduction in seizure duration with each successive session but still it was comparatively more in ketamine group. It our study depression scores were seen to be reducing with each session of ECT in both the groups. But patients in ketamine group were having better scores at the end of last session and this difference was statistically significant. Similar results were seen in the study done by Barkhori *et al*. where there was significant reduction in depression scores with ketamine as compared to sodium thiopental.[11] There were several other studies which demonstrated rapidly decreasing depression score with ketamine.[12,13] Few complications like headache, nausea and fear of awakening illusions were definitely more with ketamine but other side effects were comparable to sodium thiopental. The mechanism of improvement in mood of the depressed patients is believed to be induction of neurogenesis.[14,15] Ketamine was also seen to improve mood in patients undergoing surgery when it was used as an inducing agent.[16] As the effect of ketamine in reducing the depression scores and rapid recovery in major depression is significantly more it can be pitched above sodium thiopental as an induction agent of choice for electroconvulsive therapy in patients with drug resistant major depressive disorder,

CONCLUSION

Therefore we conclude that if the adverse effects can be made tolerable to the patients by adequate premedication with antiemetics and other rescue medications during the post procedure period ketamine is a promising agent to be used as induction agent of choice as there is clear improvement in the depression scores with repeated ketamine infusions. Ketamine can also be combined with propofol to reduce its side effects. However the effects of ketamine on other aspects of psychological behaviour is yet to be studied.

ACKNOWLEDGEMENT

We would like to thank the dean of our college for supporting our study; we also extend our gratitude of all the staff members of psychiatric department for their kind co-operation during the conduct of study.

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Source of Support: None Declared
Conflict of Interest: None Declared