The effect of ketamine versus thiopental sodium on hemodynamic profile and seizure duration during electroconvulsive therapy in patients with major depressive disorder: A randomized cross-over clinical trial

Alireza Pournajafian, Hamidreza Faiz, Mohammad Ali Motazedi Ghajar, Zahra Sadat Koleini, Masood Mohseni

Abstract

Background: Electroconvulsive therapy (ECT) is an effective treatment in major depressive disorder (MDD). Earlier studies suggest that ketamine has antidepressive effects and prolongs seizure duration in favor of therapeutic efficacy of ECT. A great concern with the use of ketamine is its possible adverse hemodynamic effects during ECT. This study was conducted to compare the hemodynamic effect and seizure duration between ketamine and sodium thiopental, a common anesthetic in ECT.

Methods: In a cross-over clinical trial, 26 patients of either sex with MDD who were candidates for ECT therapy in a university hospital were enrolled. A total of 13 patients received induction with ketamine in the first session and thiopental for the second. The sequence of treatments was vice versa in the other group. The followings were measured in all patients: blood pressure, heart rate, and oxygen saturation before induction, immediately after induction, at 1, 2, 4, and 10 minutes postinduction, and after recovery from anesthesia. Also, seizure duration, recovery time, and complications of treatments were measured. Chi square test and student t test were used for categorical data and numerical data, respectively. P values < 0.05 were considered statistically significant. Analyses were performed with SPSS software version 21.0.

Results: Heart rate, systolic and diastolic blood pressure, oxygen saturation, and recovery time were comparable between groups. Mean duration of convulsion in patients who received ketamine was significantly more than those who received STP (36±11 vs 28±9 s, p=0.001). Myalgia was less common in patients who received ketamine rather than sodium thiopental (11.5 vs 46.2%, p=0.014).

Conclusion: Ketamine prolongs seizure duration with no deleterious effects on hemodynamic parameters. Considering the antidepressant effects of ketamine, it may be a better choice, compared to thiopental sodium, for MDD patients.

Keywords: Major depressive disorder, Electroconvulsive therapy, Ketamine, Thiopental Sodium, Anesthesia, Hemodynamic

Introduction

Electroconvulsive therapy (ECT) is a therapeutic approach proved for major depression (1). To convey ECT, general anesthesia is administered for adequate analgesia and relaxation. To date, different drugs such as thiopental,
Ketamine versus thiopental sodium in ECT

methohexital, propofol, and etomidate have been adminis-
tered. The drug has varying effects on duration and
quality of seizure and hemodynamic changes (2-4). Alth-
ough ECT may be generally safe, risks and possible com-
plications like cognitive impairment and cardiovascular
complications have been noted (5-7). As a result, different
anesthetic agents have been used during the procedure to
minimize adverse effects, keeping the hemodynamic pro-
file stable, and favorably improving the quality of convul-
sion (8).

Thiopental sodium is an anesthetic widely used in general
anesthesia. Like other barbiturates, it has anticonvulsive
properties and reduces seizure duration. Ketamine is a non-
competitive high-affinity N-methyl D-aspartate (NMDA)
receptor antagonist and has antidepressant effects through
glutamate pathways (1,3). It has been suggested that those
patients who received ketamine in ECT required less ther-
apeutic sessions and had higher scores in the Hamilton rat-
ning scale (9). To our knowledge, the hemodynamic effects
of ketamine in ECT have not been evaluated. This study
was conducted to compare the effects of ketamine on sei-
zure duration and hemodynamic profile with thiopental as
the most commonly used anesthetic in ECT.

Methods

Patients with ASA physical status II-III were recruited in
a university hospital setting (Rasoul Akram Medical Cen-
ter), with no gender and age limitations, from Aug 2013 to
April 2014. All participants had the diagnosis of major de-
pression according to the Beck Depression Inventory Crite-
ria and were candidates for electroconvulsive therapy. Pa-
tients who encountered significant side effects in the first
session of therapy or missed the second session were ex-
cluded from the study. Patients with known true allergy
to ketamine, thiopental sodium, or succinylcholine and those
with documented prolonged convulsion (more than 1 mi-
ute) in the earlier treatment sessions were not included.
Written informed consent was obtained from the patients’
companions. With the approval of the medical ethics com-
mittee of the university, the clinical trial was registered in
Iranian Registry of Clinical Trials (IRCT), with the code of
201306255026N3.

Study design

In this cross-over clinical trial, 26 participants were ran-
domly allocated by sealed envelopes to receive ketamine
for the first and thiopental sodium for the second sessions
or vice versa. Each patient received both treatments. Those
who encountered significant side effects in the first session
of therapy or did not return for the next session were ex-
cluded from the study.

After admission to the ECT room, patients lied down and
one small bore intravenous catheter (usually 22G) was in-
serted on their hand or forearm. Patients were hydrated with
normal saline 5 mL·kg⁻¹ and preoxygenated before induc-
tion of anesthesia. Participants were randomly allocated to
receive Ketamine 0.3 mg/kg or thiopental sodium 2 mg/kg
for induction of anesthesia. All patients received succinyl-
choline 0.5 mg/kg as muscle relaxant. After disappearance
of muscular fasciculation or 40 seconds after anesthesia in-
duction, ECT was performed by a psychiatrist. The ma-
chine for shock delivery was Thymatron® IV device (So-
matics, LLC. Lake Bluff, IL, USA). The energy was ad-
justed on 35 voltage and subsequently increased by 10 volt-
ages if the patient did not respond or showed insufficient
seizure duration. Oxygen mask was placed on the face of
the participants immediately after shock delivery and ven-
tilated after termination of convulsion. The patients were
monitored and cared for until meeting the discharge crite-
ria. Then, IV catheter was removed and patients were trans-
ferred to the ward.

Measurements

The primary outcomes were the duration of convulsion
and occurrence of clinically significant arrhythmias. The
secondary outcomes were the duration of recovery, hemo-
dynamic profile, and postconvulsion complications, includ-
ing sialorrhea, myalgia, nausea, and agitation. Hemody-
namic parameters were recorded before and during convul-
sion in 1, 2, 4, and 10 minutes after shock delivery. Blood
pressure, heart rate, and oxygen saturation were measured
with a standard noninvasive cardiovascular monitoring sys-
tem (S1800, Saadat Company, Iran). To measure the dura-
tion of convulsion, a cuff was applied to the lower limb of
the patients and the duration of jerking movements were
recorded. Recovery was considered when patients followed
the instructions and had stable hemodynamics. Complica-
tions, including bradycardia requiring atropine administra-
tion, significant tachyarrhythmia, postconvulsion nausea,
and sialorrhea, were recorded. Sialorrhea was defined as a
frequent need for suctioning. The patients were evaluated
for the occurrence of myalgia 6 hours after ECT.

Statistical analysis

Sample size calculation was based on the estimation of
the mean and variance of the treatment difference regarding
the variable of ‘duration of convulsion’. The approach of
large sample size approximation (>12 cases in either arm)
was selected for feasibility (10). Demographic data and out-
come measurements were analyzed using chi square test for
categorical data and t student test for numerical data. P val-
ues less than 0.05 were considered as statistically signifi-
cant. All data were analyzed with SPSS version 21.0 (Chic-
go, IL, USA).

Results

In this study, 32 participants were enrolled and 26 pa-
tients remained in analysis, including 12 women and 14
men (Fig. 1. CONSORT diagram). The mean duration of
convulsion in patients who received ketamine was signifi-
cantly more than those who received STP (36±11 vs 28±9
s, p=0.001). There were no statistical significant differences
in systolic and diastolic blood pressure and heart rate be-
tween the 2 groups (Table 1). Similarly, recovery time was
comparable between the 2 groups (ketamine, 15±5 vs STP,
16±4 min; p=0.592).

Myalgia was significantly less frequent in patients who
received ketamine than those who induced with STP. Brad-
Cardia requiring atropine administration was equally recorded in both groups (3.8%). Agitation and sialorrhea were more frequent in patients receiving ketamine than their counterparts, but the difference was not statistically significant (Table 2).

**Discussion**

Ketamine has been reported to improve cognitive and antidepressant effects and to protect against memory loss after ECT (3). Previous studies compared the effects of ketamine...

**Table 1. Hemodynamic measurements in two groups**

<table>
<thead>
<tr>
<th>Time Intervals</th>
<th>Medication</th>
<th>Systolic blood pressure</th>
<th>Diastolic blood pressure</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>After induction</td>
<td>Ketamine</td>
<td>134 (26) 139 (17) 140 (20)</td>
<td>82 (14) 88 (14) 85 (14)</td>
<td>86 (11) 85 (7) 85 (9)</td>
</tr>
<tr>
<td>Min 1</td>
<td>Ketamine</td>
<td>166 (26) 170 (33) 186 (29)</td>
<td>101 (13) 93 (20) 97 (17)</td>
<td>103 (22) 95 (7) 99 (14)</td>
</tr>
<tr>
<td>Min 3</td>
<td>Ketamine</td>
<td>148 (16) 161 (23) 154 (20)</td>
<td>90 (11) 90 (18) 90 (14)</td>
<td>99 (23) 96 (15) 98 (19)</td>
</tr>
<tr>
<td>Min 5</td>
<td>Ketamine</td>
<td>138 (16) 150 (17) 144 (17)</td>
<td>85 (11) 85 (14) 85 (12)</td>
<td>93 (18) 92 (17) 92 (17)</td>
</tr>
<tr>
<td>Min 10</td>
<td>Ketamine</td>
<td>133 (15) 141 (17) 137 (16)</td>
<td>86 (8) 83 (12) 84 (10)</td>
<td>89 (18) 83 (10) 81 (9)</td>
</tr>
<tr>
<td>After convulsion</td>
<td>Ketamine</td>
<td>128 (10) 134 (16) 131 (14)</td>
<td>84 (6) 80 (8) 82 (7)</td>
<td>83 (10) 81 (8) 81 (7)</td>
</tr>
</tbody>
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<td>Thioental</td>
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<td>86 (11) 85 (7) 85 (9)</td>
<td>85 (10) 85 (15) 85 (14)</td>
</tr>
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<td>165 (36) 148 (10) 156 (27)</td>
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</tr>
</tbody>
</table>

**Table 2. The relative frequency of complications in two groups**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Ketamine (n=26)</th>
<th>Thioental (n=26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe bradycardia</td>
<td>1 (3.8)</td>
<td>1 (3.8)</td>
<td>1.000</td>
</tr>
<tr>
<td>Agitation</td>
<td>2 (7.7)</td>
<td>0 (0)</td>
<td>0.492</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (3.8)</td>
<td>2 (7.7)</td>
<td>0.952</td>
</tr>
<tr>
<td>Sialorrhea</td>
<td>3 (11.5)</td>
<td>1 (3.8)</td>
<td>0.614</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (11.5)</td>
<td>12 (46.2)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

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Med J Islam Repub Iran. 2020 (25 Feb); 34.11.
and thiopental on convulsion profile in ECT patients (3, 11). Patients receiving ketamine had longer duration of convulsion and better cognitive function and recovery from depression (12-14). Ketamine blocks NMD receptors; thus, stimulating glutamate releases and has antidepressant effects. Similarly, the results of this study showed that the administration of ketamine is associated with longer duration of convulsion with good enough recovery profile compared to thiopental sodium.

Increased blood pressure and heart rate are potential hemodynamic adverse effects of ketamine administration. However, ketamine did not cause adverse hemodynamic effects in the patients. An earlier study suggested that ketamine and etomidate provide better quality and duration of effects in the patients. An earlier study suggested that ketamine and etomidate provide better quality and duration of effects in the patients.

Recovery time was similar in the 2 groups. The duration of action of ketamine with a dose of 2 mg/kg was 10 to 15 minutes. However, the low required dose of ketamine in the ECT offers the fast recovery from anesthesia and convulsion. Ketamine 0.3mg/kg was administered, which is satisfactorily sufficient for the induction of anesthesia in ECT patients. To our knowledge, it should be administered slowly and let it affect the level of consciousness, patiently before the induction of convulsion by electrical discharge. The lower incidence of myalgia with the use of ketamine was recorded, which could be reasonably explained by its analgesic effects (15). In this study, the only disadvantage of ketamine versus STP was more frequent sialorrhea.

According to the cross-over design, every patient was compared with him/herself. Elimination of confounding factors due to differences in baseline characteristics was the strength of this study. A concern in cross-over clinical trials is the possibility of carry-over effect between treatments, which confounds the estimates of the treatment effects. Since the half-life of a single dose of administered anesthetics is in the boundary of minutes, 2 days of wash-out period makes the carry-over effect unlikely. Nevertheless, this study had some limitations. Long term effects of ECT on depression and cognitive impairment was not record. Another limitation was variable voltages used in the 2 sessions of ECT, which was applied due to psychiatric remedies.

**Conclusion**

In conclusion, ketamine seems to be a reasonable choice for anesthesia for ECT because of its convulsion profile, fast recovery from anesthesia, stable hemodynamic profile, and analgesic effect. Moreover, its antidepressant effects will make it a more favorable choice in patients with depression disorder.

**Conflict of Interests**

The authors declare that they have no competing interests.

**References**


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Med J Islam Repub Iran. 2020 (25 Feb); 34:11.