
Accumulating evidence suggests that N-methyl-d-aspartate receptor (NMDAR) antagonists (e.g. ketamine) may exert rapid antidepressant effects in MDD patients. In the present study, we evaluated the rapid antidepressant effects of ketamine compared with the electroconvulsive therapy (ECT) in hospitalized patients with MDD. In this blind, randomized study, 18 patients with DSM-IV MDD were divided into two groups which received either three intravenous infusions of ketamine hydrochloride (0.5 mg/kg over 45 min) or ECT on 3 test days (every 48 h). The primary outcome measure was the Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HDRS), which was used to rate overall depressive symptoms at baseline, 24 h after each treatment, 72 h and one week after the last (third) ketamine or ECT. Within 24 h, depressive symptoms significantly improved in subjects receiving the first dose of ketamine compared with ECT group. Compared to baseline level, this improvement remained significant throughout the study. Depressive symptoms after the second dose ketamine was also lower than the second ECT. This study showed that ketamine is as effective as ECT in improving depressive symptoms in MDD patients and have more rapid antidepressant effects compared with the ECT.


In electroconvulsive therapy (ECT), the use of anesthetics without relevant anticonvulsant properties such as ketamine and etomidate may be favorable for seizure quality. Since there is a relative paucity of studies devoted to this issue, our aim was to compare different anesthetics for ECT regarding their impact on seizure quality and different seizure parameters. We retrospectively compared ketamine (n = 912 anesthesias), etomidate (n = 227 anesthesias), thiopental (n = 2,751 anesthesias), and propofol (n = 42 anesthesias) on their influence on general seizure quality and different seizure parameters by multivariate repeated measurement regression analyses. The use of ketamine and etomidate as anesthetics led to seizures that were overall higher in quality and also longer in motor seizure activity when compared to anesthesia with thiopental and propofol. Ketamine was most favorable concerning central inhibitory potential that was indirectly quantified by concordance and postictal suppression. The worst seizure quality was observed with propofol anesthesia; further, this substance had a negative impact on autonomic activation and seizure duration. Based on the data of this retrospective study, the use of ketamine or etomidate as anesthetic in ECT might be advantageous due to the induction of high-quality seizures.

Case report


Case report


To assess the clinical utility of ketamine as an anesthetic agent for electroconvulsive therapy (ECT), based upon recent findings that ketamine may have antidepressant properties. Depressed ECT patients were randomly assigned to receive anesthesia with either ketamine or methohexital. Outcome measures included assessments of depressive severity, cognition, post-anesthesia side effects, and hemodynamics. Twenty one patients were treated with ketamine and 17 with methohexital. There were no significant differences in depression or cognitive outcomes between the two drugs. Additionally, there were no measures of post-anesthesia tolerability or hemodynamics which favored ketamine. Ketamine anesthesia does not accelerate the antidepressant effect of ECT or diminish the cognitive side effects, at least as measured in this study. Furthermore, there is no apparent benefit of ketamine for speed or quality of post-ECT recovery, and it is associated with higher systolic blood pressures after the treatments. Ketamine is associated with longer motor seizure duration than methohexital
Objectives: Recently, ketamine has attracted attention for induction of anesthesia during electroconvulsive therapy (ECT). This study compared the effects of thiopental and ketamine in patients undergoing this procedure. Method: This randomized, double-blind clinical trial included inpatients, with major depressive disorder, undergoing ECT. Subjects were randomly allocated to receive either ketamine or thiopental. Mini-Mental State Examination and Hamilton Depression Rating Scale were used to assess memory and depression, respectively, before the first and second ECT sessions as well as a few days and 1 month after the sixth session. The electrical charge, seizure duration, blood pressure, and heart rate were also recorded. Results: Of the 31 patients, 17 met the criteria for the ketamine group but 2 dropped out of the study. Therefore, 15 patients received ketamine and 14 received thiopental. Each patient underwent 6 ECT sessions. At the end of the study, depression improved significantly in both groups. However, a significant difference in depression improvement was noted only before the second ECT with ketamine compared with thiopental. Despite a significant decline in Mini-Mental State Examination scores in both groups after the first ECT, cognitive function improved afterward but was only significant in ketamine group. Seizure duration was found to be significantly longer with ketamine. Stimulus intensity used for each ECT increased gradually and linearly with a greater increase observed in thiopental group. Conclusions: Ketamine administration during ECT is well tolerated and patients may experience earlier improvement in depressive symptoms, longer seizure duration, and better cognitive performance when compared with thiopental.


Letter
OBJECTIVE: Ketamine in electroconvulsive therapy (ECT) anesthesia has been reported to be associated with better seizure quality and longer duration compared with methohexital anesthesia. Furthermore, ketamine may enhance the efficacy of ECT while having rapid independent antidepressant properties itself. However, data on the effects of ketamine with ECT are inconsistent, and there are no reports of S-ketamine. The aim of the present pilot study was to explore the effects of S-ketamine as an adjuvant to propofol on the efficacy, seizure duration, and quality of electroencephalography in patients with treatment-resistant depression. METHODS: Thirty-two patients with a recurrent severe or psychotic major depressive disorder with treatment resistance to antidepressants were included in the study. For induction of anesthesia, the patients were randomized into 2 study groups. The S-ketamine group first received S-ketamine (0.4 mg/kg) as a bolus and then propofol. The treatment-as-usual group first received saline and then propofol. RESULTS: A statistically significant and clinically relevant reduction in the depression symptom scores was found in both study groups during ECT. There was no difference in the magnitude or speed of response between the study groups, nor was there any difference in the numbers of ECT treatments, seizure thresholds, seizure durations, and the electrical doses either. The patients recovered from anesthesia equally, but the degree of posttreatment disorientation and restlessness was more marked in the S-ketamine group. CONCLUSIONS: In conclusion, a subanesthetic adjuvant dose of S-ketamine with propofol may not increase the effects of ECT in patients with treatment-resistant depression. However, S-ketamine was associated with increased posttreatment disorientation and restlessness.


Letter about Wang et al 2012


Letter

Case report


Response to Kellner 2013


OBJECTIVES: Studies now provide strong evidence that the N-methyl-D-aspartate receptor antagonist ketamine possesses rapidly acting antidepressant properties. This study aimed to determine if a low dose of ketamine could be used to expedite and augment the antidepressant effects of electroconvulsive therapy (ECT) treatments in patients experiencing a severe depressive episode. MATERIALS AND METHODS: Subjects with major depressive disorder or bipolar disorder referred for ECT treatment of a major depressive episode were randomized to receive thiopental alone or thiopental plus ketamine (0.5 mg/kg) for anesthesia before each ECT session. The Hamilton Depression Rating Scale (HDRS) was administered at baseline and at 24 to 72 hours after the first and sixth ECT sessions. RESULTS: Electroconvulsive therapy exerted a significant antidepressant effect in both groups (F2,24 = 14.35, P < 0.001). However, there was no significant group effect or group-by-time interaction on HDRS scores. In addition, post hoc analyses of the time effect on HDRS showed no significant HDRS reduction after the first ECT session for either group. CONCLUSIONS: The results of this pilot study suggest that ketamine, at a dose of 0.5 mg/kg, given just before ECT, did not enhance the antidepressant effect of ECT. Interestingly, the results further suggest that the coadministration of ketamine with a barbiturate anesthetic and ECT may attenuate the immediate antidepressant effects of the N-methyl-D-aspartate antagonist.
The aim of this study was to evaluate the effect of a ketamine:propofol combination (‘ketofol’) for electroconvulsive therapy on seizure activity, haemodynamic response and recovery parameters, and to compare with those with the effects of propofol alone. Twenty-four patients underwent a total of 144 electroconvulsive therapy sessions, allocated in this prospective, double-blind, crossover study. Patients were randomly assigned to receive 1 mg/kg ketofol (0.5 mg/kg propofol plus 0.5 mg/kg ketamine) or 1 mg/kg propofol 1% for anaesthesia induction. Seizure duration and quality, haemodynamic data, recovery parameters and side-effects were recorded and analysed between groups. Both motor and electroencephalography seizure durations in the ketofol group (29 +/- 17 and 41 +/- 17 seconds, respectively) were similar to that in the propofol group (28 +/- 13 and 38 +/- 16 seconds, respectively). Postictal suppression index was higher in the ketofol group (89.63 +/- 7.88) than in the propofol group (79.74 +/- 14.6) (P <0.05). In the ketofol group, heart rate after the seizure ended and mean arterial pressures, recorded at 0 and 5 minutes after the seizure ended, were higher than in the propofol group. Time to obeying commands was longer in the ketofol group (P <0.05). There were no untoward psychological reactions following ketofol. Although no superiority to propofol in terms of seizure duration, haemodynamic or recovery parameters was found, the ketofol mixture selected in our study provided better seizure quality than propofol. We conclude that ketofol can be an alternative strategy to enhance the seizure quality and clinical efficiency of electroconvulsive therapy.

BACKGROUND: Preliminary evidence suggests that the use of ketamine during electroconvulsive therapy (ECT) may be neuroprotective against cognitive impairment and have synergistic antidepressant effects. This study tested whether the addition of ketamine reduced cognitive impairment and enhanced efficacy over a course of ECT, in a randomised, placebo-controlled, double-blind study. METHODS: Fifty-one depressed patients treated with ultrabrief pulse-width right unilateral ECT were randomised to receive either ketamine (0.5mg/kg) or placebo (saline) in addition to thiopentone during anaesthesia for ECT. Neuropsychological outcomes (measured before ECT, after six treatments, and after the final ECT treatment) and mood outcomes (measured before ECT, and weekly after every three ECT treatments) were measured by a rater blinded to treatment condition. RESULTS: Neuropsychological outcomes did not differ between groups. The ECT-ketamine group had a slightly greater improvement in depressive symptoms over the first week of treatment and at one-week follow up, though there was no overall difference in efficacy at the end of the ECT course. No psychomimetic effects were detected. LIMITATIONS: The study was conducted in a clinical setting, so not all aspects of ECT treatment were fully controlled. Thiopentone doses differed slightly between groups, in order to accommodate the addition of ketamine to the anaesthetic. CONCLUSIONS: The addition of ketamine did not decrease cognitive impairment in patients having ultrabrief pulse-width right unilateral ECT, but was safe and slightly improved efficacy in the first week of treatment and at one-week follow up. CLINICAL TRIALS REGISTRATION: Clinicaltrials.gov ID: NCT00680433. Ketamine as an anaesthetic agent in electroconvulsive therapy (ECT).

www.clinicaltrials.gov

**BACKGROUND:** Electroconvulsive therapy (ECT) is a preferred therapy for major depressive disorder. Intravenous propofol, a sedative and hypnotic agent, is one of the choices of anesthetic for ECT. Ketamine, another anesthetic agent, providing sedation, amnesia, and analgesia, can also be used in patients undergoing ECT owing to its rapid action and persistent antidepressive effect. One adverse effect of ketamine is cardiovascular excitement, which may be reduced by propofol. Currently, the effects of combined anesthesia (propofol and ketamine) for patients with depressive disorder who have undergone ECT are unclear. The purpose of this study was to investigate the effects of the combined agents for patients undergoing ECT. **METHODS:** Forty-eight patients with Hamilton Depression Rating Scale (HDRS) scores greater than 20 were randomly divided into 3 groups (n=16 each): propofol group (group P), ketamine group (group K), and propofol plus ketamine group (group PK). Propofol (1.5 mg/kg), ketamine (0.8 mg/kg), and propofol (1.5 mg/kg) plus ketamine (0.8 mg/kg) were infused to each group of patients, respectively, before ECT by an anesthesiologist with no knowledge of the HDRS score. For the purpose of this study, the patients received a single ECT treatment and were assessed for depression using the HDRS scores (1 day before ECT and days 1, 2, 3, and 7 after the ECT treatment) by a psychiatrist with no knowledge of the randomization group. After the final assessment, the patients received further treatment as needed up to 3 treatments per week. Seizure energy index, seizure duration, and adverse effects were observed during anesthesia by a nurse with no knowledge of the study group. **RESULTS:** The HDRS scores improved earlier in group K and group PK. Decreases in HDRS scores were significantly greater in group K and group PK compared with those in group P. The adverse effects in group PK were fewer than those in group K. Seizure energy index and seizure duration in group K and group PK were higher and longer than those in group P during ECT. **CONCLUSION:** The results suggested that propofol combined with ketamine anesthesia might be the first-choice anesthesia in patients with depressive disorder undergoing ECT.


**PURPOSE:** Propofol and ketamine have become progressively popular in electroconvulsive therapy (ECT) anesthesia, although propofol shortened seizure duration and ketamine might cause cardiotoxicity, psychotic episodes, and delayed recovery. Ketofol is a combination of ketamine and propofol, and the current study was designed to evaluate the effect of ketamine, propofol, and ketofol on hemodynamic profile, duration of seizure activity, and recovery times in patients undergoing ECT. **METHODS:** Ninety patients (44 women, mean age 27.8 +/- 7.2 years) in one ECT session were enrolled and randomized to the propofol, ketamine, or ketofol group. Hemodynamic profile duration of seizure activity and recovery times were recorded. **RESULTS:** Motor seizure duration in the propofol group was significantly decreased compared to other groups (p < 0.001), whereas spontaneous breathing time in the ketamine group statistically increased compared to the propofol group (p = 0.001), and also eye-opening time (p < 0.001) and obeying-command time (p < 0.001) was significantly increased in the ketamine group compared to other groups. Heart rate (HR) at induction (ketamine 91.2 +/- 13.6 vs. propofol 77 +/- 13.4 and ketofol 79.9 +/- 15.6; p < 0.013; p < 0.08, respectively) was statistically significantly increased in the ketamine group compared to other groups, and HR at the third minute (ketamine 92 +/- 12.9 vs. propofol 79.4 +/- 9.3 and ketofol 81.5 +/- 14.2; p < 0.012, p < 0.048) was also statistically significantly increased in ketamine group compared to other groups. **CONCLUSION:** The ketofol 1:1 mixture is associated with longer mean seizure time than propofol, and shorter mean recovery times than ketamine, with better hemodynamic stability, without any important side effects in ECT anesthesia.

**BACKGROUND:** Ketamine rapidly improves depressive symptoms in patients with treatment-resistant major depressive disorder (MDD) who do not respond to multiple standard antidepressants. However, it remains unknown whether ketamine is equally effective in patients with MDD who previously also did not respond to electroconvulsive therapy (ECT). **METHODS:** This study compared 17 patients with treatment-resistant MDD who previously did not respond to ECT and 23 patients with treatment-resistant MDD who had not previously received ECT. All subjects received a single open-label infusion of ketamine (0.5 mg/kg). Patients were evaluated using the Montgomery-Asberg Depression Rating Scale (MADRS) at baseline (60 min before the infusion), as well as at 40, 80, 120, and 230 min after infusion. **RESULTS:** Depressive symptoms were significantly improved in the ECT-resistant group at 230 minutes with a moderate effect size (p < .001, d = 0.50, 95% C.I.: 0.21-0.80). At 230 minutes, the non-ECT exposed group showed significant improvement with a large effect size (p < .001, d=1.00, 95% C.I.: 0.71-1.29). **CONCLUSION:** Ketamine appears to improve depressive symptoms in patients with MDD who had previously not responded to ECT. These preliminary results encourage further investigation with a larger sample size to determine effectiveness compared to other treatment-resistant patients with MDD


In a retrospective chart review, we examined the effects of ketamine, an N-methyl-d-aspartate (NMDA) receptor antagonist, as electroconvulsive therapy (ECT) anaesthetic in patients suffering from therapy-resistant depression. We included 42 patients who received ECT treatment with either ketamine (n = 16) or the barbiturate thiopental (n = 26). We analysed the number of sessions until completion of ECT treatment (used as a surrogate parameter for outcome), psychopathology as assessed by pre- and post-ECT Mini-Mental State Examination (MMSE) and Hamilton Rating Scale for Depression (HAM-D) scores as well as ECT and seizure parameters (stimulation dose, seizure duration and concordance, urapidil dosage for post-seizure blood pressure management). The ketamine group needed significantly fewer ECT sessions and had significantly lower HAM-D and higher MMSE scores afterwards. As expected, the ketamine group needed more urapidil for blood pressure control. Taking into account the limits inherent in a retrospective study design and the rather small sample size, our results nonetheless point towards synergistic effects of ECT and ketamine anaesthesia, less cognitive side effects and good tolerability of ketamine

BACKGROUND: Certain pharmacological agents administered during electroconvulsive therapy may have the potential to prevent persistent retrograde amnesia induced during electroconvulsive therapy. This review examines mechanisms for electroconvulsive therapy-induced retrograde amnesia, and evaluates the suitability of the anaesthetic ketamine for preventing this amnestic outcome.

METHODS: A review of human studies, animal models and theoretical models in light of memory dysfunction following electroconvulsive therapy was conducted. MEDLINE was searched from 1950 to April 2009 using the MeSH terms "electroconvulsive therapy", "memory", "memory short term", "memory disorders", "excitatory amino acid antagonists", and "ketamine". PREMEDLINE was searched using the terms "electroconvulsive therapy", "amnesia" and "ketamine". Additional keyword and reference list searches were performed. No language, date constraints or article type constraints were used.

RESULTS: Disruption of long term potentiation as a mechanism for electroconvulsive therapy-induced retrograde amnesia is well supported. Based on this putative mechanism, an N-methyl-D-aspartate receptor antagonist would appear suitable for preventing the retrograde amnesia. Available evidence in animals and humans supports the prediction that ketamine, an anaesthetic agent and N-methyl-D-aspartate receptor antagonist, could effectively prevent electroconvulsive therapy-induced persistent retrograde amnesia. Whilst there are concerns about the use of ketamine with electroconvulsive therapy, such as possible psychotomimetic effects, on balance this anaesthetic agent may improve or hasten clinical response to electroconvulsive therapy.

CONCLUSIONS: A clinical trial is warranted to determine if ketamine anaesthesia during electroconvulsive therapy can lessen persistent retrograde amnesia and improve therapeutic response. Electroconvulsive therapy with ketamine anaesthesia may provide effective antidepressant action with minimal side effects.


BACKGROUND: Reports of the superiority of the antidepressant effect of ketamine during the conduct of electroconvulsive therapy (ECT) have been limited. We conducted an open-label trial of ketamine to determine whether ketamine as the anesthetic during ECT would provide a greater antidepressant effect than the antidepressant effect obtained with propofol.

METHODS: Between April 2006 and April 2007, 31 inpatients with treatment-resistant depression gave written consent for ECT and to participate in this study. An anesthesiologist who was unaware of the mental symptoms of the subjects assigned them to receive propofol or ketamine anesthetic according to the preferences of the patients, and the patients underwent 8 ECT sessions for 4 weeks. The Hamilton Depression Rating Scale (HDRS) was valuated before ECT and after the completion of the second, fourth, sixth, and eighth ECT sessions.

RESULTS: The HDRS scores improved earlier in the ketamine group, with decreases in HDRS scores that were significantly greater in the ketamine group.

CONCLUSIONS: The results suggested that it is possible to improve symptoms of depression earlier by using ketamine anesthesia.

The range of drugs available to provide anesthesia for patients undergoing electroconvulsive therapy (ECT) is ever increasing. Initially, anesthetic agents were selected on the basis of their capacity not to antagonize the induced seizure. This was not always a simple task because almost all general anesthetic agents have "in built" antiepileptic activity. Nonbarbiturate agents such as propofol have been successfully used as alternatives to thiopental and methohexitone, but this drug too has antiepileptic properties. Most recently, opioid-like drugs such as remifentanil have been used, and there has been renewed interest in ketamine, a phencyclidine derivative. Attention has also focused on whether the anesthetic agent selected may affect the cognitive impairment seen after ECT. Studies in this area are limited, but early results suggest that agents such as ketamine may have particular benefit. This article reviews the current literature dealing with anesthesia and postoperative cognitive impairment in general and with regard to ECT in particular.


Major depressive disorder is a difficult-to-treat and recurrent debilitating disorder. All approved somatic treatments for major depression to date require a significant time lapse before demonstrating an antidepressant effect. However, emerging evidence indicates a potential role for the use of ketamine to rapidly relieve symptoms of major depression. We present a case of severe, recurrent major depressive disorder that demonstrated marked improvement within 8 hours of receiving a preoperative dose of ketamine and 1 treatment of electroconvulsive therapy with bitemporal electrode placement. This case is supportive of a role of ketamine in relieving symptoms of major depressive disorder rapidly and safely.


Letter

Ten patients treated with electroconvulsive therapy (ECT) for depressive illness received anesthesia with either etomidate or ketamine. Three patients received both etomidate and ketamine anesthesia for ECT during separate episodes of depression. Patients anesthetized with ketamine for ECT had significantly less impairment of short-term memory function than did patients who received ECT with etomidate anesthesia. All patients who received both anesthetics for ECT during 2 different episodes had less memory loss during ECT with ketamine than with etomidate. These results show the importance of studying the effects of all anesthetic agents used during ECT on cognitive functions. The results imply that the effect of ECT on memory may be largely caused by effects mediated by glutamate at N-methyl-d-aspartate receptors and suggest that N-methyl-d-aspartate antagonists may offer protection from memory dysfunction during ECT.


Letter


Letter


The authors retrospectively compared the seizure duration, ictal EEG, and cognitive side effects of ketamine and methohexital anesthesia with ECT. This comparison was carried out with data from consecutive index ECT treatments that occurred immediately before and after a switch from methohexital to ketamine in 36 patients. Ketamine was well tolerated and prolonged seizure duration overall, but particularly in those who had a seizure duration shorter than 25 seconds with methohexital at the maximum available stimulus intensity. Ketamine also increased midictal EEG slow-wave amplitude. Thus, a switch to ketamine may be useful when it is difficult to elicit a robust seizure. Faster post-treatment reorientation with ketamine may suggest a lower level of associated cognitive side effects.
The use of ketamine anesthesia in electroconvulsive therapy (ECT) has been limited by its effects on blood pressure and concerns about untoward psychological reactions. However, because its effect on seizures is presumably less than that of methohexital, ketamine is listed as an alternative method to prolong seizure length. In this case series, 10 patients were given ketamine anesthesia during ECT. Whereas blood pressures were elevated above those seen with methohexital, seizure lengths actually decreased nonsignificantly with ketamine. There were no adverse psychological reactions noted with ketamine, which was generally well tolerated. It is concluded that ketamine anesthesia with the doses used in this series is unlikely to be associated with longer seizures in ECT. However, for theoretical reasons discussed, ketamine may be worth studying further in ECT.


During Phase III of nondominant unilateral ECT seizures, total energy, total peak energy, total delta energy, and 1/2-power duration of total delta energy are all less (shorter) in the unstimulated, dominant hemisphere than they are in the stimulated hemisphere. Interhemispheric differences in total energy are greatest in the lateral frontotemporal cortex, where they average 40 percent with both methohexital and ketamine anesthesias in F8 greater than F7 and T4 greater than T3. This circumstance probably explains the characteristic memory sparing associated with nondominant unilateral ECT. The magnitudes of total and peak energies in each frequency band decrease in the order: delta greater than theta greater than alpha greater than beta. Delta energy constitutes approximately three-fourths of the unilateral ECT seizure's total energy, and Phase III delta energy may be the therapeutically effective agent in this treatment. Seizures induced during ketamine anesthesia are associated with a higher percentage of delta energy, with higher magnitudes of total energy and of total and peak delta energy, and with longer 1/2-power durations of delta energy. Nondominant unilateral ECT with ketamine anesthesia offers promise as the treatment of choice for patients resistant to ECT administered with methohexital anesthesia.


Letter


No Abstract


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