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**Title:** The role of clinical pharmacology and pharmacogenetics in electroconvulsive therapy: from safety to efficacy  
**Issue Date:** 2016-01-14
Neuromuscular Blocking Agents for Electroconvulsive Therapy: A Systematic Review

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ABSTRACT

Electroconvulsive therapy (ECT) is the transcutaneous application of small electrical stimuli to the brain to induce generalized seizures for the treatment of selected psychiatric disorders. The clinical indications for ECT as an effective therapeutic modality have been considerably expanded since its introduction. Anaesthesia and neuromuscular blocking agents (NMBAs) are required to ensure patients’ safety during ECT. The optimal dose of muscle relaxant for ECT reduces muscle contractions without inducing complete paralysis. Slight residual motor convulsive activity is helpful in ascertaining that a seizure has occurred, while total paralysis prolongs the procedure unnecessarily. Suxamethonium is commonly used but nondepolarizing NMBAs are indicated in patients with certain comorbidities. In this review we summarize current concepts of N MBA management for ECT.
BACKGROUND

Electroconvulsive therapy (ECT) is a well-established psychiatric treatment; in which generalized seizures are induced by transcutaneous electrical stimuli to the brain. The aim of ECT is to induce seizure with the minimum required energy, tailored to the condition of each patient, to treat specific psychiatric disorders such as major depressive or cyclothymic disorders. ECT has evolved into a widely recognized, albeit controversial treatment modality in the practice of psychiatry. ECT is currently applied to between 5-10/100,000 persons/year in Asia and 20-100/100,000 persons/year in the Western Countries. In the United States approximately 4% of annual psychiatric admissions are solely for the purpose of ECT, resulting in about 100,000 treatments per year. In both the United Kingdom and Scandinavia, ECT appears to be declining in popularity, and in other European countries its use remains highly variable. As an example, ECT use is falling in Italy, but increasing in the Netherlands. The reason for these differences in the application of ECT is not clear, but financial considerations may be a contributing factor.

ECT owes its current acceptance to modern anaesthesia. Prior to the introduction of general anaesthesia, violent tonic-clonic convulsions associated with ECT could result in injuries such as limb fractures and compression fractures of vertebral bodies. The introduction of anaesthesia and neuromuscular transmission blockade to mitigate the tonic-clonic motor activity provided an effective means to reduce the physical and physiological trauma associated with uncontrolled tetanic muscle contractions.

Historical Perspective

Convulsive therapy for treatment of psychiatric disorders predates the use of electricity and the field of modern anaesthesiology. In the 1500s, the Swiss physician Paracelsus induced seizures by administering camphor by mouth to treat psychiatric illness. The first report of the use of seizure induction to treat mania, using camphor was published in 1785. Meduna advanced it based on the fact that patients with schizophrenia often improved when spontaneous epileptic seizures developed. He induced convulsions in a patient in 1934 by injecting a solution of oleum camphoratum, which although successful, was subsequently replaced by metrazol. The result of metrazol therapy in schizophrenic patients was reported in 1935. In 1939, Bennett reported several cases of spontaneous fractures, which occurred during convulsions induced by metrazol. He used Curare to modify metrazol-induced convulsive therapy. The introduction of electric shock therapy by Bini and Cerletti (Italy) in 1939 provided added impetus for the use of neuromuscular blockade. Bennett’s technique of using curare to block neuromuscular transmission greatly reduced the incidence of fractures and dislocations due to contraction of skeletal muscles.
seizures soon replaced metrazol therapy because it was safer and had fewer adverse side effects. The introduction of suxamethonium as a synthetic alternative to curare in 1951 led to the more widespread use of “modified” contemporary ECT.

**Contemporary use of ECT**

ECT has become an increasingly important treatment for therapy-resistant major depression, which has a prevalence ranging between 3% in Japan to 17% in the US. In general, approximately 70 percent of all patients with major depressive disorder achieve remission with pharmacotherapy. Patients who fail one or more adequate medication trials have a diminished but substantial rate of response to ECT. ECT is highly effective in the elderly, perhaps even more so than the younger age groups. ECT may also be used to treat bipolar disorder, mania and catatonia, neuroleptic malignant syndrome, Parkinson’s disease, refractory epilepsy, Tourette syndrome and refractory obsessive compulsive disorder.

The therapeutic tonic seizure that is induced by ECT usually lasts 10-15 seconds, and is followed by a clonic phase lasting 30-50 seconds, with a target seizure activity of more than 20 seconds. Electroconvulsive therapy is commonly administered 2 or 3 times per week during the immediate course of treatment, until either improvement is seen or the treatment is deemed unsuccessful. The total number of treatments administered during the short-term course of ECT varies, and is based on the presence or severity of cognitive side effects, as well as the efficacy of the treatment and evidence for clinical improvement.

**Electroconvulsive Therapy and Neuromuscular Blocking Agents (NMBAs)**

Bone fractures and dislocations have been reported when ECT treatments are performed without appropriate muscle paralysis. Consequently, neuromuscular blockers are required to minimize the convulsive motor activity, in order to prevent fractures and physical injury during the seizure, which is especially important in patients with osteoporosis or a history of spinal injury. The aims of neuromuscular blocking for ECT could be summarized as: (1) Reduction of motor activity (with accurately assessed paralysis) to avoid injury, (2) Minimal interference with seizure activity, and (3) Prompt recovery of spontaneous ventilation without residual paralysis.

It is important to await the induction of general anaesthesia before neuromuscular blocking agents are administered. Although a relatively “light level” of anaesthesia is preferred (the procedure is not painful) to avoid prolonged emergence, the anaesthetic regimen should provide loss of response to vigorous stimulation while controlling the cardiovascular responses and autonomic arousal. Cardiovascular responses consist of a brief initial increase in parasympathetic activity, followed by sympathetic response. In certain patients
the sequence described may result in bradycardia (or even sinus pause) followed by tachycardia, dysrhythmia, and hypertension. If not properly controlled, the haemodynamic response to ECT can induce myocardial ischemia and even infarction, as well as transient neurologic ischemic deficits, intracerebral hemorrhages, and cortical blindness. However, adequate monitoring and therapy of hypertension and tachycardia with short-acting drugs enables ECT to be used even in patients with a variety of severe cardiovascular impairments.

Based on its rapid onset, short duration of action, and rapid recovery, suxamethonium is considered the NMBA of choice for ECT. Small doses of nondepolarizing NMBAs such as mivacurium and rocuronium are alternatives that may be used, but the prolonged effects of nondepolarizing NMBAs need to be adequately reversed before emergence from anaesthesia. Moreover, the sensitivity to the effects of these NMBAs is highly variable, even in patients with no known risk factors or complicating neuromuscular disorders. As an example, the coefficient of variation for the 50% effective dose (ED50) of rocuronium is > 25%. Thus, even in a relatively small cohort of patients the ED50 may vary from 0.09 mg.kg\(^{-1}\) to as high as 0.25 mg.kg\(^{-1}\) (even higher in the absence of inhalational anaesthetics). Therefore, it is prudent to monitor the effects of nondepolarizing NMBAs during ECT.

Although 50% twitch depression is suggested to provide optimal conditions for endotracheal intubation, this level of blockade may be insufficient to mitigate the excessive muscle contractions during ECT. A twitch depression of 11-25% was reported appropriate in one study, but the optimal level of neuromuscular blockade for ECT remains largely unknown. Future studies are warranted to systematically examine ECT quality and outcome with different levels of neuromuscular blockade, and to test if a twitch depression of 50% is also adequate for ECT.

**Suxamethonium (Succinylcholine)**

The mean dose of suxamethonium producing 95% blockade (ED\(_{95}\)) at the adductor pollicis muscle is 0.3 to 0.35 mg.kg\(^{-1}\). The onset of skeletal muscle paralysis is achieved 30 to 60 seconds after administration of suxamethonium, and usually lasts between 5 to 10 min (5 min at the dose of 0.5 mg.kg\(^{-1}\) and 10 min at the dose of 1 mg.kg\(^{-1}\), assessed as 90% recovery from neuromuscular blockade). Although a single best dose of suxamethonium has not been identified for ECT, 0.5 mg.kg\(^{-1}\) to 1 mg.kg\(^{-1}\) is often used based on previous experience of anaesthesia providers and defined interindividual variability of its effects. Reducing the dose of suxamethonium from 1.0 to 0.60 mg.kg\(^{-1}\) shortens the duration of neuromuscular effect at the adductor pollicis with 1.5-2 min. The extent to which this dose reduction affects the duration of neuromuscular blockade at the diaphragm, laryngeal adductors, or the upper
airway muscles in the ECT setting has not been studied. When complete neuromuscular block is important, however, doses of 1.0 to 1.5 mg.kg\(^{-1}\) are generally appropriate.\(^{46}\) During the first ECT session, it has been recommended that a higher dose (1 mg.kg\(^{-1}\)) should be used.\(^{38,44}\) after which the suxamethonium dose can be adjusted based on the individual patient’s amount of motor activity.\(^ {47}\) The time until full recovery is dose-dependent and reaches 10 to 12 min after a dose of 1 mg.kg\(^{-1}\).\(^ {48}\) Using larger doses can lead to a complete absence of motor activity, which might impede monitoring of seizure adequacy.

Suxamethonium has many side effects, compelling the clinician to perform a risk-benefit analysis for individual patients prior to its administration. One of the most deleterious side effects of suxamethonium is hyperkalaemia leading to cardiovascular instability in susceptible patients. Several recent reports implicate distinct pathologic states that predispose a patient to suxamethonium-induced hyperkalaemia.\(^ {49-54}\) A common and important risk factor is prolonged immobilization,\(^ {55}\) especially in elderly patients. Concomitant presence of pathologic conditions that up-regulate the acetylcholine receptors (e.g. meningitis) can lead to a more rapid and profound increase in serum potassium levels after suxamethonium.\(^ {56}\) Other important side effects include bradycardia,\(^ {57}\) neuroleptic malignant syndrome (NMS) and malignant hyperthermia (MH).\(^ {36,57}\) Suxamethonium should, therefore, be avoided in any patient with a risk for severe hyperkalaemia\(^ {56}\) or with a history of, or susceptibility to NMS, MH, or catatonic schizophrenia.\(^ {58,59}\)

Irrespective of the choice of the anaesthetic technique, previous studies\(^ {60-63}\) have shown that ECT may produce asystole at any point during the course of a series of treatments. Conversely, even if haemodynamically significant bradyarrhythmias or asystole occur during one treatment, subsequent ECTs may be safely conducted if pertinent risk factors are eliminated (e.g. vagal tone or high potassium levels).\(^ {63}\)

**Nondepolarizing Neuromuscular Blocking Agents**

In contrast to suxamethonium, nondepolarizing NMBAs, used to achieve muscle relaxation for ECT treatment do not pose risk of side effects related to muscle fasciculation and cholinergic activation, or the potential to cause hyperkalaemia or malignant hyperthermia. The down-side of these NMBAs relates to their relatively long duration of action, typically beyond the time required for an ECT procedure, even when intermediate-acting NMBA are used. Also, there is wide variability in the sensitivity to the effects of these NMBAs, requiring that high doses be administered initially to reliably obtain neuromuscular blockade. The time to onset of effect is also variable between agents (see below) and need to be considered. Accordingly, adequate neuromuscular transmission monitoring is recommended to titrate the effect of these NMBAs, and pharmacological reversal is usually required.
Mivacurium
A nondepolarizing NMBA with a relatively short duration of action, mivacurium has been used as an alternative to suxamethonium for ECT treatment. Savarese and collaborators showed that 0.08 mg.kg$^{-1}$ of mivacurium (its ED$_{95}$) is less effective than 0.5 mg.kg$^{-1}$ suxamethonium in blocking the neuromuscular transmission, when applied 120 seconds and 30 seconds before ECT, respectively. Fredman and colleagues conducted a dose-effect study of mivacurium (0.12 to 0.2 mg.kg$^{-1}$) in a patient with susceptibility to neuroleptic malignant syndrome and history of prolonged bed-rest, and found that only 0.2 mg.kg$^{-1}$ of mivacurium given 3 min before ECT was associated with effective muscle relaxation during ECT-induced seizure. The recommended dose of 0.15 mg.kg$^{-1}$, or any of the doses smaller than 0.2 mg.kg$^{-1}$, did not effectively mitigate the tonic-clonic response to ECT. Although mivacurium can cause a significant histamine release and occasional hypotension, the authors reported no haemodynamic instability or clinical signs of histamin release. A similar dose (0.15-0.25 mg.kg$^{-1}$) appears to be sufficient for ECT in patients with myasthenia gravis, as was reported by Gitlin. Others have reported optimal neuromuscular blockade with 0.12-0.16 mg.kg$^{-1}$ (in a patient with neuroleptic malignant syndrome) or 0.15-0.25 mg.kg$^{-1}$ (patients with or without myasthenia gravis). Based on data from three patients with major comorbidities (severe osteoporosis, amyotrophic lateral sclerosis, and bradycardia), Janis and colleagues recommended the use of 0.16 or 0.2 mg.kg$^{-1}$ for ECT treatment. A smaller dose (0.11 mg.kg$^{-1}$) was also reported to adequately blunt ECT-induced muscular contraction in a patient with post-polio syndrome with high risk of severe respiratory sequelae and neuromuscular dysfunction. Mivacurium has been used as a substitute for suxamethonium to avoid (potential) adverse effects like hyperkalaemia or bradycardia. (Table 2) Of note, mivacurium is also metabolised by pseudocholinesterase, and a prolonged effect is, therefore, expected in patients with pseudocholinesterase deficiency. Mivacurium usage in the United States has declined rapidly in favour of alternative agents that are perceived to offer a more rapid onset of action and a safer cardiovascular profile. It is more commonly used in Europe, in particular in the United Kingdom.

Atracurium and Cisatracurium
The dose of atracurium to effectively modify the tonic-clonic convulsions and prevent excessive muscle contractions during ECT was reported to be 0.5 mg.kg$^{-1}$ (2.5 times its ED$_{95}$), given 2-3 min prior to the treatment. Given the profound neuromuscular blockade and the prolonged duration of action associated with this relatively high dose, nevertheless, Lui and colleagues examined if 0.3 mg.kg$^{-1}$ also provides adequate neuromuscular blockade for ECT. The authors found that 0.3 mg.kg$^{-1}$ was sufficient to keep the T1 blockade at 11-25%, whereas 0.5 mg.kg$^{-1}$ maintained T1 blockade at 0-10% throughout the ECT. As was expected, the time to recovery to a T4 ratio of 0.5 was longer following 0.5 mg.kg$^{-1}$ compared
with 0.3 mg.kg\(^{-1}\) of atracurium (9.2 ± 0.8 minutes vs. 4.3 ± 0.4 minutes). \(^{35}\) Therefore, the authors recommended that the lower dose (0.3 mg.kg\(^{-1}\)) be used for ECT to reduce the risk for prolonged neuromuscular blockade and to ascertain the occurrence of generalized seizures, as indicated by peripheral muscle activity at the time of electrographic seizures.

In another report, 10-15 mg of atracurium was compared to 2-5 mg of suxamethonium in a 64 kg patient with atypical pseudocholinesterase. \(^{72}\) The dose to produce 90 % first twitch blockade was reported as 15 and 2.5 mg for atracurium and suxamethonium, respectively. A dose of 0.5 mg.kg\(^{-1}\) of atracurium has been used in other reports in patients with cholinesterase deficiency or burn injury. \(^{52,73}\) Because of the short duration of ECT relative to the duration of action of atracurium, reversal of neuromuscular blockade with a cholinesterase inhibitor is usually recommended. \(^{27}\)

Cisatracurium, a stereoisomer of atracurium with minimal release of histamine, has largely replaced atracurium in clinical practice. At a dose of 0.05 mg.kg\(^{-1}\), the time to 90% of peak effect is approximately 4.5 min, and the maximum effect (100%) is not achieved until 7 min after its administration. \(^{74}\) Increasing the dose shortens the time to peak effect, but results in a long duration of action, which is usually unfavourable in a busy ECT setting. Despite an improved pharmacological profile with a reliable elimination, which is independent of renal or hepatic function, there are hitherto no clinical reports on the use of cisatracurium for ECT.

**Vecuronium and Rocuronium**

In appropriate doses, rocuronium has a speed of onset only marginally slower than that of suxamethonium, making it an appropriate alternative to suxamethonium for ECT. \(^{75}\) Williams and colleagues employed 0.3 mg.kg\(^{-1}\) of rocuronium in a patient with delayed motor recovery caused by suxamethonium during a prior ECT treatment. \(^{76}\) In a crossover study, Turkkal and colleagues compared rocuronium 0.3 mg.kg\(^{-1}\) versus suxamethonium 1 mg.kg\(^{-1}\) administered 90 seconds before ECT. The authors found similar ECT results in the two groups of subjects, with the exception of an increased time until the first spontaneous breath in the rocuronium group (9.46 vs. 8.07 min). Of note, the authors did not use quantitative methods to assess the neuromuscular transmission, limiting the ability to identify differences in the incidence and severity of residual paralysis. \(^{75}\)

Dodson reported the effects of a 2 mg IV dose of vecuronium in a patient who had developed bronchospasm after induction of anaesthesia and administration of 30 mg suxamethonium. \(^{77}\) The tonic-clonic response after vecuronium was similar to that after 30 mg of suxamethonium, and the authors concluded that 2 mg of vecuronium provides satisfactory neuromuscular blockade. Setoyama and colleagues administered vecuronium 0.01 mg.kg\(^{-1}\) followed
by a dose of 0.1 mg.kg\(^{-1}\) in three patients with NMS for ECT. They reported a prolonged anaesthesia time (38 vs. 19 min) in comparison to patients who received suxamethonium. \(^{78}\)

**Objective safety measures: Monitoring of the NMBA effect**

Monitoring of the neuromuscular transmission during ECT is helpful in titrating the dose of the NMBA to the desired relaxation, and confirming its effect. The isolated arm or cuff technique\(^{66,75}\) can be used to reliably monitor the motor response, particularly if electroencephalography (EEG) is not available to confirm the induction of generalized seizure activity. A forearm or leg is then isolated from circulation by inflating a blood pressure cuff to above systolic pressure after anaesthesia induction, but before NMBA administration. \(^{79}\) The technique is, however, not widely applied, as the available data is inconsistent with respect to its clinical benefit. \(^{80}\)

While the optimal relaxation level for ECT still needs to be defined in a prospective study, sufficient information is available on how to predict adequate recovery. If quantitative NMT monitoring (e.g. T1 recovery to 90% \(^{81}\) or TOF ≥0.9 \(^{59,66,68,72}\)) is not available, subjective methods such as visual and tactile assessment by a nerve stimulator, \(^{82}\) eye opening, head lift, tongue depressor, \(^{75,82,83}\) and hand grip should be considered (Table 1, 2). \(^{84,85}\) However, recently published data confirms that subjective techniques for assessment of the NMT fail to detect mild but clinically significant postoperative residual curarization. \(^{86-99}\) In fact, even very experienced observers are unable to manually detect TOF or double-burst stimulation (DBS) fade at TOF ratio of 0.4-0.6 or more. \(^{100-103}\) Therefore, quantitative measurement of the TOF ratio using acceleromyography is increasingly recommended for titrating the dose of muscle relaxants and their antagonists, and for detection of residual paralysis. \(^{33,90,96,99,104-113}\) Although the incidence of residual paralysis after ECT is unknown, recent data from postanaesthesia care units indicates an association between NMBAs and postprocedural residual paralysis as well as adverse respiratory events, and provides evidence in support of quantitative monitoring of the neuromuscular transmission. \(^{99,114}\)

**Reversal of the effects of nondepolarizing NMBA**

Tables 1 and 2 summarize the studies and case reports that compare nondepolarizing NMBAs and suxamethonium in ECT treatment. As is evident from these studies and was also outlined previously in this review, the use of a nondepolarizing NMBA is often required as a substitute for suxamethonium in patients with different comorbidities. Given the relatively prolonged duration of action of the nondepolarizing agents, nevertheless, it is often recommended that clinicians monitor the neuromuscular transmission, and confirm the return of neuromuscular function before emergence from anaesthesia. \(^{94,105,112,115-119}\) Cholinesterase inhibitors do not reverse deep levels of neuromuscular blockade, and may have undesirable autonomic side effects. \(^{100}\) Their effect may also wear off before complete clearance of an NMBA, resulting
in recurarization with the risk for adverse respiratory events. However, recurarization is unlikely after ECT, during which only a single and relatively low dose of an NMBA is given. A clinically interesting approach to neuromuscular blockade for ECT is to administer rocuronium for rapid onset of action, and to reverse the blockade with sugammadex.

Potential role of Sugammadex for ECT

Given the limitations of anticholinesterases and the complications associated with residual neuromuscular blockade, new reversal agents have been investigated. The ideal reversal agent can be given at any time after the administration of a NMBA and completion of ECT, and is efficacious irrespective of the degree of neuromuscular blockade. It has ideally a rapid onset of action and a minimal side effect profile.

Sugammadex is the first of a new class of selective muscle relaxant binding drugs developed for the rapid and complete reversal of neuromuscular blockade induced by rocuronium and vecuronium. Several studies have reported a predictable dose-response relationship with sugammadex for reversal of neuromuscular blockade. Published data from Duvaldestin and colleagues suggest that 2 mg.kg⁻¹ sugammadex is sufficient to reverse rocuronium at a posttetanic count of 1 or 2. It has been extrapolated from these findings that doses as low as 1 mg.kg⁻¹ may provide clinically satisfactory reversal of rocuronium in <5 minutes once the TOF count has returned to a value of ≥2. Available data from multiple other studies support this hypothesis. Sugammadex titration, using quantitative neuromuscular monitoring, may be a viable approach to optimizing the extent of neuromuscular blockade during ECT. Indeed, low-dose sugammadex (0.22 mg.kg⁻¹) can reverse a rocuronium-induced neuromuscular blockade at a TOF ratio of 0.5 within 2 minutes. High-dose sugammadex, on the other hand, can reverse even high degree of neuromuscular blockade (T1=0), e.g. after a high dose of rocuronium. Rapid reversal of deep blockade with high doses of sugammadex is appealing in a busy ECT setting but it may not be cost-effective. An insufficient dose of sugammadex, on the other hand, may result in incomplete decurarization, or potentially recurarization if multiple doses of rocuronium have been administered. Although the efficiency and safety of the rocuronium-sugammadex combination for ECT needs further investigation, available data suggests that sugammadex, compared with neostigmine, may provide a safer reversal of moderate neuromuscular blockade. Low-dose sugammadex may also be cost-effective for the reversal of moderate or profound neuromuscular blockade, provided that the time saving factors reported in recent trials are taken into account. Despite its use in Europe for many years, the American Food and Drug Administration have yet not approved sugammadex for clinical use for safety concerns.
<table>
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<th>Study</th>
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<tr>
<td>Hoshi et al (2011)</td>
<td>J Anaesth</td>
<td>Crossover</td>
<td>Five patients (three Ms and two Fs) with mean age of 62.8 ± 9.9 years</td>
<td>Suxamethonium</td>
<td>0.1 mg/kg</td>
<td>T1 0% for ECT then on recovery T1, 50% to T1, 90% and 90% secure duration, time to first spontaneous breathing and eye opening</td>
<td>10 ECTs (three times per week at 1- or 2-day interval), first five ECTs with (S) then with succinylcholine</td>
<td>Potential efficacy of succinylcholine as an alternative to suxamethonium for muscle relaxation during ECT.</td>
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<td>Turkkali et al. (2008)</td>
<td>J Clin Anaesth</td>
<td>Crossover</td>
<td>13 patients, 18–60 years old</td>
<td>Rocuronium</td>
<td>1 mg/kg</td>
<td>Motor seizure duration time, first spontaneous breathing, head lift and tongue depression, fast time, eye opening and Cuff technique</td>
<td>Modified ECT – three times per week, average of six to 12 ECT treatments</td>
<td>Rocuronium is an alternative to suxamethonium for ECT.</td>
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<td>Rasmussen et al. (2008)</td>
<td>J ECT</td>
<td>Clinical trial</td>
<td>36 patients (36–66 years old and eight men)</td>
<td>Suxamethonium</td>
<td>Variable doses used in facility</td>
<td>Convulsive movement, Strength of fasciculation, EEG seizure length, subjective report of myalgia</td>
<td>Unilateral, bilateral, or bitemporal ECT – 189 treatments</td>
<td>Dose adjustment of (S) is unlikely to affect complaints of myalgia.</td>
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<td>White et al. (2008)</td>
<td>Anaesth Analg</td>
<td>Parallel</td>
<td>20 patients: ECT = 10 vs. MST = 10; age, 49 ± 6 vs. 48 ± 4; weight, 84 ± 8 vs. 82 ± 10</td>
<td>Suxamethonium</td>
<td>97 ± 27 mg</td>
<td>Motor seizure, EEG seizure, Recovery time, Post-treatment Hamilton depression rating scale</td>
<td>ECT vs. MST 3–4 weeks and 10–12 for each</td>
<td>MST required lower dosage of NMBA usage and was associated with a more rapid recovery of cognitive function.</td>
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<tr>
<td>Kadar et al. (2002)</td>
<td>Anaesth Analg</td>
<td>Parallel</td>
<td>50 obese patients in three classified group based on BMI (27.14.9)</td>
<td>Suxamethonium</td>
<td>40–130 mg</td>
<td>Aspiration</td>
<td>Overall 660 ECTs (31,246,103)</td>
<td>Obese patient could be anesthetised for ECT without full stomach (aspiration) precautions.</td>
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<tr>
<td>Auriacombe et al. (2000)</td>
<td>J ECT</td>
<td>Parallel</td>
<td>37 patients, 18–86 years old; mean, 58.4, 29% M</td>
<td>Suxamethonium</td>
<td>0.7, 0.75, 0.86, and 0.89 mg/kg</td>
<td>Pre- and post-ECT agitation and serum lactate</td>
<td>246 bilateral ECTs/10 months</td>
<td>Increase of pre-ECT (S) dose prevented agitation in patients with increased serum lactate in ECTs.</td>
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<td>Munshi et al. (1999)</td>
<td>Anaesth Analg</td>
<td>Crossover</td>
<td>100 referred patients; mean age, 27.9 ± 30, 31 Ms, two groups of 50 patients</td>
<td>Suxamethonium</td>
<td>0.5 mg/kg vs. 1 mg/kg</td>
<td>EEG &amp; motor seizure duration, 5-point scale motor seizure modification, Time for 30% recovery of NM twitch height</td>
<td>Unilateral = 25; bilateral = 25–0.5 mg/kg groups 2–5; 0.1 mg/kg groups 2–4</td>
<td>The larger dose is more effective in modifying the peripheral convulsion.</td>
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<td>Cheam et al. (1999)</td>
<td>Can J Anaesth</td>
<td>Crossover</td>
<td>16 depressed otherwise healthy patients, aged 26–27, weight: 40–78 kg</td>
<td>Suxamethonium</td>
<td>0.5 mg/kg</td>
<td>Score of seizure activity, Duration of seizure, time to first breath, ability to protrude tongue and hand grip for 5 s</td>
<td>N/A</td>
<td>Seizure modification was better after low-dose suxamethonium than after low-dose mivacurium.</td>
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<td>Lui et al. (1993)</td>
<td>J Clin Anaesth</td>
<td>Parallel</td>
<td>24 patients in two groups of 12 each. 14 Ms, weight: 59 ± 3.2 vs. 62.7 ± 3.5</td>
<td>Succinylcholine</td>
<td>0.3 mg/kg IV vs. 0.3 mg/kg IV</td>
<td>EEG activity during seizure Duration of multiple-monitored ECT, Grading of tonic–colonic ECT-induced convulsion based on observation</td>
<td>Bilateral multiple-monitored ECT – total of each group ECT treatments: 36</td>
<td>Suggests lower dose of succinylcholine to ascertain the occurrence of ECT-induced seizures.</td>
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<td>Konaczeewski et al. (1988)</td>
<td>Anaesthesiol, abstract</td>
<td>Parallel</td>
<td>52 patients in three groups</td>
<td>Suxamethonium</td>
<td>50, 25, and 15 mg</td>
<td>N/A</td>
<td>N/A</td>
<td>Practical advantage of 25 mg over 50 mg, and theoretical advantage over 15 mg of suxamethonium.</td>
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<td>Pitts et al. (1998)</td>
<td>Arch Gen Psychiatry, abstract</td>
<td>N/A</td>
<td>N/A</td>
<td>Suxamethonium</td>
<td>N/A</td>
<td>N/A</td>
<td>500 ECTs</td>
<td>Modification of suxamethion in ECT.</td>
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BMI, body mass index; ECT, electroconvulsive therapy; IV, intravenous; F, female; M, male; MST, magnetic seizure therapy; N/A, not available; NMBA, neuromuscular blocking agent.
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<td>Batistaki et al.</td>
<td>J ECT</td>
<td>28-year-old man, with catatonic schizophrenia and low pseudocholinesterase, height: 180 cm, weight: 85 kg</td>
<td>Rocuronium + sugammadex</td>
<td>0.4 mg/kg + 2 mg/kg</td>
<td>TOF monitoring, bispectral index, time to first spontaneous breath, duration of seizure, recovery time to TOF = 1</td>
<td>Eight consecutive ECTs, every 48 h</td>
<td>Rocuronium used with thiopental and reversed with sugammadex can be a safe alternative for suxamethonium for ECT.</td>
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<tr>
<td>Bryson et al. (2011)</td>
<td>J ECT</td>
<td>A 73-year-old, 72-kg man with bipolar disorder referred for ECT 12 days after the initiation of chemotherapy</td>
<td>Suxamethonium</td>
<td></td>
<td></td>
<td>Prolonged neuromuscular blockade during third ECT after chemotherapy, blood pressure cuff, tibial nerve stimulator (absence of motor response), seizure duration by ECG, and spontaneous recovery of diaphragmatic movement</td>
<td>10 bilateral ECTs over 8 weeks before chemotherapy. Six ECTs in 8 days after onset of new depression episode and chemotherapy</td>
</tr>
<tr>
<td>Waghmare et al. (2010)</td>
<td>Gen Hosp Psychiatry</td>
<td>40-year-old male patient with organophosphorus poisoning</td>
<td>Suxamethonium</td>
<td>25 mg</td>
<td></td>
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<tr>
<td>Zisselman and Jaffe (2010)</td>
<td>Am J Psychiatry</td>
<td>19-year-old woman with Torsade de Pointe during first ECT, weight: N/A</td>
<td>Suxamethonium vs. rocuronium</td>
<td>30 mg vs. 15 mg</td>
<td>Absence of arrhythmia in subsequent eight ECTs</td>
<td>One ECT treatment, then nine unmodified sessions</td>
<td>Bitemporal ECT – nine ECT treatments</td>
</tr>
<tr>
<td>Birkenhager et al. (2010)</td>
<td>J ECT</td>
<td>21-year-old man with schizophrenia</td>
<td>Suxamethonium vs. mivacurium</td>
<td>90 mg vs. 12 mg</td>
<td>Bradycardia</td>
<td>Three ECTs with (S), nine ECTs with mivacurium</td>
<td>Mivacurium usage in case of bradycardia.</td>
</tr>
<tr>
<td>Setoyama et al. (2009)</td>
<td>Masui, abstract</td>
<td>Two schizophrenic and one depressive patient with neuroleptic malignant syndrome</td>
<td>Vecuronium vs. suxamethonium</td>
<td>Two times 0.01 mg/kg vs. N/A</td>
<td>Anaesthesia time, no negative report of ECT procedures</td>
<td>Modified ECT – N/A</td>
<td>Vecuronium as an alternative in NMS.</td>
</tr>
<tr>
<td>Arias et al. (2009)</td>
<td>J ECT</td>
<td>64-year-old white female</td>
<td>Suxamethonium</td>
<td>60 mg</td>
<td></td>
<td></td>
<td>Asystole because of molecular structure of (S) is unpredictable.</td>
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<tr>
<td>Williams et al. (2007)</td>
<td>J ECT</td>
<td>67-year-old, 90-kg man with pseudocholinesterase deficiency, diagnosed in first ECT</td>
<td>Suxamethonium vs. rocuronium</td>
<td>80 mg vs. 30 mg</td>
<td>Clinical and electrographic duration of seizure in first ECT</td>
<td>Right unilateral ECT – one (S) + four (R) ECT treatments</td>
<td>Suggestion of rocuronium as a substitute for ECT in pseudocholinesterase deficiency.</td>
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<tr>
<td>Holak et al. (2007)</td>
<td>Can J Anaesth</td>
<td>73-year-old man with major depression and catatonia</td>
<td>Suxamethonium</td>
<td>1–1.5 mg/kg</td>
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<td>Asystole, normal serum potassium</td>
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<td></td>
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<td></td>
<td>ECT may produce asystole at any point of procedure. Subsequent ECT may be safely conducted.</td>
</tr>
<tr>
<td>Author and Year</td>
<td>Journal</td>
<td>Subjects</td>
<td>NBMA</td>
<td>Dose</td>
<td>Clinical report/measure</td>
<td>Frequency of modality</td>
<td>Author's conclusion</td>
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<tr>
<td>Hudcova and Schumann (2006)</td>
<td>Gen Hosp Psychiatry</td>
<td>34-year-old woman (BMI = 59 kg/m²) with NMS, arrhythmia and K⁺ in third ECT by (S)</td>
<td>Suxamethonium vs. atracurium and mivacurium</td>
<td>In third ECT 140 mg N/A</td>
<td>Serum potassium, recovery time</td>
<td>ECT with (S) until restoration of physical activity</td>
<td>Nondepolarising NMBAs may eliminate the need for suxamethonium use during ECT.</td>
</tr>
<tr>
<td>Prieto Martin et al. (2006)</td>
<td>Rev Esp Anestesiol Reanim</td>
<td>35-year-old woman at 30 weeks' gestation</td>
<td>Suxamethonium N/A</td>
<td>N/A</td>
<td></td>
<td>Nine sessions (three times/week)</td>
<td>Clinical improvement and safe labour within 2 days after ECT.</td>
</tr>
<tr>
<td>Ozer et al. (2005)</td>
<td>J ECT</td>
<td>56-year-old woman with Parkinson’s disease and neuroleptic malignant syndrome</td>
<td>N/A</td>
<td>N/A</td>
<td>Improvement of neuroleptic malignant syndrome, psychiatric and parkinson’s symptoms</td>
<td>Bilateral ECT – five sessions, three times per week</td>
<td>ECT might be effective and life saving in severe, drug resistant cases of neuroleptic malignant syndrome.</td>
</tr>
<tr>
<td>Magid et al. (2005)</td>
<td>J ECT</td>
<td>A man with recent myocardial infarction (10 days before ECT)</td>
<td>Suxamethonium 80-100 mg</td>
<td>N/A</td>
<td></td>
<td>Bilateral – seven ECT treatments</td>
<td>ECT could be safe in patient with recent myocardial infarction.</td>
</tr>
<tr>
<td>Calarge and Crowe (2004)</td>
<td>Ann Clin Psychiatry, abstract</td>
<td>A patient with myasthenia gravis</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td>N/A</td>
<td>ECT was done safely, with appropriate precautions.</td>
</tr>
<tr>
<td>Liu and Modell (2001)</td>
<td>Anaesthesiology</td>
<td>64-year-old, 70-kg man with post-polio syndrome</td>
<td>Mivacurium 0.14 and 0.11 mg/kg</td>
<td>Neuromuscular response to electrical stimulation, duration of ECT</td>
<td>Four ECT treatments in 8 days</td>
<td>Mivacurium at a dose of 0.11 mg/kg was adequate in preventing muscle contraction.</td>
<td></td>
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<tr>
<td>Kadar et al. (2001)</td>
<td>Anaesth Analg</td>
<td>51-year-old, 96-kg man, family history of MH to suxamethonium</td>
<td>Rapacuronium 75–70 to 65–60 mg 0.6–0.8 mg/kg</td>
<td>Observation of motor response to tetanic stimulation</td>
<td>Four sessions</td>
<td>Rapacuronium usage in a patient at risk for MH.</td>
<td></td>
</tr>
<tr>
<td>Nishijima and Ishiguro (1999)</td>
<td>J ECT</td>
<td>Five cases of NMS</td>
<td>Suxamethonium N/A</td>
<td>N/A</td>
<td></td>
<td>Bilateral – 17 ECTs</td>
<td>ECT is a useful therapy for psychotic patients with NMS.</td>
</tr>
<tr>
<td>Trollor and Sachdev (1999)</td>
<td>Aust N Z J Psychiatry</td>
<td>13 patients with NMS, weights: N/A</td>
<td>Suxamethonium vs. atracurium</td>
<td>0.5 mg/kg 20 mg</td>
<td>Temperature, creatine kinase</td>
<td>Bilateral and unilateral – three times/week</td>
<td>The use of atracurium was associated with a prolonged duration of anaesthesia.</td>
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<tr>
<td>Dillard and Webb (1999)</td>
<td>AANA J</td>
<td>53-year-old man with suicide attempt by Dursban, weight: N/A</td>
<td>Suxamethonium</td>
<td>First ECT: 40 mg; second and third: 20 mg; third to sixth: 15 mg</td>
<td>Peripheral nerve stimulator, head lift Cholinesterase level</td>
<td>Seven ECTs 2 weeks, 10 ECTs/patient</td>
<td>Lower dose of (S) for ECT in organophosphate poisoning.</td>
</tr>
<tr>
<td>Cooper et al. (1999)</td>
<td>Anaesthesiology</td>
<td>40-year-old white catatonic woman</td>
<td>Suxamethonium vs. mivacurium</td>
<td>120 mg N/A</td>
<td>Serum potassium↑ with suxamethonium in second, third, and fourth ECTs</td>
<td>Four ECT treatments with suxamethonium and then with mivacurium</td>
<td>Suggestion of a short-acting, nondepolarising NMBA for immobile catatonic patients.</td>
</tr>
<tr>
<td>Hersot et al. (1996)</td>
<td>Br J Psychiatry</td>
<td>19-year-old, 54-kg woman with severe myalgia during her first two ECT treatments</td>
<td>Suxamethonium vs. vecuronium + suxamethonium</td>
<td>First and second ECT: 30 mg, 50 mg 1 mg before 50 mg of suxamethonium</td>
<td>Myalgia</td>
<td>At least four ECT treatments</td>
<td>Treatment with Vecuronium should be considered for ECT-induced muscle pain.</td>
</tr>
</tbody>
</table>

**Table 2 Continued**
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Journal</th>
<th>Age, Weight, Diagnosis</th>
<th>NMBA, Dose(s)</th>
<th>Procedure Details</th>
<th>Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Janis et al.</td>
<td>Can J Anaesth</td>
<td>64-, 69-, and 76-year-old men with osteoporosis, amyotrophic lateral sclerosis and cardiac arrhythmias</td>
<td>Mivacurium 0.2 and 0.16 mg/kg or 8 mg</td>
<td>Orbicularis oculi for TOF and peripheral nerve stimulation, isolated cuff to monitor seizure</td>
<td>Six ECT treatments over 13 days. Mivacurium should be used in elderly patients with comorbidities.</td>
</tr>
<tr>
<td>Jaksa and</td>
<td>Anaesth Analg</td>
<td>25-year-old, 60-kg woman with osteoporosis, amyotrophic lateral sclerosis and cardiac arrhythmias</td>
<td>Suxamethonium 0.5–1 vs. 1.2–1.58 mg/kg, 0.12, 0.15, 0.18, and 0.2 mg/kg</td>
<td>Ventilation recovery, head lift, plasma cholinesterase ↓</td>
<td>One ECT. Prolonged apnea because of organophosphate poisoning.</td>
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<td>Palahniuk (1995)</td>
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<tr>
<td>Fredman et al.</td>
<td>Anaesth Analg</td>
<td>N/A A patient with neuroleptic malignant syndrome and prolonged bed rest</td>
<td>Suxamethonium vs. mivacurium 30 mg, 7 mg vs. 0.12–0.16 mg/kg</td>
<td>Twitch response to TOF stimulation. Over 6 month ECTs, four ECT treatments.</td>
<td>Suxamethonium and mivacurium are more effective at higher doses.</td>
</tr>
<tr>
<td>Kelly and Brull</td>
<td>Can J Anaesth</td>
<td>29-year-old, 49-kg woman with NMS because of neuroleptics</td>
<td>Mivacurium 0.15–0.25 mg/kg</td>
<td>Seizure duration on EEG, creatine kinase, and TOF for adductor pollicis</td>
<td>First two ECTs, then 10 ECTs in the next 4 weeks. Mivacurium is a suitable agent for patients with neuroleptic malignant syndrome undergoing ECT.</td>
</tr>
<tr>
<td>Gillin et al.</td>
<td>Anaesth Analg, abstract</td>
<td>Four patients, one with myasthenia gravis</td>
<td>Mivacurium 6 and 5 mg</td>
<td>Bard nerve stimulator for TOF</td>
<td>Nine ECT treatments. Mivacurium is a satisfactory alternative to (S) for ECT if needed.</td>
</tr>
<tr>
<td>Burkstein and</td>
<td>Anaesthesia</td>
<td>71-year-old female, with progressive cervical myelopathy, 50 kg</td>
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<td>Denny (1993)</td>
<td></td>
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<tr>
<td>Swartz (1990)</td>
<td>J Nerv Ment Dis</td>
<td>Five patients with post-ECT agitation</td>
<td>Suxamethonium 0.7 vs. 1 mg/kg</td>
<td></td>
<td>No agitation after the higher dose of suxamethonium is administered.</td>
</tr>
<tr>
<td>Stack et al.</td>
<td>Br J Anaesth</td>
<td>76-year-old woman with plasma cholinesterase deficiency</td>
<td>Suxamethonium vs. atracurium 30 mg, 10 and 15 mg</td>
<td>Apnea, peripheral nerve stimulator. One ECT by (S) and two ECTs by (A)</td>
<td>Atracurium as a substitute for (S) in case of plasma cholinesterase deficiency.</td>
</tr>
<tr>
<td>Hickey et al.</td>
<td>Can J Anaesth</td>
<td>24-year-old, 64 kg woman with atypical plasma cholinesterase</td>
<td>Atracurium 10–15 mg vs. suxamethonium 2–5 mg</td>
<td>TOF for pollicis muscle, time for 90% first twitch blockade and recovery</td>
<td>Five ECT treatments. No advantage of atracurium over low-dose suxamethonium.</td>
</tr>
<tr>
<td>Bowersteg and</td>
<td>Convulsive Therapy</td>
<td>33 year-old white man with thermal injuries requiring ECT; weight: 47 Kg</td>
<td>Atracurium 0.5 mg/kg</td>
<td>Twitch depression measured with a force displacement transducer (Grass FT-10)</td>
<td>Bilateral, 13 ECT treatments. Atracurium is a safe alternative to suxamethonium in burned patients.</td>
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<td>Avery (1987)</td>
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<tr>
<td>Dodson</td>
<td>Br J Anaesth</td>
<td>1 patient with sensitivity to suxamethonium (bronchospasm)</td>
<td>Suxamethonium, atracurium, and mivacurium 30 mg, 2.5 mg, and 2 mg</td>
<td></td>
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</tr>
<tr>
<td>Sortye (1954)</td>
<td>Svenska Lakartidn, abstract</td>
<td>N/A</td>
<td>Suxamethonium vs. flaxedil</td>
<td>Respiratory effort and time of spontaneous return after anaesthesia</td>
<td></td>
</tr>
<tr>
<td>Thesleff et al.</td>
<td>Am J Psychiatry</td>
<td>136 patients (55 men)</td>
<td>Suxamethonium in mixture with barbiturate 0.2–0.4 mg/kg</td>
<td>512 ECT treatments. Suxamethonium is suitable for routine use in connection with ECT.</td>
<td></td>
</tr>
</tbody>
</table>

BMI, body mass index; ECT, electroconvulsive therapy; N/A, not available; NMBA, neuromuscular blocking agent; NMS, neuroleptic malignant syndrome; TOF, train-of-four; EEG, electroencephalography; MH, malignant hyperthermia.
CONCLUSION

Neuromuscular blockade has dramatically reduced the incidence of important complications such as vertebral fractures and physical injuries related to ECT. With a rapid onset of action and short duration of effect, suxamethonium remains the NMBA of choice for ECT. However, significant comorbidities may require modification of the anaesthetic regimen and avoidance of suxamethonium. Nondepolarizing NMBAs are effective when suxamethonium is contraindicated. Clinicians should use quantitative or qualitative assessment of the neuromuscular transmission and pharmacological reversal of the neuromuscular blockade when nondepolarizing NMBAs are administered. Sugammadex provides rapid and reliable reversal of neuromuscular blockade after vecuronium and rocuronium, and the combination of steroidal NMBAs and sugammadex may be an attractive alternative to suxamethonium for ECT.
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Cooper RC, Baumann PL, McDonald WM. An unexpected hyperkalemic response to succinylcholine during electroconvulsive therapy for catatonic schizophrenia. *Anesthesiology* 1999; 91: 574-5.


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