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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 NMBA 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, [1] resulting in about 100,000 treatments per year. [2,3] In both the United Kingdom and Scandinavia, ECT appears to be declining in popularity, [4] and in other European countries its use remains highly variable. [5] As an example, ECT use is falling in Italy, but increasing in the Netherlands. [5] The reason for these differences in the application of ECT is not clear, but financial considerations may be a contributing factor. [6]

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. [7] The first report of the use of seizure induction to treat mania, using camphor was published in 1785. [7] Meduna advanced it based on the fact that patients with schizophrenia often improved when spontaneous epileptic seizures developed. [8] 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. [8] He used Curare to modify metrazol-induced convulsive therapy. [9] The introduction of electric shock therapy by Bini and Cerletti (Italy) in 1939 [10] 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. [11,12] Electrical induction of

seizures soon replaced metrazol therapy because it was safer and had fewer adverse side effects. [13] The introduction of suxamethonium as a synthetic alternative to curare in 1951 led to the more widespread use of "modified" contemporary ECT. [11]

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. [14] Patients who fail one or more adequate medication trials have a diminished but substantial rate of response to ECT. [15,16] ECT is highly effective in the elderly, perhaps even more so than the younger age groups.[17,18] 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. [19,20]

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. [21] 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. [19] 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. [22-24] Consequently, neuromuscular blockers are required to minimize the convulsive motor activity, in order to prevent fractures and physical injury during the seizure, [25-27] which is especially important in patients with osteoporosis or a history of spinal injury. [25,26] 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. [7,19] 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. [28] 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. [29]

Based on its rapid onset, short duration of action, and rapid recovery,[30,31] 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 [19,28], 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%. [32] 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, [33,34] 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 [35], 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). [36] 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. [1,27,36-45] 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. [38,49,64-69] Savarese and collaborates 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. [70] 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. [28,38] Although mivacurium can cause a significant histamine release and occasional hypotension,[27,71] the authors reported no haemodynamic instability or clinical signs of histamin release. [38] 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. [67] Others have reported optimal neuromuscular blockade with 0.12-0.16 mg.kg^{-1} (in a patient with neuroleptic malignant syndrome) [59] or 0.15-0.25 mg.kg^{-1} (patients with or without myasthenia gravis). [67] 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. [66] 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. [69] Mivacurium has been used as a substitute for suxamethonium to avoid (potential) adverse effects like hyperkalaemia or bradycardia. [64,65,68] (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.[52] [35] 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. [120] Their effect may also wear off before complete clearance of an NMBA, resulting

in recurarization with the risk for adverse respiratory events. [116,121] 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.[81]

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. [122,123]

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. [124,125] 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. [126] Available data from multiple other studies[104,111,127,128] support this hypothesis. [126] 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. [129] 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. [81] 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. [130] 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. [131,132] 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 1

Conducted studies on use of NMBAs in ECT.

Study	Journal	Design	Subjects	NBMA	Dose	End point/measure	Frequency of ECTs	Outcome
Hoshi et al. (2011)[80]	J Anaesth	Crossover	Five patients (three Ms and two Fs) with mean age of 62.8 ± 5.9 years	Suxamethonium vs. rocuronium–sugammadex	0.1 mg/kg 0.6–16 mg/kg	T1 0% for ECT then on recovery T1 90%, time to T1 10% and 90%, seizure duration, time to first spontaneous breathing and eye opening	10 ECTs (three times per week at 1- or 2-day interval), first five ECTs with (S) then with rocuronium–sugammadex	Potential efficacy of rocuronium–sugammadex as an alternative to succinylcholine for muscle relaxation during ECT.
Turkkal et al. (2008)[74]	J Clin Anaesth	Crossover	13 patients, 18–60 years old	Rocuronium vs. suxamethonium	1 mg/kg 0.3 mg/kg	Motor seizure duration time, first spontaneous breath, head lift and tongue depressor test time, eye opening, Cuff technique	Modified ECT – three times per week, average of six to 12 ECT treatments	Rocuronium is an alternative to suxamethonium for ECT.
Rasmussen et al. (2008)[132]	J ECT	Clinical trial	36 patients (26–86 years old and eight men)	Suxamethonium	Variable doses used in facility	Convulsive movement, Strength of fasciculation, EEG seizure length, subjective report of myalgia	Unilateral, bifrontal, or bitemporal ECT – 189 treatments	Dose adjustment of (S) is unlikely to affect complains of myalgia.
White et al. (2006)[133]	Anaesth Analg	Parallel	20 patients: ECT = 10 vs. MST = 10; age, 49 ± 6 vs. 48 ± 4; weight, 84 ± 8 vs. 82 ± 10; M/F: 4/6	Suxamethonium vs. suxamethonium	97 ± 27 mg 38 ± 17 mg	Motor seizure, EEG seizure, Recovery time, Post-treatment Hamilton depression rating scale	ECT vs. MST/3–4 weeks and 10–12 for each	MST required lower dosage of NMBA usage and was associated with a more rapid recovery of cognitive function.
Kadar et al. (2002)[134]	Anaesth Analg	Parallel	50 obese patients in three classified group base on BMI (27,14,9)	Suxamethonium	40–120 mg Class I: 89 ± 25 Class II: 79 ± 14 Class III: 96 ± 17	Aspiration	Overall 660 ECTs (31,246,103)	Obese patient could be anaesthetised for ECT without full stomach ('aspiration') precautions.
Auriacombe et al. (2000)[135]	J ECT	Parallel	37 patients,18–86 years old; mean, 58.4, 29% M	Suxamethonium	0.7, 0.75, 0.85, and 0.89 mg/kg	Pre- and post-ECT agitation and serum lactate	245 bilateral ECTs/10 months	Increase of pre-ECT (S) dose prevented agitation in patients with increased serum lactate in ECTs.
Murali et al. (1999)[44]	Anaesth Analg	Crossover	100 referred patients; mean age, 27.9 ± 9.0, 31 Ms, two groups of 50 patients	Suxamethonium	0.5 mg/kg vs. 1 mg/kg	EEG & motor seizure duration, 5-point scale motor seizure modification, Time for 50% recovery of NM twitch height	Unilateral = 25; bilateral = 25–0.5 mg/kg groups 2–5; 0.1 mg/kg groups 2–4	The larger dose is more effective in modifying the peripheral convulsion.
Cheam et al. (1999)[136]	Can J Anaesth	Crossover	16 depressed otherwise healthy patients, aged 26–27, weight: 40–78 kg	Suxamethonium vs. mivacurium	0.5 mg/kg 0.08 mg/kg	Score of seizure activity, Duration of seizure, time to first breath, ability to protrude tongue and hand grip for 5 s	N/A	Seizure modification was better after low-dose suxamethonium than after low-dose mivacurium.
Lui et al. (1993)[35]	J Clin Anaesth	Parallel	24 patients in two groups of 12 each, 14 Ms, weight: 59 ± 3.2 vs. 62.7 ± 3.5	Atracurium	0.3 mg/kg IV vs. 0.5 mg/kg IV	EEG activity during seizure Duration of multiple-monitored ECT, Grading of tonic –colonic ECT-induced convulsion based on observation	Bilateral multiple-monitored ECT – total of each group ECT treatments: 36	Suggests lower dose of atracurium to ascertain the occurrence of ECT-induced seizures.
Konarzewski et al. (1988)[43]	Anaesthesia, abstract	Parallel	52 patients in three groups	Suxamethonium	50, 25, and 15 mg	N/A	N/A	Practical advantage of 25 mg over 50 mg, and theoretical advantage over 15 mg of suxamethonium.
Pitts et al. (1968)[40]	Arch Gen Psychiatry, abstract	N/A	N/A	Suxamethonium	N/A	N/A	500 ECTs	Modification of suxamethonium in ECT.

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.

Table 2

Case report on the use of NMBAs for ECT.

Author	Journal	Subjects	NBMA	Dose	Clinical report/measure	Frequency of modality	Author's conclusion
Batistaki et al. (2011)[137]	J ECT	26-year-old man, with catatonic schizophrenia and low pseudocholinesterase, height:180 cm; weight:85 kg	Rocuronium + sugammadex	0.4 mg/kg 2 mg/kg	TOF monitoring, bispectral index, time to first spontaneous breath, duration of seizure, recovery time to TOF = 1	Eight consecutive ECTs, every 48 h	Rocuronium used with thiopental and reversed with sugammadex can be a safe alternative for suxamethonium for ECT.
Bryson et al. (2011)[138]	J ECT	A 73-year-old, 72-kg man with bipolar disorder referred for ECT 12 days after the initiation of chemotherapy	Suxamethonium		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	10 bilateral ECTs over 8 weeks before chemotherapy. Six ECTs in 8 days after onset of new depression episode and chemotherapy	Drug induced acquired butyrylcholinesterase deficiency. With attention paid to subsequent (S) dose titration to effect, treatment continued uneventfully.
Waghmare et al. (2010)[139]	Gen Hosp Psychiatry	40-year-old male patient with organophosphorus poisoning	Suxamethonium	25 mg	Prolonged apnea	One ECT treatment, then nine unmodified sessions	Prolonged apnea because of organophosphorus poisoning.
Zisselman and Jaffe (2010)[50]	Am J Psychiatry	19-year-old woman with Torsade de Pointe during first ECT, weight: N/A	Suxamethonium vs. rocuronium	30 mg 15 mg	Absence of arrhythmia in subsequent eight ECTs	Bitemporal ECT – nine ECT treatments	Nondepolarising NMBAs as alternative to suxamethonium in case of risk of hyperkalaemia.
Birkenhager et al. (2010)[63]	J ECT	21-year-old man with schizophrenia	Suxamethonium vs. mivacurium	90 mg 12 mg	Bradycardia	Three ECTSs with (S), nine ECTs with mivacurium	Mivacurium usage in case of bradycardia.
Setoyama et al. (2009)[77]	Masui, abstract	Two schizophrenic and one depressive patient with neuroleptic malignant syndrome	Vecuronium vs. suxamethonium	Two times 0.01 mg/kg N/A	Anaesthesia time, no negative report of ECT procedures	Modified ECT – N/A	Vecuronium as an alternative in NMS.
Arias et al. (2009)[140]	J ECT	64-year-old white female	Suxamethonium	60 mg	Asystole, normal serum potassium, ECT (no change for hyperkalaemia)	Asystole in 13th ECT	Asystole because of molecular structure of (S) is unpredictable.
Williams et al. (2007)[75]	J ECT	67-year-old, 90-kg man with psuedocholinesterase deficiency, diagnosed in first ECT	Suxamethonium vs. rocuronium	80 mg 30 mg	Clinical and electrographic duration of seizure in first ECT	Right unilateral ECT – one (S) + four (R) ECT treatments	Suggestion of rocuronium as a substitute for ECT in psuedocholinesterase deficiency.
Holak et al. (2007)[62]	Can J Anaesth	73-year-old man with major depression and catatonia	Suxamethonium	1–1.5 mg/kg	Asystole, normal serum potassium	39 uneventful previous ECT treatments with asystole in 40th and safe subsequent ECTs	ECT may produce asystole at any point of procedure. Subsequent ECT may be safely conducted.

Table 2 Continued

Author	Journal	Subjects	NBMA	Dose	Clinical report/measure	Frequency of modality	Author's conclusion
Hudcova and Schumann (2006)[48]	Gen Hosp Psychiatry	34-year-old woman (BMI = 59 kg/m^2) with NMS, arrhythmia and K↑ in third ECT by (S)	Suxamethonium vs. atracurium and mivacurium	In third ECT 140 mg N/A	Serum potassium, recovery time	ECT with (S) until restoration of physical activity	Nondepolarising NMBAs may eliminate the need for suxamethonium use during ECT.
Prieto Martin et al. (2006)[141]	Rev Esp Anestesiol Reanim	35-year-old woman at 30 weeks' gestation	Suxamethonium	N/A	N/A	Nine sessions (three times/week)	Clinical improvement and safe labour within 2 days after ECT.
Ozer et al. (2005)[142]	J ECT	56-year-old woman with Parkinson's disease and neuroleptic malignant syndrome	N/A	N/A	Improvement of neuroleptic malignant syndrome, psychiatric and parkinson's symptoms	Bilateral ECT – five sessions, three times per week	ECT might be effective and life saving in severe, drug resistant cases of neuroleptic malignant syndrome.
Magid et al. (2005)[143]	J ECT	A man with recent myocardial infarction (10 days before ECT)	Suxamethonium	80–100 mg	N/A	Bilateral – seven ECT treatments	ECT could be safe in patient with recent myocardial infarction.
Calarge and Crowe (2004)[144]	Ann Clin Psychiatry, abstract	A patient with myasthenia gravis	N/A	N/A	N/A	N/A	ECT was done safely, with appropriate precautious.
Liu and Modell (2001)[68]	Anaesthesiology	64-year-old, 70-kg man with post-polio syndrome	Mivacurium	0.14 and 0.11 mg/kg	Neuromuscular response to electrical stimulation, duration of ECT	Four ECT treatments in 8 days	Mivacurium at a dose of 0.11 mg/kg was adequate in preventing muscle contraction.
Kadar et al. (2001)[145]	Anaesth Analg	51-year-old, 96-kg man, family history of MH to suxamethonium	Rapacuronium	75–70 to 65–60 mg 0.6–0.8 mg/kg	Observation of motor response to tetanic stimulation	Four sessions	Rapacuronium usage in a patient at risk for MH.
Nisijima and Ishiguro (1999)[146]	J ECT	Five cases of NMS	Suxamethonium	N/A	N/A	Bilateral – 17 ECTSs	ECT is a useful therapy for psychotic patients with NMS.
Trollor and Sachdev (1999)[147]	Aust N Z J Psychiatry	13 patients with NMS, weights: N/A	Suxamethonium vs. atracurium	0.5 mg/kg 20 mg	Temperature, creatine kinase	Bilateral and unilateral – three times/week	The use of atracurium was associated with a prolonged duration of anaesthesia.
Dillard and Webb (1999)[81]	AANA J	53-year-old man with suicide attempt by Dursban, weight: N/A	Suxamethonium	First ECT: 40 mg; second and third: 20 mg; third to sixth: 15 mg	Peripheral nerve stimulator, head lift Cholinesterase level	Seven ECTs/2 weeks, 10 ECTs/patient	Lower dose of (S) for ECT in organophosphate poisoning.
Cooper et al. (1999)[64]	Anaesthesiology	40-year-old white catatonic woman	Suxamethonium vs. mivacurium	120 mg N/A	Serum potassium↑ with suxamethonium in second, third, and fourth ECTs	Four ECT treatments with suxamethonium and then with mivacurium	Suggestion of a short-acting, nondepolarising NMBA for immobile catatonic patients.
Herriot et al. (1996)[148]	Br J Psychiatry	19-year-old, 54-kg woman with severe myalgia during her first two ECT treatments	Suxamethonium vs. vecuronium + suxamethonium	First and second ECT: 30 mg, 50 mg 1 mg before 50 mg of suxamethonium	Myalgia	At least four ECT treatments	Pretreatment with Vecuronium should be considered for ECT-induced muscle pain.

Janis et al. (1995)[65]	Can J Anaesth	64-, 69-, and 76-year-old men with osteoporosis, amyotrophic lateral sclerosis and cardiac arrhythmias	Mivacurium	0.2 and 0.16 mg/kg or 8 mg	Orbucularis oculi for TOF and peripheral nerve stimulator, isolated cuff to monitor seizure	Six ECT treatments over 13 days	Mivacurium should be used in elderly patients with comorbidities.
Jaksa and Palahniuk (1995)[57]	Anaesth Analg	25-year-old, 60-kg woman	d-tubucorare suxamethonium	3 mg 50 mg	Ventilation recovery, head lift, plasma cholinesterase↓	One ECT	Prolonged apnea because of organophosphate poisoning.
Fredman et al. (1994)[38]	Anaesth Analg	N/A A patient with neuroleptic malignant syndrome and prolonged bed rest	Suxamethonium Mivacurium	0.5–1 vs. 1.2–1.58 mg/kg 0.12, 0.15, 0.18, and 0.2 mg/kg	Twitch response to TOF stimulation	Over 6 month ECTs, four ECT treatments	Suxamethonium and mivacurium are more effective at higher doses.
Kelly and Brull (1994)[58]	Can J Anaesth	29-years-old, 49-kg woman with NMS because of neuroleptics	Suxamethonium vs. mivacurium	30 mg, 7 mg 0.12–0.16 mg/kg	Seizure duration on EEG, creatine kinase, and TOF for adductor pollicis	First two ECTs, then 10 ECTs in the next 4 weeks	Mivacurium is a suitable agent for patients with neuroleptic malignant syndrome undergoing ECT.
Gitlin et al. (1993)[66]	Anaesth Analg, abstract	Four patients, one with myasthenia gravis	Mivacurium	0.15–.25 mg/kg	N/A	N/A	N/A
Burnstein and Denny (1993)[67]	Anaesthesia	71-year-old female, with progressive cervical myelopathy, 50 kg	Mivacurium	6 and 5 mg	Bard nerve stimulator for TOF	Nine ECT treatments	Mivacurium is a satisfactory alternative to (S) for ECT if needed.
Swartz (1990)[149]	J Nerv Ment Dis	Five patients with post-ECT agitation	Suxamethonium	0.7 vs. 1 mg/kg	N/A	20 ECT with 0.7, then 15 sessions with 1.0 mg/kg	No agitation after the higher dose of suxamethonium is administered.
Stack et al. (1988)[72]	Br J Anaesth	76-year-old woman with plasma cholinesterase deficiency	Suxamethonium vs. atracurium	30 mg 10 and 15 mg	Apnea, peripheral nerve stimulator	One ECT by (S) and two ECTs by (A)	Atracurium as a substitute for (S) in case of plasma cholinesterase deficiency.
Hickey et al. (1987)[71]	Can J Anaesth	24-year-old, 64 kg woman with atypical plasma cholinesterase	Atracurium vs. suxamethonium	10–15 mg 2–5 mg	TOF for pollicis muscle, time for 90% first twitch blockade and recovery	Five ECT treatments	No advantage of atracurium over low-dose suxamethonium.
Dwersteg and Avery (1987)[51]	Convulsive Therapy	33 year-old white man with thermal injuries requiring ECT; weight: 47 Kg	Atracurium	0.5 mg/kg	Twitch depression measured with a force displacement transducer (Grass FT-10)	Bilateral, 13 ECT treatments	Atracurium is a safe alternative to suxamethonium in burned patients.
Dodson (1985)[76]	Br J Anaesth	1 patient with sensitivity to suxamethonium (bronchospasm)	Suxamethonium, atracurium, and mivacurium	30 mg, 2.5 mg, and 2 mg	N/A	N/A	Mivacurium provided satisfactory modification of ECT.
Sorbye (1954)[150]	Svenska Lakartidn, abstract	N/A	Suxamethonium vs. flaxedil	N/A	N/A	N/A	N/A
Thesleff et al. (1952)[151]	Am J of Psychiatry	136 patients (55 men)	Suxamethonium in mixture with barbiturate	0.2–0.4 mg/kg	Respiratory effort and time of spontaneous return after anaesthesia	512 ECT treatments	Suxamethonium is suitable for routine use in connection with ECT.

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.

REFERENCES

1. Asnis GM, Fink M, Saferstein S. ECT in metropolitan New York hospitals: a survey of practice, 1975-1976. *Am J Psychiatry* 1978; 135: 479-82.
2. Hermann RC, Dorwart RA, Hoover CW, Brody J. Variation in ECT use in the United States. *Am J Psychiatry* 1995; 152: 869-75.
3. Holden C. A guarded endorsement for shock therapy. Science 1985; 228: 1510-1.
4. Pankratz WJ. Electrtoconvulsive therapy: the position of the Canadian Psychiatric Association. *Can J Psychiatry* 1980; 25: 509-14.
5. Sienaert P, van den Broek WW. Electroconvulsive therapy in continental Western Europe: A literature review. In: Swartz CM, ed. Electroconvulsive and Neuromodulation Therapies**.** New York: Cambridge University Press, 2009; 246-55.
6. Philpot M, Treloar A, Gormley N, Gustafson L. Barriers to the use of electroconvulsive therapy in the elderly: a European survey. *Eur Psychiatry* 2002; 17: 41-5.
7. Prudic J. Electroconvulsive Therapy. In: Sadock BJ, Sadock VA, eds. Kaplan & Sadock's comprehensive textbook of psychiatry. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2005; 2968-83
8. Bennett BT, Fitzpatrick CP. Fractures of the spine complicating metrazol therapy. *JAMA* 1939; 112: 2240-44.
9. Bennett AE. Preventing traumatic complications in convulsive shock therapy by curare. *JAMA* 1940; 114: 322-4.
10. Faedda GL, Becker I, Baroni A, Tondo L, Aspland E, Koukopoulos A. The origins of electroconvulsive therapy: Prof. Bini's first report on ECT. *J Affect Disord* 2010; 120: 12-5.
11. Dorkins HR. Suxamethonium-the development of a modern drug from 1906 to the present day. *Med Hist* 1982; 26: 145-68.
12. Bennett AE. Curare: a preventive of traumatic complications in convulsive shock therapy (including a preliminary report on a synthetic curare-like drug). 1940. *Convuls Ther* 1997; 13: 93-107.
13. Cerletti U. Electroconvulsive Therapy. In: Sackler AM, Marti-Ibanez F, Saclcler RR, eds. The Great Physiodynamic Therapies in Psychiatry: an historical appraisal. New York: Hoeber-Harper, 1956; 91-120.
14. Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *Am J Psychiatry* 2006; 163: 1905-17.
15. Prudic J, Haskett RF, Mulsant B, Malone KM, Pettinati HM, Stephens S, Greenberg R, Rifas SL, Sackeim HA. Resistance to antidepressant medications and short-term clinical response to ECT. *Am J Psychiatry* 1996; 153: 985-92.
16. Prudic J, Sackeim HA, Devanand DP. Medication resistance and clinical response to electroconvulsive therapy. *Psychiatry Res* 1990; 31: 287-96.
17. Benbow SM. ECT in the elderly. *Br J Psychiatry* 1987; 150: 877.
18. Mulsant BH, Rosen J, Thornton JE, Zubenko GS. A prospective naturalistic study of electroconvulsive therapy in late-life depression. *J Geriatr Psychiatry Neurol* 1991; 4: 3-13.
19. American Psychiatric Association, Committee on Electroconvulsive Therapy. The Practice of Electroconvulsive Therapy. Recommendations for treatment, training, and privileging: a task force report of the APA. 2nd ed. Washington D.C.: American Psychiatric Press, 2001.
20. Wilkins KM, Ostroff R, Tampi RR. Efficacy of electroconvulsive therapy in the treatment of nondepressed psychiatric illness in elderly patients: a review of the literature. *J Geriatr Psychiatry Neurol* 2008; 21: 3-11.
21. Sackeim HA, Devanand DP, Prudic J. Stimulus intensity, seizure threshold, and seizure duration: impact on the efficacy and safety of electroconvulsive therapy. *Psychiatr Clin North Am* 1991; 14: 803-43.

22. Sarpel Y, Togrul E, Herdem M, Tan I, Baytok G. Central acetabular fracture-dislocation following electroconvulsive therapy: report of two similar cases. *J Trauma* 1996; 41: 342-4.

23. Nott MR, Watts JS. A fractured hip during electroconvulsive therapy. *Eur J Anaesthesiol* 1999; 16: 265-7.

24. Fink M. Convulsive therapy: a review of the first 55 years. *J Affect Disord* 2001; 63: 1-15.

25. Taylor S. Electroconvulsive therapy: a review of history, patient selection, technique, and medication management. *South Med J* 2007; 100: 494-8.

26. Pandya M, Pozuelo L, Malone D. Electroconvulsive therapy: what the internist needs to know. *Cleve Clin J Med* 2007; 74: 679-85.

27. Wagner KJ, Mollenberg O, Rentrop M, Werner C, Kochs EF. Guide to anaesthetic selection for electroconvulsive therapy. *CNS Drugs* 2005; 19: 745-58.

28. Ding Z, White PF. Anesthesia for electroconvulsive therapy. *Anesth Analg* 2002; 94: 1351-64.

29. Gaines GY 3rd, Rees DI. Anesthetic considerations for electroconvulsive therapy. *South Med J* 1992; 85: 469-82.

30. Combs JM, Combs GN. A literature review of the newest muscle relaxant: ORG 9426. *CRNA* 1994; 5: 104-12.

31. Lee C. Goodbye suxamethonium! Anaesthesia 2009; 64 Suppl 1: 73-81.

32. Kopman AF, Lien CA, Naguib M. Neuromuscular dose-response studies: determining sample size. *Br J Anaesth* 2011; 106: 194-8.

33. Eikermann M, Hunkemoller I, Peine L, et al. Optimal rocuronium dose for intubation during inhalation induction with sevoflurane in children. *Br J Anaesth* 2002; 89: 277-81.

34. Eikermann M, Renzing-Kohler K, Peters J. Probability of acceptable intubation conditions with low dose rocuronium during light sevoflurane anaesthesia in children. *Acta Anaesthesiol Scand* 2001; 45: 1036-41.

35. Lui PW, Ma JY, Chan KK. Modification of tonic-clonic convulsions by atracurium in multiple-monitored electroconvulsive therapy. *J Clin Anaesth* 1993; 5: 16-21.

36. Durant NN, Katz RL. Suxamethonium. *Br J Anaesth* 1982; 54: 195-208.

37. Gaines GY 3rd, Rees DI. Electroconvulsive therapy and anesthetic considerations. *Anesth Analg* 1986; 65: 1345-56.

38. Fredman B, Smith I, d'Etienne J, White PF. Use of muscle relaxants for electroconvulsive therapy: how much is enough? *Anesth Analg* 1994; 78: 195-6.

39. Weiner RD, Coffey CE. Indications for use of electroconvulsive therapy. In: Frances AJ, Hales RE, eds. Review of Psychiatry, vol 7. Washington DC: Am Psychiatr Press 1988; 458-481.

40. Pitts FN, Jr., Woodruff RA, Jr., Craig AG, Rich CL. The drug modification of ECT. II. Succinylcholine dosage. *Arch Gen Psychiatry* 1968; 19: 595-9.

41. Sadock BJ, Sadock VA. Kaplan & Sadock's concise textbook of clinical psychiatry. 3rd ed. Philadelphia*: Lippincott Williams & Wilkins*, 2008.

42. Weinger MB, Partridge BL, Hauger R, Mirow A. Prevention of the cardiovascular and neuroendocrine response to electroconvulsive therapy: I. Effectiveness of pretreatment regimens on hemodynamics. *Anesth Analg 1991*; 73: 556-62.

43. Konarzewski WH, Milosavljevic D, Robinson M, Banham W, Beales F. Suxamethonium dosage in electroconvulsive therapy. *Anaesthesia* 1988; 43: 474-6.

44. Murali N, Saravanan ES, Ramesh VJ, et al. An intrasubject comparison of two doses of succinylcholine in modified electroconvulsive therapy. *Anesth Analg* 1999; 89: 1301-4.

45. Weiner RD, Coffey CE, Fochtmann L, Greenberg R, Isenberg KE, Kellner CH, Moench L, Sackeim HA. The Practice of Electroconvulsive Therapy. Recommendations for treatment, training, and privileging: a task force report of the American Psychiatric Association. 2nd ed. Washington D.C.: American Psychiatric Press, 2001.

46. Kopman AF, Zhaku B, Lai KS. The "intubating dose" of succinylcholine: the effect of decreasing doses on recovery time. *Anesthesiology* 2003; 99:

1050-4.

47. Folk JW, Kellner CH, Beale MD, Conroy JM, Duc TA. Anesthesia for electroconvulsive therapy: a review. *J ECT* 2000; 16: 157-70.
48. Vanlinthout LE, van Egmond J, de Boo T, Lerou JG, Wevers RA, Booij LH. Factors affecting magnitude and time course of neuromuscular block produced by suxamethonium. *Br J Anaesth* 1992; 69: 29-35.
49. Hudcova J, Schumann R. Electroconvulsive therapy complicated by life-threatening hyperkalemia in a catatonic patient. *Gen Hosp Psychiatry* 2006; 28: 440-2.
50. Belin RP, Karleen CI. Cardiac arrest in the burned patient following succinyldicholine administration. *Anesthesiology* 1966; 27: 516-8.
51. Zisselman MH, Jaffe RL. ECT in the treatment of a patient with catatonia: consent and complications. *Am J Psychiatry* 2010; 167: 127-32.
52. Dwersteg JF, Avery DH. Atracurium as a muscle relaxant for electroconvulsive therapy in a burned patient. *Convuls Ther* 1987; 3: 49-53.
53. Tolmie JD, Joyce TH, Mitchell GD. Succinylcholine danger in the burned patient. *Anesthesiology* 1967; 28: 467-70.
54. Tobey RE. Paraplegia, succinylcholine and cardiac arrest. *Anesthesiology* 1970; 32: 359-64.
55. Sarubin J, Gebert E. Serum potassium rise following depolarizing muscle relaxants in immobilized patients . *Anaesthesist* 1981; 30: 246-50.
56. Martyn JA, Richtsfeld M. Succinylcholine-induced hyperkalemia in acquired pathologic states: etiologic factors and molecular mechanisms. *Anesthesiology* 2006; 104: 158-69.
57. Claudius C, Garvey LH, Viby-Mogensen J. The undesirable effects of neuromuscular blocking drugs. *Anaesthesia* 2009; 64 Suppl 1: 10-21.
58. Jaksa RJ, Palahniuk RJ. Attempted organophosphate suicide: a unique cause of prolonged paralysis during electroconvulsive therapy. *Anesth Analg* 1995; 80: 832-3.
59. Kelly D, Brull SJ. Neuroleptic malignant syndrome and mivacurium: a safe alternative to succinylcholine? *Can J Anaesth* 1994; 41: 845-9.
60. McCall WV. Asystole in electroconvulsive therapy: Report of four cases. *J Clin Psychiatry* 1996; 57: 199-203.
61. Burd J, Kettl P. Incidence of asystole in electroconvulsive therapy in elderly patients. *Am J Geriatr Psychiatry* 1998; 6: 203-11.
62. Wells DG, Zelcer J, Treadrae C. ECT-induced asystole from a sub-convulsive shock. *Anaesth Intensive Care* 1988; 16: 368-71.
63. Holak EJ, Scott JP, Pagel PS. Electroconvulsive therapy-induced asystole: occurrence after 39 previous uneventful treatments. *Can J Anaesth* 2007; 54: 772-3.
64. Birkenhager TK, Pluijms EM, Groenland TH, van den Broek WW. Severe bradycardia after anesthesia before electroconvulsive therapy. *J ECT* 2010; 26: 53-4.
65. Cooper RC, Baumann PL, McDonald WM. An unexpected hyperkalemic response to succinylcholine during electroconvulsive therapy for catatonic schizophrenia. *Anesthesiology* 1999; 91: 574-5.
66. Janis K, Hess J, Fabian JA, Gillis M. Substitution of mivacurium for succinylcholine for ECT in elderly patients. *Can J Anaesth* 1995; 42: 612-3.
67. Gitlin MC, Jahr JS, Margolis MA, McCain J. Is mivacurium chloride effective in electroconvulsive therapy? A report of four cases, including a patient with myasthenia gravis. *Anesth Analg* 1993; 77: 392-4.
68. Burnstein RM, Denny N. Mivacurium in electroconvulsive therapy. *Anaesthesia* 1993; 48: 1116.
69. Liu S, Modell JH. Anesthetic management for patients with postpolio syndrome receiving electroconvulsive therapy. *Anesthesiology* 2001; 95: 799-801.
70. Savarese JJ, Ali HH, Basta SJ, Embree PB, Scott RP, Sunder N, Weakly JN, Wastila WB, el-Sayad HA. The clinical neuromuscular pharmacology of mivacurium chloride (BW B1090U). A short-acting nondepolarizing ester neuromuscular blocking drug. *Anesthesiology* 1988; 68: 723-32.
71. Savarese JJ, Ali HH, Basta SJ, Scott RP, Embree PB, Wastila WB, Abou-Donia MM, Gelb C. The

cardiovascular effects of mivacurium chloride (BW B1090U) in patients receiving nitrous oxide-opiate-barbiturate anesthesia. *Anesthesiology* 1989; 70: 386-94.

72. Hickey DR, O'Connor JP, Donati F. Comparison of atracurium and succinylcholine for electroconvulsive therapy in a patient with atypical plasma cholinesterase. *Can J Anaesth* 1987; 34: 280-3.
73. Stack CG, Abernethy MH, Thacker M. Atracurium for ECT in plasma cholinesterase deficiency. *Br J Anaesth* 1988; 60: 244-5.
74. Kopman AF, Klewicka MM, Kopman DJ, Neuman GG. Molar potency is predictive of the speed of onset of neuromuscular block for agents of intermediate, short, and ultrashort duration. *Anesthesiology* 1999; 90: 425-31.
75. Turkkal DC, Gokmen N, Yildiz A, Iyilikci L, Gokel E, Sagduyu K, Gunerli A. A cross-over, post-electroconvulsive therapy comparison of clinical recovery from rocuronium versus succinylcholine. *J Clin Anesth* 2008; 20: 589-93.
76. Williams J, Rosenquist P, Arias L, McCall WV. Pseudocholinesterase deficiency and electroconvulsive therapy. *J ECT* 2007; 23: 198-200.
77. Dodson ME. Short Acting Neurmuscular Blockers and ECT. *Br J Anaesth* 1985; 57: 933-4.
78. Setoyama K, Hirata T, Saeki H, Morimoto Y, Tsuruta S, Matsumoto M, Sakabe T. Anesthetic management for electroconvulsive therapy in the patients with a history of neuroleptic malignant syndrome. *Masui* 2009; 58: 633-6.
79. Fink M, Johnson L. Monitoring the duration of electroconvulsive therapy seizures: 'cuff' and EEG methods compared. *Arch Gen Psychiatry* 1982; 39: 1189-91.
80. Jan Wise ME, Mackie F, Zamar AC. Investigation of the 'cuff' method for assessing seizure duration in electroconvulsive therapy. *Psychiatric Bulletin* 2000; 24: 301.
81. Hoshi H, Kadoi Y, Kamiyama J, Nishida A, Saito H, Taguchi M, Saito S. Use of rocuronium-sugammadex, an alternative to succinylcholine, as a muscle relaxant during electroconvulsive therapy. *J Anesth* 2011; 25: 286-90.
82. Dillard M, Webb J. Administration of succinylcholine for electroconvulsive therapy after organophosphate poisoning: a case study. *AANA J* 1999; 67: 513-7.
83. Grayling M, Sweeney BP. Recovery from neuromuscular blockade: a survey of practice. *Anaesthesia* 2007; 62: 806-9.
84. Viby-Mogensen J. Postoperative residual curarization and evidence-based anaesthesia. *Br J Anaesth* 2000; 84: 301-3.
85. Plaud B, Debaene B, Donati F, Marty J. Residual paralysis after emergence from anesthesia. *Anesthesiology* 2010; 112: 1013-22.
86. Heier T, Caldwell JE, Feiner JR, Liu L, Ward T, Wright PM. Relationship between normalized adductor pollicis train-of-four ratio and manifestations of residual neuromuscular block: a study using acceleromyography during near steady-state concentrations of mivacurium. *Anesthesiology* 2010; 113: 825-32.
87. Eriksson LI. Evidence-based practice and neuromuscular monitoring: it's time for routine quantitative assessment. *Anesthesiology* 2003; 98: 1037-9.
88. Hayes AH, Mirakhur RK, Breslin DS, Reid JE, McCourt KC. Postoperative residual block after intermediate-acting neuromuscular blocking drugs. *Anaesthesia* 2001; 56: 312-8.
89. Cammu G, de Baerdemaeker L, den Blauwen N, de Mey JC, Struys M, Mortier E. Postoperative residual curarization with cisatracurium and rocuronium infusions. *Eur J Anaesthesiol* 2002; 19: 129-34.
90. Gatke MR, Viby-Mogensen J, Rosenstock C, Jensen FS, Skovgaard LT. Postoperative muscle paralysis after rocuronium: less residual block when acceleromyography is used. *Acta Anaesthesiol Scand* 2002; 46: 207-13.
91. Kim KS, Lew SH, Cho HY, Cheong MA. Residual paralysis induced by either vecuronium or rocuronium after reversal with pyridostigmine. *Anesth Analg* 2002; 95: 1656-60.
92. McCaul C, Tobin E, Boylan JF, McShane AJ. Atracurium is associated with postoperative

residual curarization. *Br J Anaesth* 2002; 89: 766-9.

93. Mortensen CR, Berg H, el-Mahdy A, Viby-Mogensen J. Perioperative monitoring of neuromuscular transmission using acceleromyography prevents residual neuromuscular block following pancuronium. *Acta Anaesthesiol Scand* 1995; 39: 797-801.
94. Kopman AF, Yee PS, Neuman GG. Relationship of the train-of-four fade ratio to clinical signs and symptoms of residual paralysis in awake volunteers. *Anesthesiology* 1997; 86: 765-71.
95. Baillard C, Gehan G, Reboul-Marty J, Larmignat P, Samama CM, Cupa M. Residual curarization in the recovery room after vecuronium. *Br J Anaesth* 2000; 84: 394-5.
96. Debaene B, Plaud B, Dilly MP, Donati F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. *Anesthesiology* 2003; 98: 1042-8.
97. Caldwell JE. Reversal of residual neuromuscular block with neostigmine at one to four hours after a single intubating dose of vecuronium. *Anesth Analg* 1995; 80: 1168-74.
98. Beemer GH, Rozental P. Postoperative neuromuscular function. *Anaesth Intensive Care* 1986; 14: 41-5.
99. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS, Nisman M. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the postanesthesia care unit. *Anesthesiology* 2008; 109: 389-98.
100. Viby-Mogensen J, Jensen NH, Engbaek J, Ording H, Skovgaard LT, Chraemmer-Jorgensen B. Tactile and visual evaluation of the response to train-of-four nerve stimulation. *Anesthesiology* 1985; 63: 440-3.
101. Kopman AF. A piezoelectric neuromuscular monitor. *Anesth Analg* 1994; 79: 1210-1.
102. Dupuis JY, Martin R, Tessonnier JM, Tetrault JP. Clinical assessment of the muscular response to tetanic nerve stimulation. *Can J Anaesth* 1990; 37: 397-400.
103. Capron F, Fortier LP, Racine S, Donati F. Tactile fade detection with hand or wrist stimulation using train-of-four, double-burst stimulation, 50-hertz tetanus, 100-hertz tetanus, and acceleromyography. *Anesth Analg* 2006; 102: 1578-84.
104. Shields M, Giovannelli M, Mirakhur RK, Moppett I, Adams J, Hermens Y. Org 25969 (sugammadex), a selective relaxant binding agent for antagonism of prolonged rocuronium-induced neuromuscular block. *Br J Anaesth* 2006; 96: 36-43.
105. Eikermann M, Groeben H, Husing J, Peters J. Accelerometry of adductor pollicis muscle predicts recovery of respiratory function from neuromuscular blockade. *Anesthesiology* 2003; 98: 1333-7.
106. Viby-Mogensen J, Jensen E, Werner M, Nielsen HK. Measurement of acceleration: a new method of monitoring neuromuscular function. *Acta Anaesthesiol Scand* 1988; 32: 45-8.
107. Meakin GH, Meretoja OA, Motsch J, Taivainen T, Wirtavuori K, Schonstedt R, Perkins R, McCluskey A. A dose-ranging study of rapacuronium in pediatric patients. *Anesthesiology* 2000; 92: 1002-9.
108. El-Orbany MI, Joseph NJ, Salem MR. The relationship of posttetanic count and train-of-four responses during recovery from intense cisatracurium-induced neuromuscular blockade. *Anesth Analg* 2003; 97: 80-4.
109. Han T, Kim H, Bae J, Kim K, Martyn JA. Neuromuscular pharmacodynamics of rocuronium in patients with major burns. *Anesth Analg* 2004; 99: 386-92.
110. Gijsenbergh F, Ramael S, Houwing N, van Iersel T. First human exposure of Org 25969, a novel agent to reverse the action of rocuronium bromide. *Anesthesiology* 2005; 103: 695-703.
111. Sorgenfrei IF, Norrild K, Larsen PB, Stensballe J, Ostergaard D, Prins ME, Viby-Mogensen J. Reversal of rocuronium-induced neuromuscular block by the selective relaxant binding agent sugammadex: a dose-finding and safety study. *Anesthesiology* 2006; 104: 667-74.
112. Murphy GS, Szokol JW, Franklin M, Marymont

JH, Avram MJ, Vender JS. Postanesthesia care unit recovery times and neuromuscular blocking drugs: a prospective study of orthopedic surgical patients randomized to receive pancuronium or rocuronium. *Anesth Analg* 2004; 98: 193-200.

113. Fezing AK, d'Hollander A, Boogaerts JG. Assessment of the postoperative residual curarisation using the train of four stimulation with acceleromyography. *Acta Anaesthesiol Belg* 1999; 50: 83-6.
114. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Analg* 2010; 111: 120-8.
115. Maybauer DM, Geldner G, Blobner M, Puhringer F, Hofmockel R, Rex C, Wulf HF, Eberhart L, Arndt C, Eikermann M. Incidence and duration of residual paralysis at the end of surgery after multiple administrations of cisatracurium and rocuronium. *Anaesthesia* 2007; 62: 12-7.
116. Murphy GS, Szokol JW, Marymont JH, Greenberg SB, Avram MJ, Vender JS. Residual neuromuscular blockade and critical respiratory events in the postanesthesia care unit. *Anesth Analg* 2008; 107: 130-7.
117. Arbous MS, Meursing AE, van Kleef JW, de Lange JJ, Spoormans HH, Touw P, Werner FM, Grobbee DE. Impact of anesthesia management characteristics on severe morbidity and mortality. *Anesthesiology* 2005; 102: 257-68.
118. Warner MA. Perioperative mortality: intraoperative anesthetic management matters. *Anesthesiology* 2005; 102: 251-2.
119. Brull SJ, Naguib M, Miller RD. Residual neuromuscular block: rediscovering the obvious. *Anesth Analg* 2008; 107: 11-4.
120. Caldwell JE. Clinical limitations of acetylcholinesterase antagonists. *J Crit Care* 2009; 24: 21-8.
121. Miller RD, Van Nyhuis LS, Eger EI 2nd, Vitez TS, Way WL. Comparative times to peak effect and durations of action of neostigmine and pyridostigmine. *Anesthesiology* 1974; 41: 27-33.
122. Srivastava A, Hunter JM. Reversal of neuromuscular block. *Br J Anaesth* 2009; 103: 115-29.
123. Hunter JM, Flockton EA. The doughnut and the hole: a new pharmacological concept for anaesthetists. *Br J Anaesth* 2006; 97: 123-6.
124. Puhringer FK, Gordon M, Demeyer I, Sparr HJ, Ingimarsson J, Klarin B, van Duijnhoven W, Heeringa M. Sugammadex rapidly reverses moderate rocuronium- or vecuronium-induced neuromuscular block during sevoflurane anaesthesia: a dose-response relationship. *Br J Anaesth* 2010; 105: 610-9.
125. Duvaldestin P, Kuizenga K, Saldien V, Claudius C, Servin F, Klein J, Debaene B, Heeringa M. A randomized, dose-response study of sugammadex given for the reversal of deep rocuronium- or vecuronium-induced neuromuscular blockade under sevoflurane anesthesia. *Anesth Analg* 2010; 110: 74-82.
126. Kopman AF. Sugammadex dose requirements at posttetanic counts of 1 to 2: cost implications. *Anesth Analg* 2010; 110: 1753-4.
127. Suy K, Morias K, Cammu G, Hans P, van Duijnhoven WG, Heeringa M, Demeyer I. Effective reversal of moderate rocuronium- or vecuronium-induced neuromuscular block with sugammadex, a selective relaxant binding agent. *Anesthesiology* 2007; 106: 283-8.
128. Plaud B, Meretoja O, Hofmockel R, Raft J, Stoddart PA, van Kuijk JH, Hermens Y, Mirakhur RK. Reversal of rocuronium-induced neuromuscular blockade with sugammadex in pediatric and adult surgical patients. *Anesthesiology* 2009; 110: 284-94.
129. Schaller SJ, Fink H, Ulm K, Blobner M. Sugammadex and neostigmine dose-finding study for reversal of shallow residual neuromuscular block. *Anesthesiology* 2010; 113: 1054-60.
130. Eleveld DJ, Kuizenga K, Proost JH, Wierda JM. A temporary decrease in twitch response during reversal of rocuronium-induced muscle relaxation with a small dose of sugammadex. *Anesth Analg* 2007; 104: 582-4.
131. Chambers D, Paulden M, Paton F, Heirs M, Duffy S, Hunter JM, Sculpher M, Woolacott N. Sugammadex for reversal of neuromuscular block

after rapid sequence intubation: a systematic review and economic assessment. *Br J Anaesth* 2010; 105: 568-75.

132. Paton F, Paulden M, Chambers D, Heirs M, Duffy S, Hunter JM, Sculpher M, Woolacott N. Sugammadex compared with neostigmine/glycopyrrolate for routine reversal of neuromuscular block: a systematic review and economic evaluation. *Br J Anaesth* 2010; 105: 558-67.
133. Rasmussen KG, Petersen KN, Sticka JL, Wieme LJ, Zosel JH, Marienau ME, Ryan DA, Schroeder DR, Stevens SR, Hooten WM, Spackman TN. Correlates of myalgia in electroconvulsive therapy. *J ECT* 2008; 24: 84-7.
134. White PF, Amos Q, Zhang Y, Stool L, Husain MM, Thornton L, Downing M, McClintock S, Lisanby SH. Anesthetic considerations for magnetic seizure therapy: a novel therapy for severe depression. *Anesth Analg* 2006; 103: 76-80.
135. Kadar AG, Ing CH, White PF, Wakefield CA, Kramer BA, Clark K. Anesthesia for electroconvulsive therapy in obese patients. *Anesth Analg* 2002; 94: 360-1.
136. Auriacombe M, Reneric JP, Usandizaga D, Gomez F, Combourieu I, Tignol J. Post-ECT agitation and plasma lactate concentrations. *J ECT* 2000; 16: 263-7.
137. Cheam EW, Critchley LA, Chui PT, Yap JC, Ha VW. Low dose mivacurium is less effective than succinylcholine in electroconvulsive therapy. *Can J Anaesth* 1999; 46: 49-51.
138. Batistaki C, Kesidis K, Apostolaki S, Kostopanagiotou G. Rocuronium antagonized by sugammadex for series of electroconvulsive therapy (ECT) in a patient with pseudocholinesterase deficiency. *J ECT* 2011; 27: e47-8.
139. Bryson EO, Aloysi AS, Perez AM, Popeo D, Kellner CH. Prolonged Succinylcholine Action During Electroconvulsive Therapy (ECT) After Cytarabine, Vincristine, and Rituximab Chemotherapy. *J ECT*; 27: e42-3.
140. Waghmare A, Kumar CN, Thirthalli J. Suxamethonium induced prolonged apnea in a patient receiving electroconvulsive therapy. *Gen Hosp Psychiatry* 2010; 32: 447.
141. Arias L, O'Brien JJ, Kimball JN. Electroconvulsive therapy- and succinylcholine-related asystole. *J ECT* 2009; 25: 144.
142. Prieto Martin RM, Palomero Rodriguez MA, et al. Electroconvulsive therapy in the third trimester of pregnancy: a case report. *Rev Esp Anestesiol Reanim* 2006; 53: 653-6.
143. Ozer F, Meral H, Aydin B, Hanoglu L, Aydemir T, Oral T. Electroconvulsive therapy in drug-induced psychiatric states and neuroleptic malignant syndrome. *J ECT* 2005; 21: 125-7.
144. Magid M, Lapid MI, Sampson SM, Mueller PS. Use of electroconvulsive therapy in a patient 10 days after myocardial infarction. *J ECT* 2005; 21: 182-5.
145. Kadar AG, Kramer BA, Barth MC, White PF. Rapacuronium: an alternative to succinylcholine for electroconvulsive therapy. *Anesth Analg* 2001; 92: 1171-2.
146. Nisijima K, Ishiguro T. Electroconvulsive therapy for the treatment of neuroleptic malignant syndrome with psychotic symptoms: a report of five cases. *J ECT* 1999; 15: 158-63.
147. Trollor JN, Sachdev PS. Electroconvulsive treatment of neuroleptic malignant syndrome: a review and report of cases. *Aust N Z J Psychiatry* 1999; 33: 650-9.
148. Herriot PM, Cowain T, McLeod D. Use of vecuronium to prevent suxamethonium-induced myalgia after ECT. *Br J Psychiatry* 1996; 168: 653-4.
149. Swartz CM. Electroconvulsive therapy emergence agitation and succinylcholine dose. *J Nerv Ment Dis* 1990; 178: 455-7.
150. Sorbye R. Succinylcholine halogens compares with flaxedil as muscle relaxant in electroshock therapy. *Sven Lakartidn* 1954; 51: 1680-8.
151. Thesleff S, Dardel OV, Holmberg G. Succinylcholine iodide; a new muscular relaxant. *Br J Anaesth* 1952; 24: 238-44.