Anesthesia for Electroconvulsive Therapy

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The use of electroconvulsive therapy (ECT) to provoke a generalized epileptic seizure was first described in 1938 and was performed without anesthesia for almost 30 yr (1). Now the number of ECT procedures performed each year under general anesthesia in the United States exceeds the number of coronary revascularization, appendectomy, and herniorrhaphy procedures (2). In recent years, ECT has assumed an increasingly important role in the treatment of severe and medication-resistant depression and mania, as well as in the treatment of schizophrenic patients with affective disorders, suicidal drive, delusional symptoms, vegetative dysregulation, inanition, and catatonic symptoms (2,3). Typically, the acute phase of ECT is performed three times a week for 6 to 12 treatments. In successful cases, initial clinical improvement is usually evident after three to five treatments (3,4). Maintenance therapy can be performed at progressively increasing intervals from once a week to once a month to prevent relapses.

To optimize the anesthetic management of patients undergoing ECT, it is important to understand the physiologic responses to the electrical stimulus, the effect of anesthetic drugs on the ECT response, and the pharmacologic effects of the drugs used to attenuate the side effects related to ECT. In 1986, Gaines and Rees (5) published a comprehensive review regarding the psychiatric and anesthetic considerations in caring for patients undergoing ECT. More recently, Folk et al. (6) reviewed the preanesthetic management of ECT patients with coexisting diseases. This review article is intended to provide an update on the anesthetic management of patients undergoing ECT.

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Physiologic Responses to ECT

When an electrical current is applied to the brain via transcutaneous electrodes, the resultant electroencephalographic (EEG) spike and wave activity is accompanied by a generalized motor seizure and an acute cardiovascular response, which results in a marked increase in cerebral blood flow and intracranial pressure (7). The maximal blood flow velocity increases approximately 133% above the baseline value (8). However, the magnitude of the acute hyperdynamic response to ECT appears to be independent of the duration of the motor and EEG seizure activity (Fig. 1) (9). The hemodynamic response to ECT can produce myocardial ischemia and even infarction (10), as well as transient neurologic ischemic deficits, intracerebral hemorrhages, and cortical blindness (11,12). Short-term memory loss is common after ECT (1,3), and more serious cognitive dysfunction has been described in the ECT literature, even though there is no scientific evidence of direct neuronal damage (13). However, use of brief pulse stimulation, unilateral nondominant electrode placement, and individual stimulus titration have all been alleged to minimize cognitive dysfunction after ECT (2,3,14,15).

The typical cardiovascular response to ECT consists of generalized autonomic nervous system stimulation, with an initial parasympathetic-induced bradycardia lasting 10 to 15 s followed immediately by a more prominent sympathetic response that results in transient tachycardia and hypertension lasting 5 min or longer. The cardiovascular response is associated with the release of catecholamines and occasional cardiac arrhythmias (16,17). Systolic blood pressure (SBP) is transiently increased by 30%–40%, and heart rate (HR) is increased by 20% or more, resulting in a two- to fourfold increase in the rate-pressure product (RPP), an index of myocardial oxygen consumption (16–18). Bilateral ECT produces a larger increase in the RPP than unilateral ECT (19). Older patients typically manifest a larger increase in RPP after ECT. The peak HR and SBP values occur 3–5 min after the application of the electrical stimulus (9); the magnitude varies with the quality of the EEG seizure

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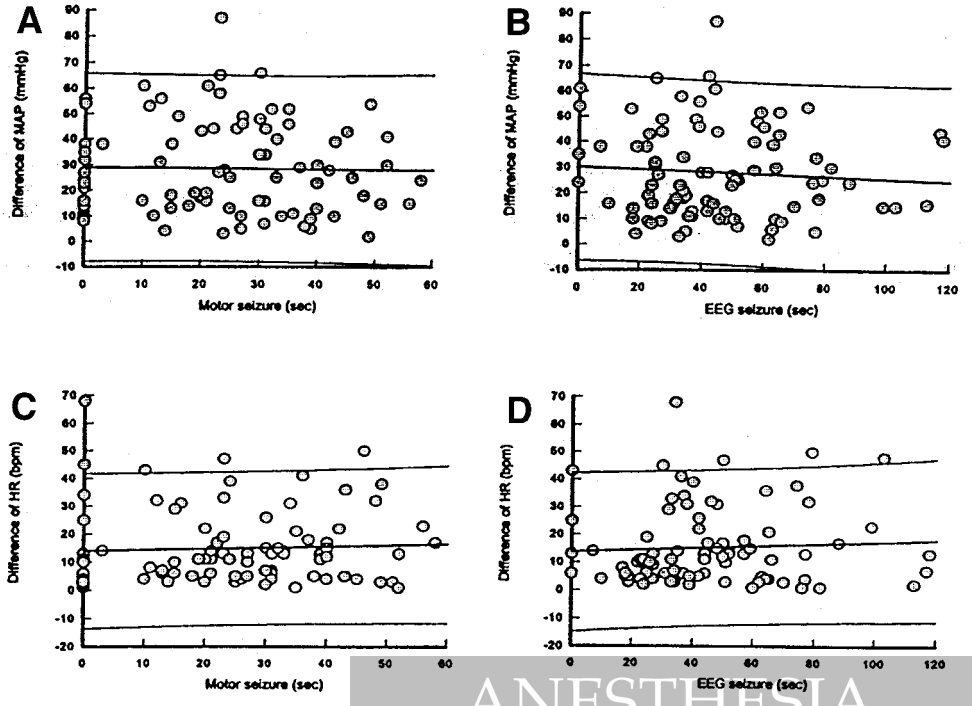

Figure 1. The correlation between the maximal changes in mean arterial blood pressure (MAP) (a,b) and heart rate (HR) (c,d) values and the duration of motor and electroencephalographic (EEG) seizure activity. The changes of MAP and HR values do not correlate with the duration of motor or EEG seizure activity (9).

(20) and can provide clinically useful information for stimulus dose regulation.

Hyperventilation-induced hypocapnia ($Paco_2$ of 2%) appears to augment the HR (47% vs 28%) and RPP (82% vs 60%) responses compared with normocapnic conditions (P_{ET} of 5%) (21). It is interesting to note that the HR and RPP responses correlated with seizure duration in hyperventilated patients, but not in patients with normal end-tidal CO_2 values. In patients with compromised cardiac function, ECT can result in myocardial ischemia and infarction (10,22). As a result of the acute hemodynamic responses, ECT can result in ventricular tachycardia (23) and even cardiac rupture (24). Patients with preexisting cardiac diseases are at an increased risk of developing cardiac complications during and after ECT (25–27). Furthermore, left-ventricular systolic and diastolic function was decreased from 20 min to 6 h after ECT treatments even in patients without cardiac diseases (28,29).

In addition to acute neurologic and cardiovascular effects, the ECT-induced seizure activity is accompanied by a generalized convulsion that has resulted in fracture-dislocations (30,31) and muscle aches (32) (Table 1). Other complications related to ECT include nausea, headache, emergence agitation, and sudden death (33,34).

Anesthetic Drugs Used for ECT

The efficacy of ECT in alleviating acute depression is dependent on the duration of the induced seizure (1–3). EEG seizure activity lasting from 25 to 50 s is alleged to produce the optimal antidepressant response. Patients experiencing an initial seizure duration of <15 s or >120 s achieve a less favorable response to ECT (35). Because many of the anesthetic drugs used for ECT have anticonvulsant properties, they would be expected to decrease the duration of ECT-induced seizure activity in a dose-dependent manner. Use of larger than necessary dosages of general anesthetics will shorten the duration of ECT-induced seizure activity and could adversely affect the efficacy of the ECT treatments. Therefore, there is a delicate balance between achieving an adequate anesthetic state and an optimal duration of EEG seizure activity (Table 2). In the current health care environment, use of general anesthetic techniques with a rapid onset and recovery is essential to facilitate fast-tracking and permits the discharge of these patients within 1–2 h after the ECT treatment.

Methohexital

Methohexital remains the most widely used general anesthetic for ECT and is considered the "gold standard" against which all other anesthetics are compared (Table 2, Fig. 2) (36–38). Of interest, a recent regional survey from Edinburgh, Scotland (37), found that most patients received a methohexital dose (1.5 ± 0.3 mg/kg) exceeding the dose range recommended by the Royal College of Psychiatrists (0.75–0.9 mg/kg) and the American Psychiatric Association (0.75–1.0 mg/kg). An explanation for the larger methohexital

Table 1. Common Physiologic Responses and Side Effects Associated with Electroconvulsive Therapy

Variable	Response
Central nervous system	Increased blood flow velocity, intracranial pressure, and cerebral metabolism; dizziness, amnesia, confusion, agitation, and headaches
Cardiovascular system	Increased blood pressure, heart rate, and cardiac output; cardiac arrhythmias
Musculoskeletal system	Myoclonic-toxic contractions, bone fractures/dislocations, muscle and joint pain
Miscellaneous responses	Increased salivation, nausea and vomiting, dental damage, and oral cavity lacerations

Table 2. Effects of IV Anesthetic and Cardiovascular Drugs on the Duration of ECT-Induced Seizure Activity (relative to methohexital or saline, respectively)

Drug	Increased	No change	Decreased
Anesthetic drugs	Etomidate (36,42,43) Alfentanil (94,95)[b] Remifentanil (96)[b]	Methohexital (36–39)[a]	Thiopental (39,40), thiamylal (39), lorazepam (52), midazolam (54), ketamine (51), fentanyl (75), propofol (36,40,44–48)
Cardiovascular drugs	Aminophylline (114) Caffeine (115,116)	Clonidine (84), esmolol (74,86), labetalol (81), dexmedetomidine (83), nifedipine (79), nicardipine (81), nitroglycerin (86), trimethaphan (93), nitroprusside (92)	Diltiazem (82), lidocaine (9,75), labetalol (74,75), Esmolol (76,78)

Reference numbers are cited in parentheses.
ECT = electroconvulsive therapy.
[a] Compared with saline, methohexital decreases ECT seizure duration.
[b] Increased seizure time because of an anesthetic-sparing effect.

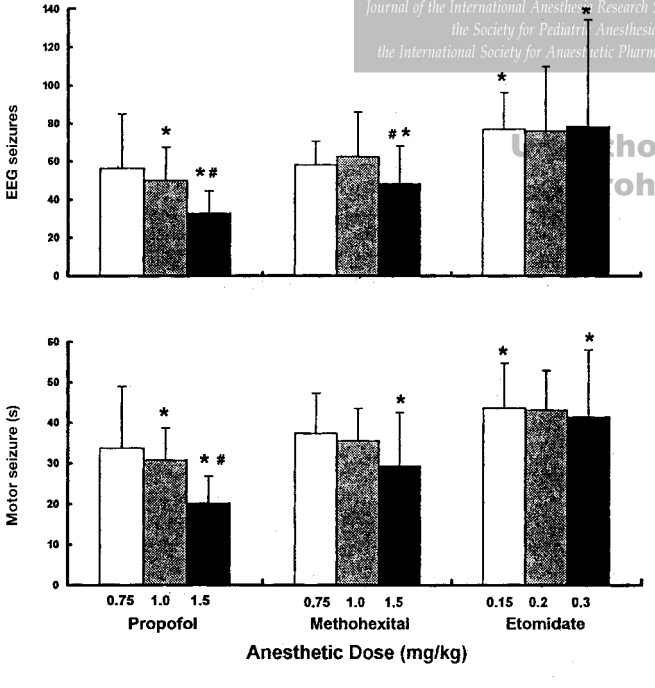

Figure 2. Duration of motor and electroencephalographic (EEG) seizures in patients receiving propofol, methohexital, and etomidate. Open bars = 0.75 or 0.15 mg/kg doses; hatched bars = 1.0 or 0.2 mg/kg doses; solid bars = 1.5 or 0.3 mg/kg doses. Error bars = SD. *Significantly different from the other drugs in the same dosage group ($P < 0.05$); #significantly different from lower doses of the same drug ($P < 0.05$) (36).

dosage may relate to the concurrent chronic medications that the patients were receiving at the time of their ECT treatments, as well as to chronic consumption of alcohol and centrally active drugs (e.g., benzodiazepines) known to increase the anesthetic requirement. Minimally effective doses of methohexital compare favorably with other IV anesthetics with respect to its effect on the duration of seizure activity (Table 2). It has been suggested that divided doses of methohexital would minimize its depressant effect on seizure activities and could lead to improved outcomes after ECT (38). With respect to speed of recovery of cognitive function after ECT, propofol and etomidate offered no advantage over methohexital (36). Therefore, unless there is a specific contraindication to barbiturates (e.g., acute intermittent porphyria), methohexital should be considered the drug of choice for the induction of anesthesia in this patient population.

Thiopental/Thiamylal

Compared with methohexital (0.5–1.0 mg/kg), both thiopental (1.5–2.5 mg/kg) and thiamylal (1.5–2.5 mg/kg) shorten the EEG seizure duration (39). The frequency of sinus bradycardia and premature ventricular contractions was also increased with thiopental and thiamylal compared with methohexital (39). Compared with propofol, the middle cerebral artery flow velocities immediately after ECT were significantly higher with thiopental (40), and suppression of ECT-induced hemodynamic changes with thiopental was comparable to that with sevoflurane anesthesia (41).

Therefore, there is no obvious reason to use either thiopental or thiamylal for ECT procedures.

Etomidate

When compared with methohexital, thiopental, and propofol, anesthetic induction with etomidate (0.15–0.3 mg/kg) is generally associated with a longer seizure duration and may be helpful in patients with short seizure times (<20 s) despite a maximal electrical stimulus (36,42,43). As a result of etomidate's reduced cardiovascular depressant properties and ability to enhance seizure activity, the acute hemodynamic response to ECT is accentuated compared with the barbiturates and propofol. Furthermore, early recovery after etomidate can be delayed because of post-ECT confusion and an increased incidence of emetic symptoms compared with methohexital and propofol.

Propofol

Propofol appears to have more potent anticonvulsant effects during ECT than other IV anesthetics (Table 2) (36,44–48). However, the use of a minimally hypnotic dose of propofol (0.75 mg/kg) was associated with a seizure duration that was comparable to standard hypnotic doses of methohexital (Fig. 2) (36). The ECT seizure duration after larger dosages of propofol (1.0–1.5 mg/kg) was significantly shorter than after methohexital, etomidate, and thiopental (36,40). However, even the largest doses of propofol (1.5 mg/kg) may result in a duration of EEG seizure activity that is considered clinically acceptable (45,46). Furthermore, the measurements of seizure quality (including postictal suppression index and mean integrated amplitude) after propofol anesthesia were not significantly different from those after methohexital (45).

Because use of propofol can significantly shorten the duration of seizure activity, its effect on the antidepressant action of ECT has been a concern (47–49). Two reports have compared the antidepressant efficacy of ECT by using the Hamilton Rating Scale for Depression (a 17-item scale that evaluates mood, vegetative and cognitive symptoms of depression, and comorbid anxiety symptoms) and the Beck Depression Inventory (a 21-item self-report rating inventory that measures characteristic attitudes and symptoms of depression) when propofol or methohexital was administered as the primary anesthetic (48,49). Even though the seizure duration was consistently shorter with propofol (versus methohexital), the Hamilton Rating Scale for Depression scores were improved to a similar degree in both anesthetic groups after they completed a standard series of ECT treatments. The magnitude of improvement in the patients' depression symptoms was apparently unrelated to either the total duration of seizure activity during the series of ECT treatments or the concurrent use of tricyclic antidepressant (TCA) drugs (47). Given the well known cardiovascular depressant effects of propofol, the acute hemodynamic response during the ECT procedure is reduced with propofol compared with etomidate, methohexital, and thiopental (36,39). However, emergence from propofol anesthesia is only marginally faster than with other IV anesthetics (36,39,48), and recovery of cognitive function is similar to methohexital during the early recovery period (36,50).

Ketamine

Ketamine, a unique IV anesthetic with sedative and analgesic properties, has also been used to induce a hypnotic state for ECT (51). With ketamine, hemodynamic variables are increased compared with those of other IV drugs because of its intrinsic sympathomimetic activity. Surprisingly, the EEG seizure duration was decreased compared with methohexital, even with small doses of ketamine. Although there were no adverse psychological reactions to ketamine, the enhanced hemodynamic response and resultant increase in intracranial pressure make ketamine less desirable than methohexital and propofol for routine ECT treatments.

Benzodiazepines

Use of benzodiazepines can alter both the ECT seizure threshold and the duration of seizure activity. Although the administration of lorazepam before ECT was not associated with a change in the seizure threshold, the seizure duration was significantly decreased (52). Nevertheless, in patients with catatonia, the concurrent use of lorazepam has been associated with a superior response to ECT treatments (53). When IV midazolam was compared with thiopental for ECT, it significantly reduced the duration of seizure activity (54). In a case report, the anticonvulsant effect produced by large doses of lorazepam or midazolam was successfully reversed with flumazenil given immediately before the ECT treatments (55). Because of their prominent anticonvulsant activity, benzodiazepines should be avoided before ECT.

Sevoflurane

Because most ECT procedures are performed in locations remote from the operating room, IV anesthetics are considered preferable to the inhaled (volatile) anesthetics. Nevertheless, sevoflurane (1.7%) in combination with nitrous oxide 50% in oxygen was comparable to thiopental in suppressing the acute hemodynamic response during ECT (41). The use of a larger concentration of sevoflurane (3.4%) was more effective than thiopental in blunting the acute hemodynamic response without producing

cardiac arrhythmias. The seizure duration and recovery time after ECT with sevoflurane were similar to those with thiopental. Although this volatile anesthetic can be used to produce an adequate anesthetic state for ECT, it is more time consuming and possesses no obvious advantage when compared with the commonly used IV anesthetics, except for women requiring ECT in the late stages of pregnancy, when it may reduce post-ECT uterine contractions (56).

Muscle Relaxants

When ECT is performed without any muscle relaxant, the patient will require vigorous physical restraint during the seizure and will experience severe muscle pain after the procedure. To prevent myalgias (32), as well as more serious musculoskeletal complications (e.g., bone fractures or dislocations) (30,31), muscle relaxants are often administered during ECT procedures.

Succinylcholine. Succinylcholine remains the most commonly used muscle relaxant to reduce the intense muscle contractions associated with ECT-induced seizure activity (37). Although the dose recommended by the Royal College of Psychiatrists is 0.5 mg/kg, larger dosages (0.75–1.5 mg/kg) are often used in clinical practice (57). In patients with a history of post-ECT agitation related to increased levels of plasma lactate, increasing the dose of succinylcholine may decrease the emergence delirium (58). However, use of larger dosages of succinylcholine should be avoided in patients with a history of bradyarrhythmias (59). Even small doses of this rapid and short-acting muscle relaxant can produce side effects (e.g., myalgias, hyperthermia, and hyperkalemia) in at-risk patients with a history of susceptibility to malignant hyperthermia (MH), neuroleptic malignant syndrome (NMS), catatonic schizophrenia, and organophosphate poisoning (60–62). Therefore, an ultra-short-acting nondepolarizing muscle relaxant would be a valuable addition to the anesthesiologist's armamentarium.

Mivacurium. Mivacurium is the drug most often administered as an alternative to succinylcholine during ECT (57,60,63–65). In a patient with NMS who developed an MH-like reaction after succinylcholine administration for ECT (60), mivacurium was used during subsequent treatments and resulted in effective attenuation of muscle contractions without producing acute increases in muscle enzyme levels. In another report, mivacurium was successfully used in three older patients with severe osteoporosis, amyotrophic lateral sclerosis, and cardiac arrhythmias (65). When mivacurium (0.08 mg/kg) was compared with succinylcholine (0.5 mg/kg), succinylcholine was more effective than mivacurium in preventing muscle contractions during ECT (63). Fredman et al. (57) performed a dose-ranging assessment of mivacurium in a patient with a history of NMS and found that only a full intubating dose of mivacurium (0.2 mg/kg IV) was associated with effective muscle relaxation during ECT-induced seizures. Gitlin et al. (65) also found that mivacurium doses of 0.15–0.25 mg/kg IV were required for ECT in patients with myasthenia gravis. Of concern, a full intubating dose of mivacurium can be associated with clinically significant histamine release and occasional hypotension and requires the use of anticholinesterase drugs to reverse residual paralysis after ECT.

Atracurium/cisatracurium. Patients receiving atracurium 0.5 mg/kg IV had significantly fewer ECT-induced moderate to severe muscle contractions compared with patients receiving a 0.3 mg/kg dose (16% vs 86%) (66). As expected, patients receiving atracurium 0.5 mg/kg IV required more time to achieve a train-of-four ratio of 0.5 compared with patients receiving the 0.3 mg/kg dose (9.2 ± 0.8 min vs 4.3 ± 0.4 min). These investigators recommended that a small dose of atracurium be used if one needs to avoid using succinylcholine and mivacurium for ECT treatments. However, a small dose of atracurium (10–15 mg) in a patient with atypical plasma cholinesterase (67) had an onset of action of 6 min, and the time to 90% first twitch recovery was 16 min (even after reversal with edrophonium and atropine). Although the use of atracurium has been largely replaced by cisatracurium in clinical practice, there are no clinical reports describing the use of this improved formulation of atracurium for ECT.

Vecuronium/rocuronium. Vecuronium has been used for pretreatment in patients with severe succinylcholine-induced myalgias (32). There have been no clinical reports describing the use of rocuronium for ECT. Given the pharmacodynamic profiles of these aminosteroid nondepolarizing muscle relaxants, it does not appear that these drugs offer any advantages in the ECT setting.

Rapacuronium. Rapacuronium is a newer aminosteroid muscle relaxant with a rapid onset and short duration of action. This nondepolarizing muscle relaxant has been used for ECT treatments in a patient with a positive family history of MH (68). Rapacuronium dosages of 0.6–0.8 mg/kg provided effective muscle relaxation for ECT, and this was readily reversible with edrophonium and atropine at the end of the seizure. Unfortunately, the occurrence of respiratory complications (e.g., bronchospasm) when rapacuronium was administered as part of a rapid-sequence induction technique led to its withdrawal from the market in the United States (69).

Drugs Used to Control Cardiovascular Responses

Because acute cardiovascular responses secondary to ECT can result in serious complications (10,11,25–27), many different drugs have been used to attenuate the

acute parasympathetic and sympathetic responses (16–18). The parasympathetic effects of ECT often result in increased salivation, transient bradycardia, and occasionally even asystole, especially when repeated stimuli are administered as part of a seizure threshold determination (70). The sympathetic effects of ECT typically result in tachycardia, hypertension, and occasionally even myocardial ischemia and infarction, as mentioned previously. Anticholinergic drugs are often used to block the parasympathetic responses, whereas the acute sympathetic responses are attenuated with β-blockers, calcium channel blockers, α_2 agonists, and direct-acting vasodilators. Rapid, short-acting opioid analgesics also possess sympatholytic effects and have recently been investigated as adjuvants during ECT. Some of these drugs can produce adverse effects on the duration of the ECT-induced seizure activity (Table 2). Therefore, the selection of adjuvants should be tailored to the needs of the individual patient.

Anticholinergic drugs. When atropine was administered as premedication before ECT, it resulted in significantly higher RPP values (71). However, Mokriski et al. (39) reported that atropine 0.6 mg IV given before the induction of anesthesia decreased the frequency of premature atrial contractions and bradycardia and increased the frequency of tachycardia after ECT.

Glycopyrrolate is an anticholinergic drug that lacks central nervous system activity. As a result of its ability to reduce oral secretion and bradycardia during ECT without producing post-ECT side effects, glycopyrrolate has become the anticholinergic drug of choice for ECT. In an elderly population (72), no significant post-ECT complications were reported when patients received glycopyrrolate for premedication. In a placebo-controlled study, cognitive function after ECT was similar in patients receiving glycopyrrolate (0.2 mg IV) or saline (73). Because the primary benefit of using an anticholinergic drug appears to be its antisialagogue effect, glycopyrrolate (0.1–0.3 mg IV) is a better choice than atropine for ECT because it would be associated with less post-ECT tachycardia.

β-Blockers. To attenuate the acute sympathetic response to ECT, both esmolol (a short-acting β_1-receptor blocker) and labetalol (a mixed α- and β-blocker) have been most extensively studied. When esmolol (1–1.3 mg/kg) or labetalol (0.1–0.2 mg/kg) was administrated before the induction of anesthesia, they both produced significant amelioration of the acute cardiovascular response to ECT (74). However, SBP values were significantly lower during the early recovery period with labetalol (versus esmolol) pretreatment.

In a placebo-controlled, double-blinded study (75), pretreatment with esmolol (1.0 mg/kg) or labetalol (0.3 mg/kg) immediately before the induction of anesthesia significantly reduced the hemodynamic response to ECT compared with fentanyl (1.5 μg/kg) or lidocaine (1.0 mg/kg) (Fig. 3). It is interesting to note that esmolol more effectively attenuated the blood pressure response than labetalol. In contrast to esmolol, pretreatment with labetalol, fentanyl, or lidocaine significantly reduced the EEG seizure duration and increased the frequency with which a second electrical stimulus was required (Table 3) (75). However, there is controversy about the relative effects of esmolol and labetalol on the duration of seizure activity (Table 2) (76–78). To minimize the potential adverse effect of labetalol on the duration of seizure activity, labetalol can be administered immediately before or after the electrical stimulation is applied.

Calcium channel blockers. When the acute blood pressure response to ECT was not adequately controlled with labetalol alone (79), nifedipine combined with labetalol was found to be safe and resulted in more effective control of the hemodynamic response in older patients. In patients with hypertension, sublingual nifedipine 10 mg, given 20 min before their ECT treatments, also attenuated the acute increase in the mean arterial blood pressure (MAP) (80).

The effects of nicardipine alone and in combination with labetalol have also been investigated with respect to its ability to control the acute hyperdynamic response to ECT (Fig. 4) (81). When administered as a rapid infusion, nicardipine (5 mg IV) produced a significant decrease in MAP. It is interesting to note that larger doses of nicardipine (10–15 mg) failed to produce a significantly larger decrease in MAP than the 5-mg dose. Bolus administration of nicardipine 1.25–5 mg IV produced a rapid onset of its hemodynamic effects without exacerbating the cardiovascular depressant effects of methohexital (1 mg/kg IV) (81). Unfortunately, the decrease in MAP after the 5-mg bolus dose was accompanied by a reflex increase in HR. Therefore, the acute hyperdynamic response to ECT was most effectively controlled by a bolus dose of 1.25 to 2.5 mg IV in combination with labetalol 10 mg IV. This combination produced a 20% decrease in MAP immediately before ECT and produced a lower MAP at the time of discharge from the recovery area compared with labetalol alone. It is important to note that the use of small-dose nicardipine did not alter the ECT-induced seizure duration (81).

In a placebo-controlled study, diltiazem (10 mg IV) significantly reduced HR and MAP after the induction of anesthesia and reduced the increases in these variables after the ECT stimulus (82). However, the use of diltiazem was associated with a shortened seizure duration. Therefore, small-dose nicardipine (or nifedipine) in combination with labetalol (0.1–0.2 mg/kg IV) appears to be a more effective regimen for controlling the acute hemodynamic response in older hypertensive patients undergoing ECT.

α_2 Agonists/antagonists. The acute hemodynamic effects of the α_2-adrenergic agonist dexmedetomidine

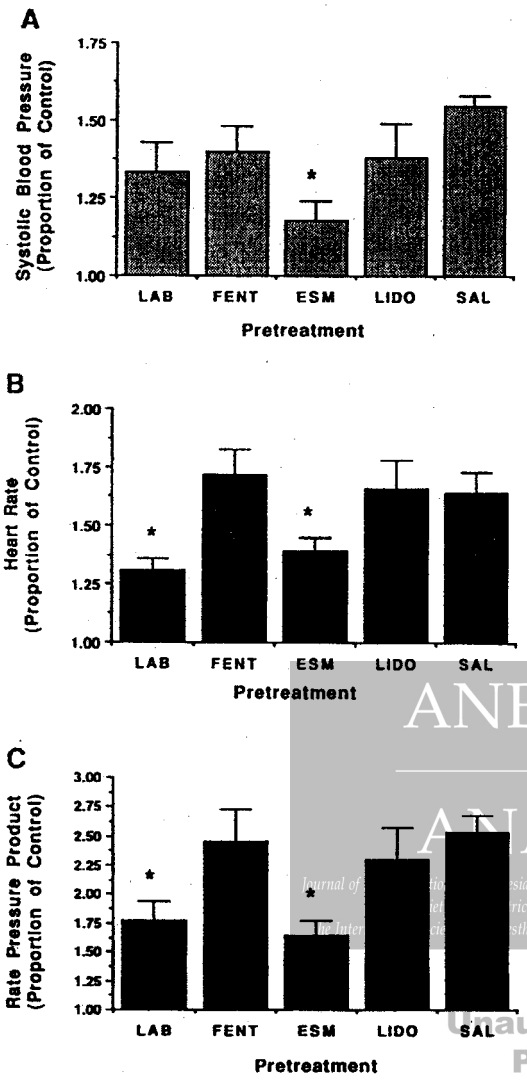

Figure 3. Effect of drug pretreatments on systolic blood pressure (A), heart rate (B), and rate-pressure product (C). Data are mean maximal values during the seizure as a proportion of control (preoperative) values for labetalol (LAB), fentanyl (FENT), esmolol (ESM), lidocaine (LIDO), and saline (SAL). *Significant ($P < 0.05$) compared with preoperative values. Esmolol attenuated the blood pressure response to ECT, and both labetalol and esmolol decreased the heart rate and rate-pressure product responses to electroconvulsive therapy (75).

have been investigated in patients undergoing ECT (83). Dexmedetomidine 0.5 or 1.0 μg/kg IV, given 10–30 min before the induction of anesthesia, produced dose-related increases in the level of the patient's pre-ECT sedation. However, dexmedetomidine failed to decrease the peak MAP and HR responses after the ECT stimulus and prolonged the recovery time after ECT. Although it had no effect on seizure duration, dexmedetomidine did not appear to be beneficial in controlling the acute hyperdynamic response associated with ECT.

The α_2-adrenergic agonist/antagonist clonidine has also been investigated in the ECT setting (84). Oral clonidine (0.05–0.3 mg) given 60 to 90 min before the induction of anesthesia produced a dose-related antihypertensive effect by decreasing the MAP values immediately before the electrical stimulus was applied. However, clonidine produced no significant change in either the HR or the magnitude of the increase in MAP after the stimulus was applied. Clonidine produced no adverse effects on the duration of motor and EEG seizure activity or prolongation of the recovery time.

Finally, a recent study (85) reported that the postsynaptic α_1-adrenergic antagonist urapidil (25 mg IV) was as effective as labetalol (0.2 mg/kg IV) in attenuating the increase in blood pressure associated with ECT but did not prevent the increase in HR. Therefore, it would appear that clonidine, a mixed α_2 agonist/antagonist, is the most beneficial drug in this class for achieving hemodynamic stability during ECT. However, careful dose titration is required to achieve the optimal outcome.

Direct vasodilators. When nitroglycerin (NTG) 3 μg/kg IV was given 2 min before ECT, post-ECT hemodynamic variables were all significantly lower compared with esmolol 2 mg/kg IV (86). It is important to note that neither NTG nor esmolol produced a change in the ECT-induced seizure duration. In another study, the administration of NTG 0.4 mg as a sublingual spray before ECT significantly attenuated the acute hypertensive response after the ECT stimulus (87). When 2% NTG ointment was applied 45 min before ECT (88), it also effectively attenuated the increase in HR and MAP after ECT, and it should be considered for ECT patients who are at a high risk of developing myocardial ischemia. It is interesting to note that NTG partially inhibits the increase in cerebral blood flow velocity associated with ECT (8).

Nitroprusside, another peripheral-acting vasodilator, has been used in patients with intracranial aneurysms, dissecting aortic aneurysm, and critical aortic stenosis requiring ECT (89–91). The combination of a β-blocker and an infusion of nitroprusside prevented tachycardia and hypertension and attenuated the expected increase in flow velocity in the middle cerebral artery after ECT (8). Furthermore, there is no evidence that nitroprusside decreases the ECT-induced seizure duration (92).

Ganglionic blockers. Trimethaphan, a ganglionic blocker, administered by IV bolus injection in doses of 5, 10, and 15 mg, is able to control the hyperdynamic responses during ECT without altering the duration of seizure activity (93). It is important that no rebound hypertension, post-ECT hypotension, cardiac arrhythmias, or other side effects were noted.

Local anesthetics. Lidocaine has also been administered to blunt the cardiovascular responses after ECT (9,75). Despite producing dose-related decreases in the duration of both motor and EEG seizure activity (Table 4) (9), lidocaine (1 mg/kg IV) failed to effectively

Table 3. Effect of Drug Pretreatment on the ECT-Invoked EEG Seizure Activity (75)

Variable	EEG seizure duration (s)	Required second stimulus (%)	Inadequate seizure (%)
Labetalol 0.3 mg/kg	36.9 ± 4.5*	20	10
Fentanyl 1.5 μg/kg	43.6 ± 4.1*	20	0
Esmolol 1 mg/kg	45.8 ± 5.9	10	0
Lidocaine 1 mg/kg	26.5 ± 7.2*	60	30
Saline (placebo)	56.5 ± 12.5	0	0

ECT = electroconvulsive therapy; EEG = electroencephalography.
* Significantly different from control (saline) values ($P < 0.05$).

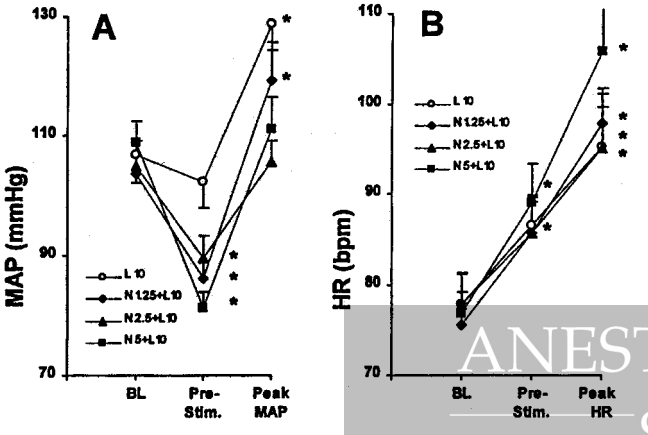

Figure 4. (A) Mean arterial blood pressure (MAP) and (B) heart rate (HR) values after bolus administration of labetalol 10 mg (L 10) alone (○) and in combination with nicardipine 1.25 mg (N 1.25) (◆), 2.5 mg (N 2.5) (▲), and 5 mg (N 5) (■). Mean and SD data are presented for the baseline (BL), prestimulation period (Pre-Stim.), and peak values after the induction of seizure (Peak MAP or HR). *Significant differences versus baseline values ($P < 0.05$) (81).

attenuate the acute hemodynamic response associated with ECT (Fig. 3) (75).

Opioid analgesics. Alfentanil was evaluated in combination with methohexital or propofol during anesthesia for ECT (94,95). In an observer-blinded, prospective, randomized, cross-over study, alfentanil (10 μg/kg IV) reduced the doses of methohexital and propofol required to induce unconsciousness by 33%, resulting in a prolongation of the ECT-induced seizure duration (95). In this interaction study, the durations of motor and EEG seizure durations were longest with the methohexital/alfentanil combination and shortest with propofol alone. However, recovery times were shorter in patients receiving propofol alone compared with methohexital/alfentanil and methohexital alone. In another report (94), alfentanil (25 μg/kg IV) in combination with methohexital (20 mg IV) was associated with a 45% increase in the EEG seizure duration compared with a standard 0.75 mg/kg dose of methohexital alone. In a recent study (96) comparing the effect of a methohexital (0.5 mg/kg) and remifentanil (1 μg/kg) combination with that of methohexital (0.75 mg/kg) alone, the anesthetic-sparing effect of remifentanil resulted in prolongation of the seizure time from 27 to 38 s. However, the hemodynamic changes and recovery times were similar in both groups.

It is interesting to note that when fentanyl (1.5 μg/kg IV) was administered with a standard 0.75 mg/kg dose of methohexital, the seizure duration was reduced (Table 3) (75). Fentanyl also failed to attenuate the acute hemodynamic response to ECT (Fig. 3). Therefore, the increased seizure duration associated with the short-acting opioid analgesics alfentanil and remifentanil appears to be related to a reduction in the IV anesthetic dosage requirements. In ECT patients with borderline seizure times, adjunctive use of a potent rapid and short-acting opioid analgesic could be very beneficial.

Standard General Anesthetic Technique

The essential elements of anesthesia for ECT include rapid loss of consciousness, effective attenuation of the hyperdynamic response to the electrical stimulus, avoidance of gross movements, minimal interference with seizure activity, and prompt recovery of spontaneous ventilation and consciousness. Therefore, the use of rapid and short-acting anesthetic drugs (e.g., methohexital, propofol, succinylcholine, esmolol, and labetalol) facilitates the ECT procedure. Although the rapid and short-acting opioid analgesics (e.g., alfentanil and remifentanil) have anesthetic-sparing properties, their role in ECT is yet to be clearly defined.

Although patients are required to fast overnight for solid food, clear liquids are allowed for taking oral medication up to 1 h before the procedure. Patients with cardiovascular disease should be encouraged to take all chronic antihypertensive medications before ECT. To prevent post-ECT myalgias, patients can be premedicated with enteric-coated aspirin (650 mg orally) or acetaminophen (650 mg orally). In younger patients at risk for severe ECT-induced myalgias, headaches, or both, ketorolac 30 mg IV can also be administered before the induction of anesthesia. Finally, to minimize the pain on injection of methohexital and propofol, lidocaine 0.5–1 mL can be injected into the IV catheter immediately before administering the induction drug.

Table 4. Effect of Lidocaine on the Mean Hamilton Rating Scale for Depression (HAM-D) and the Mini-Mental State Examination (MMSE) score, as well as the Dynamic Energy, Duration of Motor and Electroencephalogram (EEG) Seizure Activity, and Times to the Peak Hemodynamic Variables After the Electrical Stimulus (9)

Variable	Saline	Lidocaine 50 mg	Lidocaine 100 mg	Lidocaine 200 mg
HAM-D score	15 ± 13	15 ± 10	13 ± 10	14 ± 9
MMSE score	28 ± 2	29 ± 3	29 ± 1	29 ± 3
Electrical stimulus delivered				
Dynamic energy (J)	37 ± 17	41 ± 15	38 ± 13	43 ± 18
Stimulus strength (V)	174 ± 36	183 ± 37	176 ± 27	170 ± 39
Motor seizure (s)	37 ± 13	25 ± 11*	17 ± 12*†	1 ± 3*†
EEG seizure (s)	64 ± 21	52 ± 43	32 ± 17*†	18 ± 10*†
Time to peak value after ECT stimulus				
Mean arterial blood pressure (min)	3.8 ± 2.2	4.5 ± 2.1	5.0 ± 2.2	3.4 ± 2.1
Heart rate (bpm)	4.8 ± 2.7	4.4 ± 1.6	5.2 ± 2.1	5.1 ± 2.8

Data are means ± SD.
* Significantly different from the Saline Control group ($P < 0.05$).
† Significantly different from the Saline and Lidocaine 50 mg groups ($P < 0.05$).

Because ECT is typically performed three times a week for 3–4 wk and each procedure lasts only a few minutes, tracheal intubation is not recommended except in very specific situations (e.g., late pregnancy or emergency treatments with full-stomach precautions). In a recent series (97) evaluating anesthesia outcome in obese patients undergoing elective ECT, there was no evidence of regurgitation or aspiration in >650 consecutive general anesthetics administered at 2 major medical centers.

Ventilation is assisted with a face mask with a standard circle or a simple bag-valve-mask system. For obese patients with sleep apnea syndrome, a Guedel oral airway can be used to facilitate assisted ventilation during the procedure. Appropriate resuscitative equipment must be available, as must a laryngoscope, tracheal tube, and laryngeal mask airway for management of an airway emergency. Noninvasive hemodynamic monitoring is recommended except in rare cases in which arterial cannulation is required to control blood pressure in patients with cerebral aneurysms. Standard EEG and electromyographic monitoring (or a tourniquet technique to isolate the circulation to an extremity before the muscle relaxant is administered) are used to quantify the durations of the motor and EEG seizure activity. A bite-block should be carefully placed before application of the electrical stimulus to protect the patient's teeth and to minimize the risk of lacerating the tongue.

During the recovery period, the most common side effects are confusion, agitation, amnesia, and headache. Because headaches occur in up to 45% of patients receiving ECT (98), intranasal administration of the 5-hydroxytryptamine-1 agonist sumatriptan may be beneficial in patients developing post-ECT headaches despite prophylaxis with ketorolac. Nausea and vomiting, as well as dizziness, are infrequent complications after ECT. Rare complications after ECT include acute cardiovascular (10,26) and neurologic (11,12) events, splenic rupture (99), and pulmonary edema (100). Standard noninvasive hemodynamic variables and oxygen saturation should be monitored for 15–30 min after ECT (101). Emergence agitation after ECT is usually treated by administering a small dose of midazolam (0.5–1 mg IV) (102). However, increasing (or decreasing) the dose of the succinylcholine and adding a small bolus of methohexital (10 mg IV) at the end of the seizure may also be helpful in reducing the incidence of post-ECT agitation.

Special Patient Populations

Patients with Cerebral Aneurysms

Because ECT provokes abrupt changes in both systemic and cerebral hemodynamics, the cerebrovascular changes increase wall stress in aneurysms, leading to enlargement or rupture (34). The increase in cerebral blood flow velocity during ECT is generally less with propofol than thiopental (40). Although nicardipine (0.02 mg/kg) failed to block the increase in cerebral blood flow velocity associated with ECT (8), both β-blockers and NTG partially inhibit the increase in cerebral blood flow velocity. In a patient with a cerebral aneurysm, administration of nitroprusside 30 μg/min IV in combination with atenolol 50 mg orally effectively controlled the acute cardiovascular changes associated with ECT (103).

Patients with Subdural Hemorrhage and Intracranial Mass Lesion

In a case report involving a patient with a subdural hemorrhage (104), ECT was not found to extend the subdural hemorrhage or intracranial complications. These authors suggested that the use of a dose-titration method of ECT with unilateral electrode placement away from the site of the lesion minimizes

the risk of adverse neurologic outcomes. The use of neuroimaging scans during and after the course of ECT was recommended. In patients with a cerebral mass lesion, special efforts should be made to reduce intracranial pressure by pretreating the patient with steroids and diuretics and by hyperventilating the patient before applying the electrical stimulus (105).

Patients with Preexisting Cardiovascular Disease

To minimize myocardial ischemia, controlling known risk factors (e.g., hypertension, angina, arrhythmias, diabetes mellitus, and congestive heart failure) are important before ECT. Although etomidate can be used for the induction of anesthesia to minimize hypotension, this anesthetic is associated with an enhanced hyperdynamic response after ECT. Pretreatment with β-blockers is strongly recommended in patients with coronary artery disease (106). In a small case series (107), ECT successfully converted atrial fibrillation (AF) to normal sinus rhythm in four of six patients. ECT was also successfully performed in a series of AF patients receiving anticoagulation therapy (107). Considering the high risk of embolization with AF, these authors recommended full anticoagulation therapy before ECT treatments in this patient population.

In patients with preexisting bradycardia (or sick sinus syndrome), pretreatment with atropine is strongly recommended, especially in patients with myasthenia gravis who are receiving pyridostigmine (59,108). In these cases, avoiding an excessively large dose of succinylcholine and threshold titration should reduce the likelihood of asystole during ECT. In patients with permanent pacemakers, a temporary conversion to fixed-rate pacing before ECT is recommended to minimize the risk of interference with pacemaker functioning as a result of inhibitory myopotentials (109). In patients with an automatic internal cardioverter-defibrillator, the device should be deactivated before the electrical current is applied and should be reactivated in the early recovery period (110).

If a depressed patient presents with severe hypertension, headaches, and episodes of flushing, the presence of a pheochromocytoma should be excluded before initiating ECT because it remains one of the few absolute contraindications to ECT (111).

Patients with NMS

NMS is a serious side effect produced by antipsychotic drugs. NMS shares some clinical similarities to MH, and well known triggering drugs (e.g., succinylcholine and sevoflurane) should be avoided (112,113). Patients with NMS will manifest increases in temperature and serum creatine kinase levels after the administration of a triggering drug (113). Nondepolarizing muscle relaxants (e.g., mivacurium) have been successfully used in place of succinylcholine in this patient population (60).

Patients with Inadequate ECT-Induced Seizure Activity

Etomidate is the induction drug of choice in patients experiencing inadequate seizure activity when a maximal electrical stimulus is applied (36). Alternatively, use of a reduced dose of methohexital in combination with alfentanil or remifentanil will prolong the duration of seizure activity (95,96). Aminophylline has also been reported to lengthen ECT-induced seizures (114). In a case report, theophylline 100–200 mg, infused approximately 30 min before the ECT treatment, prolonged the seizure duration. In 55 ECT treatment sessions, no serious cardiovascular complications were observed. Caffeine is the other drug reported to prolong seizure activity during ECT (115,116).

Pregnant Patients

Pregnancy-induced depression can be successfully treated with ECT. However, there are potential complications for both the mother (e.g., aspiration and premature labor) and the fetus (e.g., spontaneous abortion and death) (117,118). In addition to securing the patient's airway with a tracheal tube after a rapid-sequence induction with cricoid pressure, consideration should be given to the prophylactic use of tocolytic therapy in pregnant patients with a history of premature labor or uterine contractions. For parturients in the later stages of pregnancy, use of sevoflurane as an alternative to methohexital may reduce the risk of uterine contractions after ECT (56).

Patients Receiving Concurrent Psychiatric Drugs

Current practice guidelines recommend that antidepressant medications be discontinued before starting a course of ECT (3). TCAs, monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors, and lithium are all medications that are often administered to depressed patients presenting for ECT. In patients taking an MAOI, meperidine and all indirect-acting sympathomimetic drugs should be avoided. Given the intrinsic anticholinergic properties of TCA drugs, anticholinergics are unnecessary. At therapeutic doses, an MAOI can decrease MAP and increase the postural decline in MAP without affecting the HR (119). In a clinical report (120), changes in MAP and HR during ECT were not significantly different in patients receiving chronic treatment with an MAOI compared with a similar patient population not receiving these drugs.

Use of the selective serotonin reuptake inhibitor venlafaxine was compared with TCA in patients undergoing ECT (121). The seizure durations were similar in both groups, and neither drug significantly

increased the MAP or produced heart rhythm abnormalities. However, a prolonged bradycardia was observed in a patient receiving venlafaxine (122), and post-ECT hypotension and bradycardia were observed in a patient receiving fenfluramine, phentermine, and fluoxetine (123). In a study involving 13 depressed patients receiving moclobemide (300 mg/d orally), a selective and reversible MAOI, there were no clinically relevant side effects during ECT treatments (124). However, the use of lithium can delay recovery from muscle relaxants (125). Chronic administration of TCA drugs and the atypical antidepressants (e.g., mianserin, iprindole, fluoxetine, zimelidine, or viloxazine) can prolong recovery from anesthesia even 2 to 5 days after the last dose.

Summary

ECT is a simple procedure performed on a highly diverse patient population with severe, drug-resistant depression and other psychiatric disorders (Table 5). Despite its proven effectiveness, ECT remains one of the most controversial treatments in all of medicine (126). When appropriately administered, ECT is an extremely safe and effective procedure in a wide variety of high-risk patient populations (127). Unfortunately, the relapse rate during the 6- to 12-mo period after completion of an acute course of ECT exceeds 50% unless the patient receives maintenance ECT or combination pharmacotherapy (128).

The anesthetic management for ECT typically involves the use of an induction dose of an IV anesthetic (e.g., methohexital or propofol) followed by a muscle relaxant (e.g., succinylcholine or mivacurium). A wide variety of cardiovascular drugs (e.g., esmolol or labetalol) are administered to minimize the acute hemodynamic changes produced by the electrical stimulus and the resultant generalized seizure activity. Standard noninvasive monitors are used during the procedure, and the airway is typically managed with a face mask. An antisialagogue (e.g., glycopyrrolate) is used to decrease oral secretion, and a Guedel airway device may be used in patients prone to upper airway obstruction (e.g., those with sleep apnea syndrome or who are morbidly obese). The availability of new brain monitors (e.g., EEG bispectral index, patient state index, auditory evoked potential index) (129) may improve the ability of anesthesiologists to titrate anesthetic drugs to optimize the conditions for ECT.

The optimal dosages of the anesthetic, muscle relaxant, and sympatholytic drugs require careful titration to the needs of the individual patient, and further adjustments should be made during the course of a series of ECT treatments on the basis of the patient's earlier responses. In a recent editorial by Kellner (130), a simple modal approach to ECT treatment was advocated. Unfortunately, patients vary widely in their sensitivity to these drugs, depending on their age, body habitus, concurrent drug usage, and underlying medical conditions. Given the large number of elderly patients with underlying cardiovascular diseases (e.g., hypertension, coronary artery disease, and peripheral vascular disease), careful titration of the patients' sympatholytic drugs (e.g., labetalol, esmolol, nicardipine, and clonidine) is also important to obtain the best possible outcome with ECT. The "one size fits all" approach advocated by Kellner (130) is not supported by scientific data and would result in suboptimal care for many patients undergoing ECT treatments in the future.

In conclusion, practicing anesthesiologists should be aware of the anesthetic factors that influence the duration of seizure activity, because the effectiveness of ECT treatments is predicated on achieving an adequate EEG seizure (>30 s). Because these patients may be receiving a wide variety of psychotropic and cardiovascular drugs, anesthesiologists should also be aware of potential adverse drug interactions. Despite the advanced age and presence of coexisting medical diseases in many patients undergoing ECT treatments, this therapy has remained remarkably safe and effective for treating severe depression.

Table 5. Psychiatric Diagnoses for Which ECT Has Been Alleged to be Effective (1–3)

- Major depression, single or recurrent episode
- Bipolar major depression, depressed or mixed type
- Mania (bipolar disorder), mania or mixed type
- Schizophrenia
  - Catatonia
  - Schizophreniform or schizoaffective disorder
- Atypical psychosis
- Other conditions
  - Organic delusional disorder
  - Organic mood disorder
  - Acute psychotic disorder
  - Obsessive-compulsive disorder
  - Dysthymia
- Miscellaneous conditions
  - Parkinson's disease
  - Neuroleptic malignant syndrome
  - Secondary catatonia
  - Lethal catatonia

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