Succinylcholine Shortage and Electroconvulsive Therapy

To the Editor: Drug shortages have become more common in recent years, and in 2009, 46% of scarce agents were intravenous drugs (1). The preferred muscle relaxant for ECT is succinylcholine, whose fast action and short half-life make it ideal for this brief procedure (2). Although deliveries of succinylcholine continue, there is no guarantee that production can be maintained to meet current demand. Nondepolarizing muscle relaxants are an alternative to succinylcholine. However, these agents have longer half-lives and require reversal with an acetylcholinesterase inhibitor such as neostigmine and a muscarinic antagonist such as glycopyrrolate or atropine. (Sugammadex, which rapidly reverses neuromuscular blockade by rocuronium without relying on the inhibition of acetylcholinesterase, is not approved by the U.S. Food and Drug Administration [3]). Accordingly, use of nondepolarizing muscle relaxants for ECT anesthesia introduces the risk of prolonging treatment and adverse effects.

The ECT Task Group of the National Network of Depression Centers (NNDC), a network of 22 depression and bipolar disorder experts in geographically dispersed academic medical centers, has been tracking the shortage of succinylcholine and its effects across the network of sites. Half of these sites reported shortages lasting from a few weeks to 2 months; some sites needed to reactively conserve while others ran out for periods of time. Some anesthesiologists are reluctant to use alternatives because the risks of using nondepolarizing agents outweigh the risks of not administering ECT. Consequently, ECT was temporarily unavailable for new cases at some hospitals, including in some U.S. Department of Veterans Affairs facilities (T. Khazan, personal communication, June 2011). The unpredictability of the supply of succinylcholine has led the NNDC to focus on two major issues: how best to conserve supplies of succinylcholine and possible alternatives during this shortage.

Strategies to conserve supply include reserving succinylcholine for high utilizers, such as ECT programs. In addition, seldom-used supplies in emergency carts have been reduced and shunted to ECT services. Pharmacies have ordered smaller single-use doses or have split larger doses. Finally, ECT practitioners have reduced their use by attempting to stay on the lower end of the recommended dose range for ECT (0.75–1 mg/kg).

Despite succinylcholine being the preferred ECT muscle relaxant, other nondepolarizing agents such as atracuronium, cisatracuronium, pancuronium, rocuronium, and vecuronium can be used (2). Rocuronium has the fastest onset of action and a relatively brief recovery of twitch response following reversal (4). In a recent small study of thirteen patients, a rocuronium dose of 0.3 mg/kg was used in a crossover design with succinylcholine (4). Rocuronium is a nondepolarizing muscle relaxant with an action onset time of 1–2 minutes, although time to peak action tends to be longer. The dose of rocuronium in this study was lower than that typically used for rapid sequence induction (0.6 mg/kg), and it was reversed with neostigmine (20 μg/kg) and atropine (10 μg/kg). The study found that the time before the first spontaneous breath was significantly longer in the rocuronium group compared with the succinylcholine group (9.46 minutes and 8.07 minutes, respectively, p=0.02). Otherwise, rocuronium was found to be a safe alternative to succinylcholine with no significant hemodynamic differences.

Rocuronium has been used at six of 22 NNDC sites at various doses in recent months. These centers have reported that ECT recovery time is longer with rocuronium than with succinylcholine, and patients require repeat boluses of an anesthetic agent. Nonetheless, one patient recalled feeling weakness. Also, in contrast to the study by Turkkal et al. (4), NNDC sites reported several adverse effects related to the combination of neostigmine and atropine or glycopyrrolate, including urinary retention and incontinence, fecal incontinence, worse postictal delirium, and more bradycardia and hypotension. As ECT itself induces acute autonomic changes, ECT patients may be more vulnerable to adverse effects associated with posttreatment reversal agents that modulate parasympathetic tone.

A review of practices at our centers suggests that the following approach could be helpful when using rocuronium:

- Use a dose of 0.25–0.3 mg/kg.
- Administer rocuronium within 30 seconds of the anesthetic agent and wait 4 minutes for its full action, monitoring muscle twitch response to peripheral nerve stimulation.
- Reverse rocuronium with 20 μg/kg of neostigmine. If the patient has received glycopyrrolate pretreatment, then reversal may not be needed after treatment. Clinicians should nevertheless watch for bradycardia.

ECT clinicians need to be aware of current drug shortages and how they may affect ECT practice. Collaborating with local institutional pharmacies and anesthesiology colleagues is vital to staying abreast of shortages and to developing contingency plans to conserve succinylcholine. Nondepolarizing muscle relaxants like rocuronium have a slow onset of action and longer half-lives, and reversal agents introduce risks of adverse effects as well. Although there are no formal risk-benefit analyses that assess the use of these alternative agents compared with delaying ECT, we believe that ECT should not be withheld because of lack of succinylcholine, as our most severely ill patients often urgently depend on ECT. Agents like rocuronium can be used safely with a proper understanding of pharmacology to minimize the risk to patients. Therefore, ECT clinicians need to be knowledgeable about the use of alternative muscle relaxants and should discuss these alternatives with their anesthesiology team members.

References

1. Jensen V, Rappaport B: The reality of drug shortages: the case of the injectable agent propofol. N Engl J Med 2010; 363:806–807
2. American Psychiatric Association: The Practice of Electroconvulsive Therapy: Recommendations for Treatment, Training, and Privileging: A Task Force Report of the American Psychiatric Association, 2nd ed. Washington, DC, American Psychiatric Publishing, 2001
3. Hoshi J, 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: 286–290

4. Turkkal D, 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; 20:589–593

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Do All Relapses in Schizophrenia Warrant Resumption of Medication?

To the Editor: In the March 2011 issue of the *Journal*, Subotnik et al. (1) detail the high likelihood of relapse with even small degrees of medication nonadherence in first-episode schizophrenia patients. This study provides clinicians, patients, and their families with important information as they consider treatment decisions.

However, the authors also assert that nonadherence is the "greatest obstacle to *recovery* and relapse prevention" (emphasis ours). It may seem logically obvious that lack of relapse is a precondition for recovery, but this may not be so. If by recovery we mean functional recovery (e.g., the capacity to work, have meaningful relationships, and have a satisfying life), positive symptoms have less relevance than cognitive and negative symptoms. Antipsychotics do little, if anything, to help these crucial factors, but they do have serious toxicities that increase morbidity and mortality. Their overall impact is such that patients routinely discontinue them (2). One of the great drivers of nonadherence in schizophrenia may be that many patients want recovery rather than a reduction in positive symptoms; psychiatrists who view clinical outcomes primarily as positive symptom control emphasize compliance.

When psychosis worsens, it is standard practice to resume treatment with or increase the dosage of antipsychotics, despite the fact that many "relapses" are mild—either requiring no hospitalization (3) or otherwise lacking clinical significance (4). While clearly the mildness of these relapses may be attributable to the rapid resumption of medication, there may be a subgroup of patients who could weather increased positive symptoms, or perhaps even learn from them, without resuming medication, as can occur in relapses during addiction recovery. In current practice, the option of not resuming medication is rarely considered or offered, and patients can become trapped in the mental health system—both by their disease and by their treatment. Small wonder that so many try to "break away" through nonadherence.

Importantly, we believe, some succeed. Some patients achieve substantial recovery without antipsychotic medication, sometimes by finding ways to work around their positive symptoms. Empowerment, often attained through work, family, or community, is a crucial ingredient (5). However, our general failure to seriously engage in shared decision making by helping patients make informed choices impedes empowerment. We suggest accepting medication discontinuation as a reasonable path—albeit one with substantial risks—that some patients and families might want to pursue. And if they do, they should not have to give up their doctors to do so. Respecting a patient's right to consider this alternative path to recovery is a physician's role. Researching how we can promote meaningful recovery is essential.

References

1. Subotnik KL, Nuechterlein KH, Ventura J, Gitlin MJ, Marder S, Mintz J, Hellemann GS, Thornton LA, Singh IR: Risperidone nonadherence and return of positive symptoms in the early course of schizophrenia. Am J Psychiatry 2011; 168:286–292
2. Lewis S, Lieberman J: CATIE and CUtLASS: can we handle the truth? Br J Psychiatry 2008; 192:161–163
3. Gitlin M, Nuechterlein K, Subotnik KL, Ventura J, Mintz J, Fogelson DL, Bartzokis G, Aravagiri M: Clinical outcome following neuroleptic discontinuation in patients with remitted recent onset schizophrenia. Am J Psychiatry 2001; 158:1835–1842
4. Wunderink L, Nienhuis FJ, Sytema S, Slooff CJ, Knegtering R, Wiersma D: Guided discontinuation versus maintenance treatment in remitted first-episode psychosis: relapse rates and functional outcome. J Clin Psychiatry 2007; 68:654–661
5. Warner R: Recovery from schizophrenia and the recovery model. Curr Opin Psychiatry 2009; 22:374–380

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Response to Gordon and Green Letter

To the Editor: The correlational relationship between psychotic symptoms and functional outcome is weak, as Gordon