

Succinylcholine Should Be Avoided in Patients on Statin Therapy



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PARAPHRASING that an old soldier never dies, he just fades away, this author has written of succinylcholine, “A drug capable of generating so many controversies, surviving so many crises, so uniquely short acting and rapid in onset, and inexpensive, will not just die.”¹ Indeed, succinylcholine still invites attention. In this issue of ANESTHESIOLOGY, Turan *et al.* skillfully document that patients who were receiving statin medications for hypercholesterolemia had greater myoglobinemia and fasciculation after intravenous administration of 1.5 mg/kg succinylcholine than did similar patients not taking statin medications.² Because the myoglobinemia remained well below its normal renal toxicity threshold, the authors suggested that the muscular injury probably is of limited clinical consequences. Nevertheless, this new finding should provoke a timely reassessment of the role of succinylcholine.

First of all, quantification of the succinylcholine-statin interaction is timely and important, considering the widespread, ever-increasing use of statin drugs in our health-conscious aging population and considering that both succinylcholine and the statin drugs frequently cause muscle damage.²

Turan *et al.* appropriately excluded from their study patients with American Society of Anesthesiologists status greater than III and those undergoing orthopedic and spinal surgeries and surgeries involving extensive muscle manipulations. They also excluded patients with hepatic, renal, or neuromuscular pathologies and those with chronic pain and risk of malignant hyperthermia.² I have no qualms with a conclusion



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that *absent other concerns*, statin therapy *per se* may not necessarily contraindicate succinylcholine. I am, however, concerned with patients disqualified from this study, especially the vulnerable seniors with reduced functional reserves. Other unanswered questions remain because statins vary in their propensity to cause muscle damage, and patients vary in their existing muscle damage and in the succinylcholine interaction.

Indications for succinylcholine, or any drug, must be reevaluated periodically as more is learned about it. When they introduced succinylcholine to the United States 59 yr ago, Foldes *et al.* concluded in their 1952 publication that succinylcholine approximated most closely the definition of ideal relaxant.³ Upon reevaluation, however, Savarese and Kitz⁴ called for a major effort to replace succinylcholine with a “nondepolarizing succinylcholine,” and Savarese

*et al.*⁵ immediately launched that effort in 1975. Lee classified the disadvantages of succinylcholine and noted that the list kept growing, whereas the drug’s specific indications kept dwindling.⁶ Many short-acting compounds intended to replace succinylcholine, including rapacuronium and TAAC3, have proved promising. Unfortunately, none have succeeded.^{7–9} Vecuronium, rocuronium, and cisatracurium excelled on their own virtues and gained wide clinical acceptance, but they also failed to completely retire succinylcholine. Currently, the rocuronium-sugammadex combination beats succinylcholine in practically all outcome measures.⁸ Unfortunately, sugammadex is still unavailable in the United States. Another series of compounds, the CW002-related neuromuscular blocking agents, are promising but remain experimental.^{10,11} Meanwhile, the advantages and disadvantages of succinylcholine and its indications should be updated in light of the current study by Turan *et al.*

Photograph: J. P. Rathmell.

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Economic reality requires all healthcare providers to be cost-conscious, and succinylcholine is indeed inexpensive. However, the cost of a drug must be evaluated in proper context. *Mind the dollar and the penny will take care of itself.* A Duke University study showed that American patients were willing to pay \$33 out of pocket to avoid succinylcholine myalgia.¹² This finding alone should go a long way toward paying for an intubation dose of a replacement nondepolarizing relaxant at less than \$10. Besides myalgia, how much would an informed consumer pay to avoid sinus arrest, catecholamine release, the possibility of masseter spasm,¹³ chances of prolonged paralysis and malignant hyperthermia, fasciculation and increased oxygen consumption, and accelerated oxygen desaturation in the event of ventilatory failure and apnea?¹⁴ On balance, it appears penny-wise to deny patients an intubation dose of a nondepolarizing relaxant, which is also inexpensive relative to the statin drugs and other healthcare costs these patients face. After all, many inexpensive drugs have been removed from anesthesia practice; why not succinylcholine? In addition, the cost advantage of succinylcholine will be diluted if a nondepolarizing relaxant is administered soon afterward and if the cost is compared on a *per minute* basis. Admittedly, succinylcholine, at less than \$2 an intubation dose, could be the only relaxant affordable in geographic areas of extreme low cost of living.

Are there indications for which succinylcholine is irreplaceable? One is obvious. In patients with unbreakable laryngospasm but no intravenous access (mostly pediatric), succinylcholine is uniquely advantageous. Its intramuscular injection could be lifesaving. However, I cannot tell how often this situation is unpreventable and how often an intravenous line cannot be established quickly at the first sign of trouble. In addition, succinylcholine remains popular in rapid-sequence intubation. This is significant because the full-stomach precaution is being applied quite liberally to many patients nowadays. Furthermore, for procedures of short duration, succinylcholine can provide profound relaxation to the last minute while still allowing rapid spontaneous recovery to occur. Finally, in the cannot-intubate-cannot-ventilate scenario, succinylcholine allows a chance for spontaneous breathing to return before serious harms ensue. These advantages of succinylcholine based on rapid recovery will diminish when sugammadex becomes available to encapsulate rocuronium or vecuronium in a "rescue reversal,"⁷ a situation for which the high cost of sugammadex is justifiable.

Compare succinylcholine with thiopental, another drug of great historic importance. They grew popular together and for decades were routinely found together on anesthesia carts and in stock rooms in large quantities. Both have benefitted millions and millions of patients for decades. Both feature rapid onset, speedy recovery from induction dose, cumulation on further use, and low cost. However, succinylcholine has more disadvantages and more serious side effects. After all, it is structurally, conformationally, and functionally two molecules of acetylcholine joined end on end, and therefore a nicotinic compound

with predictable poor specificity as relaxant.¹ Amazingly, years after the obsolescence of thiopental, succinylcholine is still used electively in more than a few hospitals.

A Chinese proverb states, "Spare no virtue even if minor, do no harm even if trivial." We owe this duty to our patients, as soon as the risk/benefit and the cost/benefit ratios so indicate. Considering the great number of patients receiving statin therapy and the prevalence of muscle injury, no additional harm of succinylcholine is trivial to the society. In conclusion, succinylcholine still has a few indications based on specific advantages. Its ultimate fate in anesthesia will not be clear until clinicians gain experience with sugammadex. Meanwhile, it should be avoided in patients receiving statin therapy, unless specifically indicated.

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