

increased by propofol administration in our study. This immune reaction was unquestionably diminished as well but to a lesser extent.⁶

Moreover, the additives EDTA and sodium metabisulfite are biologically active and are used to retard bacterial contamination in propofol formulations. Whereas sulfite supports lipid peroxidation in propofol emulsions⁷ and increases proinflammatory interleukin-6 release in lipopolysaccharide-injured rat lungs,⁸ antiinflammatory properties of EDTA may have beneficial effects in patients with sepsis and systemic inflammatory response syndrome. Accordingly, surgical intensive care unit patients who received propofol with EDTA had significantly reduced mortality rates in comparison with those who received propofol without EDTA.⁹ In contrast, clinical variables and incidence of adverse events were not affected by propofol/EDTA in patients after cardiac surgery.¹⁰

The administration of propofol formulations with EDTA or sodium metabisulfite may thus increase the variability of the inflammatory response. For that reason, we used a single propofol formulation without EDTA or sulfite (Propofol-Lipuro 20 mg/ml, B. Braun Melsungen, Melsungen, Germany) in our study.¹ This preparation contains refined soybean oil, medium-chain triglycerides, glycerol, egg lecithin, and sodium oleate.

In conclusion, it is essential to take the immunomodulatory properties of different anesthetic drugs and their potential additives into account to avoid misinterpretation of clinical reports. However, the amount of reliable data on inflammatory effects of additive drugs is limited and often conflicting; therefore, more experimental and clinical studies are needed.

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References

- Schilling T, Kozian A, Senturk M, Huth C, Reinhold A, Hedenstierna G, Hachenberg T: Effects of volatile and intravenous anesthesia on the alveolar and systemic inflammatory response in thoracic surgical patients. *ANESTHESIOLOGY* 2011; 115:65-74
- De Conno E, Steurer MP, Wittlinger M, Zalunardo MP, Weder W, Schneider D, Schimmer RC, Klagofer R, Neff TA, Schmid ER, Spahn DR, Z'graggen BR, Urner M, Beck-Schimmer B: Anesthetic-induced improvement of the inflammatory response to one-lung ventilation. *ANESTHESIOLOGY* 2009; 110: 1316-26
- Schilling T, Kozian A, Kretzschmar M, Huth C, Welte T, Bhling F, Hedenstierna G, Hachenberg T: Effects of propofol and desflurane anaesthesia on the alveolar inflammatory response to one-lung ventilation. *Br J Anaesth* 2007; 99:368-75
- O'Donnell NG, McSharry CP, Wilkinson PC, Asbury AJ: Comparison of the inhibitory effect of propofol, thiopentone and midazolam on neutrophil polarization *in vitro* in the presence or absence of human serum albumin. *Br J Anaesth* 1992; 69:70-4
- Allaouchiche B, Debon R, Goudable J, Chassard D, Duflo F: Oxidative stress status during exposure to propofol, sevoflurane and desflurane. *Anesth Analg* 2001; 93:981-5
- Marik PE: Propofol: An immunomodulating agent. *Pharmacotherapy* 2005; 25: 28S-33S
- Baker MT, Dehring DJ, Gregerson MS: Sulfite supported lipid peroxidation in propofol emulsions. *ANESTHESIOLOGY* 2002; 97:1162-7
- Haitisma JJ, Lachmann B, Papadakos PJ: Additives in intravenous anesthesia modulate pulmonary inflammation in a model of LPS-induced respiratory distress. *Acta Anaesthesiol Scand* 2009; 53:176-82
- Herr DL, Kelly K, Hall JB, Ulatowski J, Fulda GJ, Cason B, Hickey R, Nejman AM, Zaloga GP, Teres D: Safety and efficacy of propofol with EDTA when used for sedation of surgical intensive care unit patients. *Intensive Care Med* 2000; 26 Suppl 4:S452-62
- Wahr J, Vender J, Gilbert HC, Spiess B, Horrow JC, Maddi R: Effect of propofol with and without EDTA on haemodynamics and calcium and magnesium homeostasis during and after cardiac surgery. *Intensive Care Med* 2000; 26 Suppl 4:S443-51

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There Is Lack of Evidence that Succinylcholine Should Be Avoided in Patients on Statin Therapy

To the Editor:

I read with great concern the recent editorial from Dr. Lee, the title of which provided a very strong message to the readers of *ANESTHESIOLOGY*: "Succinylcholine Should Be Avoided in Patients on Statin Therapy."¹ The editorial was in reference to the article by Turan *et al.* from the Department of Outcomes Research at the Anesthesiology Institute at Cleveland Clinic in Cleveland, Ohio.² The Cleveland Clinic authors performed a well designed study and were correct when they concluded that despite statistically significant results, the difference on plasma myoglobin concentration attributed to the use of succinylcholine in patients taking statins was likely to be small and probably of limited clinical consequences.

Lee based the strong and conclusive title of his editorial on a hypothesis that the negative finding of Turan *et al.*'s study was probably due to the fact that subjects at high risk for the development of high myoglobin plasma concentrations were excluded from the protocol, and that the inclusion of those subjects would have led to different results. He specifically mentioned the elderly population as a particularly vulnerable group because of its limited functional reserve. Although only another well designed study will be able to answer this question, I hypothesize that, if pursued, the study will find similar results as the one found by Turan *et al.* Elderly pa-

These letters were sent to the author of the above-referenced article (by Turan *et al.*), who declined to reply. Only the author of the editorial (by Lee) replied.—James C. Eisenach, M.D., Editor-in-Chief.

tients are probably less prone to a possible combined effect of statin and succinylcholine, simply because they have less muscle mass. If this clinical effect in fact existed, we would be observing a pandemic of perioperative renal failure caused by myoglobinuria during the past several years, since statins are prescribed frequently for the elderly population undergoing surgical procedures in the United States,³ and succinylcholine has not been contra-indicated in the same population. In contrast, postoperative myoglobinuria leading to kidney injury is not a common clinical entity, being only reported in few case reports that attributed inappropriate patient positioning as a possible cause.⁴

Scientific writing techniques teach us that certain parts of manuscripts are particularly powerful in conveying the manuscript's message, and the title is definitely one of them. This fact has led certain peer-reviewed journals to restrict the use of conclusive titles by authors in order to limit the influence of the author's conclusion on readers' conclusions. I personally believe that conclusive titles are important and should be allowed to point out important study results based on scientific evidence, but this was not the case in Lee's editorial.

If readers are misled by the title of Lee's editorial, it could lead to a change in practice that may increase the use of high doses of rocuronium in substitution for succinylcholine, and certainly could create a favorable clinical setting for the widespread use of sugammadex. Despite early favorable safety studies, sugammadex lacks the several decades of clinical experience of succinylcholine, which were crucial to understand the safety profile of succinylcholine. This change in practice would substantially increase the market for sugammadex because of the high prevalence of statin use among surgical patients. I understand that Lee has demonstrated in a well designed, industry-sponsored study the beneficial reversal effects of sugammadex on rocuronium-induced neuromuscular block, compared with spontaneous succinylcholine,⁵ and therefore he might have a negative personal experience with succinylcholine. This was further confirmed by Lee's suggestion that succinylcholine should be removed from the anesthesia practice: "After all, many inexpensive anesthesia drugs have been removed from anesthesia practice, why not succinylcholine?" Again, another strong statement, supported by not enough evidence. It is unknown if patients are willing to pay the cost of sugammadex in cases where high doses of rocuronium are used instead of succinylcholine. It is also unknown the effects high doses of rocuronium can have on operating room utilization costs in countries where sugammadex is still not available, such as the United States. Also important to note is that succinylcholine postoperative myalgias can be reduced by a number of low-cost interventions, such as the perioperative use of another cheap drug, lidocaine.⁶

Succinylcholine has been used for several decades by anesthesiologists. Although it has well established contraindications, such as in patients with a history of malignant hyperthermia and

spine cord injury, it is also a cheap and highly efficacious drug with clear indications for its use by anesthesiologists. Based on the current literature, there is no evidence that succinylcholine should be avoided in patients receiving statins. There is evidence after Turan *et al.*'s study that succinylcholine is likely safe for otherwise healthy patients taking statins.

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References

1. Lee C: Succinylcholine should be avoided in patients on statin therapy. *ANESTHESIOLOGY* 2011; 115:6-7
2. Turan A, Mendoza ML, Gupta S, You J, Gottlieb A, Chu W, Saager L, Sessler DI: Consequences of succinylcholine administration to patients using statins. *ANESTHESIOLOGY* 2011; 115: 28-35
3. Kalarickal PL, Fox CJ, Tsai JY, Liu H, Kaye AD: Perioperative statin use: An update. *Anesthesiol Clin* 2010; 28:739-51
4. de Menezes Ettinger JE, dos Santos Filho PV, Azaro E, Melo CA, Fahel E, Batista PB: Prevention of rhabdomyolysis in bariatric surgery. *Obes Surg* 2005; 15:874-9
5. Lee C, Jahr JS, Candiotti KA, Warriner B, Zornow MH, Naguib M: Reversal of profound neuromuscular block by sugammadex administered three minutes after rocuronium: A comparison with spontaneous recovery from succinylcholine. *ANESTHESIOLOGY* 2009; 110: 1020-5
6. Schreiber JU, Lysakowski C, Fuchs-Buder T, Tramèr MR: Prevention of succinylcholine-induced fasciculation and myalgia: A meta-analysis of randomized trials. *ANESTHESIOLOGY* 2005; 103:877-84

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We Do Not Have Evidence that Avoidance of Succinylcholine in Patients Receiving Statins Will Improve Outcomes

To the Editor:

It is always helpful when a clinical study demonstrates that a commonly used medication lacks a potentially harmful side effect. Such was the case in the recent article by Turan *et al.*, in which it was demonstrated that succinylcholine produced an inconsequentially greater release of myoglobin in patients receiving statins than in patients not receiving statins.¹ Importantly, there was no difference in plasma potassium, plasma creatine kinase, or postoperative myalgias. Equally importantly, there was no comparison group in which patients receiving statins were randomly assigned to receive either no relaxant or a relaxant other than succinylcholine.

Curiously, the editorial by Lee that discussed the study by Turan *et al.* was titled "Succinylcholine Should Be Avoided in Patients on Statin Therapy."^{1,2} Where did Lee find the evidence for this conclusion within the study by Turan *et al.*? Where is the evidence that avoiding succinylcholine and using either no relaxant or an alternative relaxant would result