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LETTERS

INTERMEDIATE ACTING NEUROMUSCULAR BLOCKING AGENTS AND POSTOPERATIVE RESPIRATORY COMPLICATIONS

Neostigmine reversal doesn't improve postoperative respiratory safety

Matthew J Meyer *research fellow*¹, Brian T Bateman *assistant professor*^{1 2}, Tobias Kurth *director of research*^{3 4 5}, Matthias Eikermann *associate professor*^{1 6}

¹Department of Anaesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA; ²Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; ³Inserm Unit 708-Neuroepidemiology, Bordeaux, France; ⁴University of Bordeaux, Bordeaux, France; ⁵Division of Preventive Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; ⁶Universitätsklinikum Essen, Klinik fuer Anaesthesie und Intensivmedizin, Essen, Germany

We recently reported an association between the intraoperative administration of intermediate acting non-depolarizing neuromuscular blocking agents and severe postoperative respiratory complications (oxygen desaturation, reintubation, and unplanned admission to intensive care).¹ In secondary analyses we examined standard techniques to abate the effects of postoperative residual neuromuscular blockade—neostigmine administration and neuromuscular transmission monitoring. We found that their use did not reduce the risk of respiratory outcomes.

In the main and secondary analyses we used propensity score matching to control for confounding factors associated with the use of neuromuscular blocking agents. However, our methods did not account for confounding factors related to the use of neostigmine.

We conducted additional analyses to evaluate whether these recommended strategies to reduce the risk of residual neuromuscular blockade help reduce the risk of respiratory complications associated with neuromuscular blocking agents. For each variable—neostigmine administration and neuromuscular transmission monitoring—we used a propensity matched cohort. For the neostigmine administration cohort, one group of patients received neostigmine and the other did not. For the neuromuscular transmission monitoring cohort, one group of patients had documented qualitative neuromuscular transmission monitoring (visual or tactile assessment of muscle response to peripheral nerve stimulation) and the other did not. The propensity score model for both variables included information on age, sex, weight, body mass index, American Society of Anesthesiologists physical status classification, surgical service, case duration, emergency status, volatile anesthesia, nitrous oxide, Charlson comorbidity index, and

administration of intermediate acting non-depolarizing neuromuscular blocking agents.

Just like the author of a rapid response to our publication,² we expected neostigmine and neuromuscular transmission monitoring to reduce respiratory events. However, analysis of 14 813 matched pairs in the neostigmine administration cohort (table 1¹) and 17 126 matched pairs in the qualitative neuromuscular transmission monitoring cohort (table 2²) showed that neither neostigmine administration nor qualitative neuromuscular transmission monitoring reduced the risk of postoperative respiratory events.

Our data show that the intraoperative use of neostigmine and neuromuscular transmission monitoring has little effect, and neostigmine administration may even increase the risk of postoperative deoxygenation. Accordingly, although neostigmine has been shown to reverse shallow levels of neuromuscular blockade,³ under the conditions studied neostigmine and qualitative neuromuscular transmission monitoring did not mitigate the increased risk of postoperative respiratory complications linked to the use of non-depolarizing neuromuscular blocking agents. Furthermore, neostigmine may affect postoperative respiratory function,⁴ and the mechanism of this effect needs to be further explored.

Competing interests: This study was funded only by academic research funds; TK has received investigator initiated research funding from the French National Research Agency, the US National Institutes of Health, the Migraine Research Foundation, and the Parkinson's Disease Foundation. He has received honorariums from Allergan, the American Academy of Neurology, and Merck for educational lectures, from the *BMJ* for editorial services, and from MAP Pharmaceutical for contributing

to a scientific advisory panel. ME has received investigator initiated research funding from Merck, Pfizer, and the ResMed Foundation, as well as the Department of Anesthesia and Critical Care and Pain Medicine of the Massachusetts General Hospital. He has received honorariums from Hill-Rom for giving advice, and from the American Thoracic Society, Brown University, University of Michigan, and Vanderbilt University for educational lectures, and from the *Journal of Anesthesiology* for editorial services; the authors have no financial relationships with any organisation or company that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

- 1 Grosse-Sundrup M, Henneman JP, Sandberg WS, Bateman BT, Uribe JV, Nguyen NT, et al. Intermediate acting non-depolarizing neuromuscular blocking agents and risk of postoperative respiratory complications: prospective propensity score matched cohort study. *BMJ* 2012;345:e6329. (16 October.)
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- 3 Bevan DR, Donati F, Kopman AF. Reversal of neuromuscular blockade. *Anesthesiology* 1992;77:785-805.
- 4 Herbstreit F, Zigrann D, Ochterbeck C, Peters J, Eikermann M. Neostigmine/glycopyrrolate administered after recovery from neuromuscular block increases upper airway collapsibility by decreasing genioglossus muscle activity in response to negative pharyngeal pressure. *Anesthesiology* 2010;113:1280-8.

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Tables

Table 1 | Associations between neostigmine administration and risk of respiratory outcome events in propensity score matched cohort (n=29 626)

Outcome	Not received	Received	Odds ratio (95% confidence interval)
Total (n)	14 813	14 813	Not applicable
Oxygen desaturation <90%	657	739	1.13 (1.02 to 1.26)
Oxygen desaturation <80%	150	164	1.09 (0.88 to 1.37)
Reintubation	116	129	1.11 (0.87 to 1.43)
In-hospital death	63	49	0.78 (0.54 to 1.13)

Table 2| Associations between qualitative neuromuscular transmission monitoring and risk of respiratory outcome events in propensity score matched cohort (n=34 252).

Outcome			
Not received	Received	Odds ratio (95% confidence interval)	
Total (n)	17 126	17 126	Not applicable
Oxygen desaturation <90%	835	814	0.97 (0.88 to 1.08)
Oxygen desaturation <80%	185	177	0.96 (0.78 to 1.18)
Reintubation	135	164	1.22 (0.97 to 1.53)
In-hospital death	75	60	0.80 (0.57 to 1.12)