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Accessibility
INTERMEDIATE ACTING NEUROMUSCULAR BLOCKING AGENTS AND POSTOPERATIVE RESPIRATORY COMPLICATIONS

Neostigmine reversal doesn’t improve postoperative respiratory safety

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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 1⇓) and 17 126 matched pairs in the qualitative neuromuscular transmission monitoring cohort (table 2⇓) 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

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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.


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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)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Not received</th>
<th>Received</th>
<th>Odds ratio (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (n)</td>
<td>14 813</td>
<td>14 813</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Oxygen desaturation &lt;90%</td>
<td>657</td>
<td>739</td>
<td>1.13 (1.02 to 1.26)</td>
</tr>
<tr>
<td>Oxygen desaturation &lt;80%</td>
<td>150</td>
<td>164</td>
<td>1.09 (0.88 to 1.37)</td>
</tr>
<tr>
<td>Reintubation</td>
<td>116</td>
<td>129</td>
<td>1.11 (0.87 to 1.43)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>63</td>
<td>49</td>
<td>0.78 (0.54 to 1.13)</td>
</tr>
</tbody>
</table>
Table 2] Associations between qualitative neuromuscular transmission monitoring and risk of respiratory outcome events in propensity score matched cohort (n=34 252).

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