

# Reply to "Is neostigmine safe and effective for neuromuscular blockade reversal in patients recovering from general anesthesia?"

## Wentao Ji, Xiaoting Zhang, Lulong Bo

Faculty of Anesthesiology, Changhai Hospital, Naval Medical University, Shanghai, China

*Correspondence to:* Lulong Bo. Faculty of Anesthesiology, Changhai Hospital, Naval Medical University, Shanghai 200433, China. Email: bartbo@smmu.edu.cn.

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We thank Wu *et al.* (1) for the interest in our study that aimed to investigate the efficacy and safety of neostigmine for neuromuscular blockade reversal in patients under general anesthesia via meta-analysis (2). They raised two valuable comments.

Firstly, we performed a sensitivity analysis by removing Xu *et al.*'s study (3) which had the most influence on the overall pooled estimates. As we noted that, the  $I^2$  statistic was decreased from 92% to 86%. We also presented the overall pooled mean difference (MD) of length of stay in the post-anesthesia care unit (PACU), which was changed from

-17.73 to -18.58, still indicating a significant difference.

Secondly, Yao *et al.*'s study (4) was mistakenly enrolled into the subgroup of dosage  $\geq$ 40 µg/kg. We have reanalyzed the data and the new pooled results were shown in *Figure 1*. Based on the dosage of neostigmine, compared to that in the control group, the length of PACU stay was significantly shortened in both the neostigmine  $\geq$ 40 µg/kg (MD =-19.91; 95% CI: -27.73 to -12.09; P<0.0001; I<sup>2</sup>=91%) and neostigmine <40 µg/kg (MD =-16.03; 95% CI: -26.51 to -5.55; P=0.003; I<sup>2</sup>=83%) groups. The results did not change the conclusion of our meta-analysis.

	Neostigmine			Control			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	IV, Random, 95% CI
1.1.1 ≥40									
Chen 2019	19.1	7.2	162	36.2	10.1	165	21.4%	-17.10 [-19.00, -15.20]	
Xu 2011	29.2	6	15	56.9	5.4	15	19.4%	-27.70 [-31.79, -23.61]	+
Zhu 2020	49.3	10.7	40	63.5	21.3	42	15.4%	-14.20 [-21.45, -6.95]	-
Subtotal (95% CI)			217			222	56.1%	-19.91 [-27.73, -12.09]	◆
Heterogeneity: Tau <sup>2</sup> = 41.97; Chi <sup>2</sup> = 22.86, df = 2 (P < 0.0001); l <sup>2</sup> = 91%									
Test for overall effect:	Z = 4.99	(P < (	.00001	)					
1.1.2 <40									
Xu 2011	32.6	5.3	15	56.9	5.4	15	19.6%	-24.30 [-28.13, -20.47]	•
Yao 2021	51.3	15.4	11	59.6	20.9	19	9.1%	-8.30 [-21.38, 4.78]	
Zhu 2020	51.3	11.5	38	63.5	21.3	42	15.1%	-12.20 [-19.61, -4.79]	-
Subtotal (95% CI)			64			76	43.9%	-16.03 [-26.51, -5.55]	•
Heterogeneity: Tau <sup>2</sup> = 67.96; Chi <sup>2</sup> = 11.89, df = 2 (P = 0.003); l <sup>2</sup> = 83%									
Test for overall effect: $Z = 3.00 (P = 0.003)$									
Total (95% CI)			281			298	100.0%	-18.58 [-23.73, -13.42]	•
Heterogeneity: Tau <sup>2</sup> = 31.46; Chi <sup>2</sup> = 36.07, df = 5 (P < 0.00001); I <sup>2</sup> = 86%									
Test for overall effect: Z = 7.06 (P < 0.00001)									
Test for subgroup differences: $Chi^2 = 0.34$ , df = 1 (P = 0.56), $l^2 = 0\%$									

Figure 1 Forest plots of the length of stay in the PACU. PACU, post-anesthesia care unit.

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