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Halothane augments the interaction between succinylcholine and pancuronium

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We previously reported that prior administration of succinylcholine prolonged the pancuronium-induced neuronmuscular block during halothane anesthesia [1]. Recent publications [2–3], however, have reported conflicting results in which the same dose of succinylcholine did not affect the duration of the pancuronium-induced neuromuscular block during neuroleptanesthesia. Therefore, it is possible that halothane may have affected our previous results. The present study was performed to investigate if halothane augments the interaction between succinylcholine and pancuronium.

The Study was approved by the local Ethics Committee. Informed consent was obtained from 30 adult patients (ASA class I; aged 18–60 years), none of whom was taking medication or suffering from an illness known to affect neuromuscular function. All patients were premedicated with a combination of pethidine 1 mg·kg^{-1} and atropine 0.01 mg·kg^{-1}, i.m. 1 h before induction of anesthesia. They were randomly divided into groups of the same size according to the anesthetic agents used. The two groups were similar in age and weight. In the neuroleptanesthesia (NLA) group (n = 15), anesthesia was induced with droperidol 0.15 mg·kg^{-1}, thiopental 2 mg·kg^{-1}, and fentanyl 4–5 μg·kg^{-1}, and the trachea was intubated with a cuffed tube facilitated by transtracheal administration of 4% lidocaine. Anesthesia was maintained with 60% nitrous oxide in oxygen with intermittent administration of thiopental and fentanyl. In the halothane group (n = 15), anesthesia was induced by inhalation of 2% inspired halothane and 50% nitrous oxide in oxygen. The tracheal intubation was facilitated with 4% lidocaine and anesthesia was maintained with 0.8%–1.0% end-tidal halothane and 60% nitrous oxide in oxygen. Ventilation was controlled to achieve normocapnia throughout the experiment. Rectal or esophageal temperature was monitored and kept between 36°C and 37°C. After tracheal intubation, ulnar nerve stimulation was started via surface electrodes at the wrist with supramaximal train-of-four (TOF) stimuli of 0.2-ms duration at 2 Hz every 10 s. The force of evoked adduction of the thumb was measured with a transducer and recorded continuously. After stable baseline contraction was obtained, patients were pre-treated with a bolus injection of 1 mg·kg^{-1} succinylcholine (n = 5), 2 mg·kg^{-1} succinylcholine (n = 5) or without succinylcholine (n = 5). After full recovery from succinylcholine-induced neuromuscular block and in a comparable amount of time in patients without succinylcholine, all patients were given pancuronium 0.02 mg·kg^{-1}, i.v. and inhibition of the first twitch of TOF (T_1) and the TOF ratio (T_4/T_1) were noted. The degrees of changes in T_1 and the TOF ratio after pancuronium were compared between patients with succinylcholine pretreatment and those without the drug using analysis of variance and Duncan's multiple range test.

After recovery from complete neuromuscular block by 1 or 2 mg·kg^{-1} of succinylcholine, T_1 significantly increased ($P < 0.01$, paired t-test) to 116.9 ± 4.1% and 137.9 ± 4.1%, respectively, in the NLA group, and to 107.9 ± 3.0% and 116.4 ± 5.1%, respectively, in the halothane group. The TOF ratio was not reduced in either group. Subsequently administered pancuronium 0.02 mg·kg^{-1} reduced T_1 and the TOF ratio significantly more in patients with succinylcholine pretreatment than in those without succinylcholine in the halothane group. In contrast, only changes in the TOF ratio were sig-

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Table 1. Maximum effect of pancuronium 0.02 mg·kg^{-1} on first twitch (T_1) of train-of-four (TOF) and TOF ratio with and without prior succinylcholine during halothane (Hal) or neuroleptanesthesia (NLA)

	Maximum effect of pancuronium 0.02 mg·kg^{-1} on T_1 (% of control)		TOF ratio	
Succinylcholine	NLA group	Hal group	NLA group	Hal group
None	66.7 ± 5.6	49.1 ± 4.3	0.49 ± 0.04	0.40 ± 0.05
1 mg·kg^{-1}	53.4 ± 12.7	25.7 ± 8.5*	0.31 ± 0.06*	0.16 ± 0.04*
2 mg·kg^{-1}	55.1 ± 5.5	14.5 ± 0.5*	0.20 ± 0.03*	0.07 ± 0.01*

Each value is mean ± SEM, $n = 5$.
* Significant difference from values without succinylcholine pretreatment in each group.

nificantly greater with succinylcholine pretreatment than without succinylcholine in the NLA group (Table 1).

Succinylcholine pretreatment augmented the pancuronium-induced reduction in T_1 and the TOF ratio in the halothane group, whereas it augmented only the TOF ratio reduction in the NLA Group. Considering that the degree of reduction in the TOF ratio is a more sensitive index than that in T_1 when assessing neuromuscular block [4], the above finding indicates that halothane augmented the interaction between succinylcholine and subsequently administered pancuronium. In addition, the finding that the degree of succinylcholine-induced augmentation was more with 2 mg·kg^{-1} of succinylcholine than with 1 mg·kg^{-1} suggests that the interaction is dose-dependent. Similarly, onset of the phase II block of succinylcholine is also dose-dependent and is accelerated by inhalation anesthetics [5]. The latter block has been attributed to a desensitization of the endplate and resulting nondepolarizing type of block. Although the TOF ratio was not found to be reduced after succinylcholine in this study, it is conceivable that the intubating dose of succinylcholine may have desensitized the endplate to such a degree that it did not induce an apparent neuromuscular block by itself. This reduction in the margin of safety of the neuromuscular transmission may have contributed to the augmentation of the subsequent pancuronium-induced nondepolarizing neuromuscular block. The above speculation is consistent with the finding that myasthenic patients, in whom the number of functional acetylcholine receptors are reduced at the neuromuscular junction, develop the phase II block immediately after the administration of an intubating dose of succinylcholine [6].

The findings of this study indicate that succinylcholine does increase the neuromuscular effects of the subsequently administered pancuronium both during neuroleptanesthesia and halothane anesthesia. The interaction between succinylcholine and subsequent pancuronium was augmented during halothane anesthesia compared with neuroleptanesthesia. Halothane has been reported not only to potentiate the neuromuscular block induced by nondepolarizing relaxants, but also to accelerate onset of the phase II block [5]. Our finding suggests that even the intubating dose of succinylcholine induces the phase II block and thereby increases the pancuronium-induced neuromuscular block during halothane anesthesia. This potentiation by halothane may explain the differences among the previous reports [1–3] on the interaction between succinylcholine and pancuronium.

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