Correspondence

Temperature, the benzoylcholine substrate, and fluoride inhibition of pseudocholinesterase

To the Editor:

The magnitude of sevoflurane's (and enflurane's) effect on fluoride inhibition of pseudocholinesterase (PCHE) deserves attention in modern anesthetic practice. Nearly all studies dealing with this topic[1–3] refer to the study of Kambam *et al.*[4] who reported an inhibition of PCHE between 16 to 73% with 10 to 100 μmol·L^{-1} fluoride, the concentrations usually obtained during sevoflurane (and enflurane) anesthesia. Since we could not confirm this inhibition with mivacurium and butyrylthiocholine as substrates and at temperatures between 28 to 37°C[3,5] we investigated fluoride inhibition of PCHE with benzoylcholine at 25°C, the substrate and temperature Kambam *et al.* used in their study, and at 37°C, the temperature currently recommended for determination of enzymatic activity.

After approval by our Local Ethics Committee and with written informed consent, serum samples of eight healthy volunteers were obtained, spiked with fluoride (0, 10, 50 and 100 μmol·L^{-1}) and adjusted to 25°C and 37°C, respectively. Thereafter, 50 μmol·L^{-1} benzoylcholine were added, and at timed interval aliquots were withdrawn to measure the concentrations of benzoylcholine by high-performance liquid chromatography. After calculating the half-lives with KINETICA 2000 (InnaPhase Corp. Philadelphia, PA, USA) a one-factor (fluoride concentration) analysis of variance with a post hoc Dunnett test was performed at each temperature, using the fluoride-free sample as the control category. The results are presented in the Figure. At 25°C there was an increase of the benzoylcholine half-time of 9.3% with 10 μmol·L^{-1} fluoride, and a 36% increase with 50 μmol·L^{-1} fluoride. The 68% increase in benzoylcholine half-time was significant ($P < 0.05$) at a concentration of 100 μmol·L^{-1}. In contrast, no change was observed over the same range of fluoride concentrations at 37°C.

We thus confirm one aspect of the study of Kambam *et al.*[4] who measured PCHE activity at 25°C with a photometric assay. In contrast, when using a high-performance liquid chromatography assay at clinically relevant body temperature (37°C) and with fluoride concentrations up to 100 μmol·L^{-1}, fluoride inhibition of PCHE is not apparent, whether using the substrates mivacurium and butyrylthiocholine[3,5] or benzoylcholine, as reported here. In conclusion, the influence of substrate and temperature on fluoride inhibition of PCHE must be taken into consideration when interpreting the results of investigations with sevoflurane and enflurane.

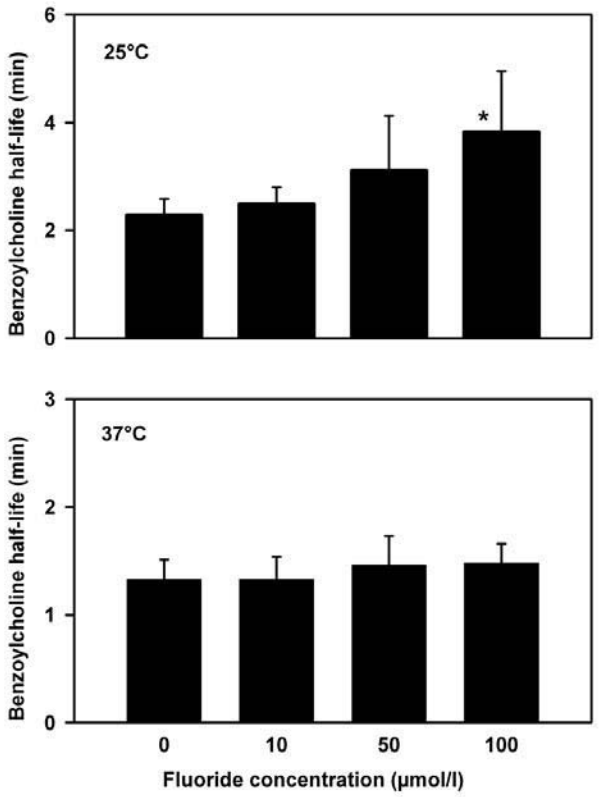

FIGURE Dependence of the benzoylcholine half-lives on the fluoride concentration (0, 10, 50, and 100 μmol·L^{-1}) at 25°C and 37°C. Data are presented as mean ± standard deviation. * $P < 0.05$ *vs* 0 μmol·L^{-1} fluoride at the corresponding temperature.

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Landiolol and peri-induction tachycardia

To the Editor:
We read with interest the recently published article by Yamazaki *et al.*[1] The authors describe the role of landiolol, a new β_1 selective antagonist in attenuating tachycardia in response to tracheal intubation. The authors conclude that landiolol [0.1 mg·kg^{-1} (L1 group) and 0.3 mg·kg^{-1} (L3 group)] prevents tachycardia without affecting blood pressure. However, the results indicate that there was no difference in heart rate (HR) values between the control group and L1 group. We believe that this may be related to the anesthetic induction technique, which comprised propofol (2 mg·kg^{-1}) and succinylcholine (1 mg·kg^{-1}). It is well known that propofol[2] as well as succinylcholine[3] are associated with a decrease in HR. Further, it is unclear as to when vecuronium was administered during the induction-intubation sequence: as this may have presented an additional confounding factor. Thus, it appears that a dose of 0.1 mg·kg^{-1} of landiolol was unable to attenuate the tachycardia in response to tracheal intubation independently from the effects of the anesthetic agents. Further, the mean HR values ranged between 70 to 90 beats·min^{-1} (SD ± 10) in all the groups at all stages. Although the increase in HR was statistically significant, the magnitude of change was clinically insignificant, barring perhaps one minute after intubation.

Therefore, it seems that the conclusions drawn by the authors should be revised. The study does not demonstrate that a dose of 0.1 mg·kg^{-1} of landiolol produced any significant change in HR as compared with the control group. Perhaps the drug should be evaluated in combination with other anesthetic techniques. Although the authors suggest that studies should be performed in patients with heart disease to demonstrate beneficial effects of landiolol, most patients with coronary artery disease are usually receiving beta blockers preoperatively. Long acting drugs such as atenolol may confer an anti-ischemic benefit during the entire perioperative period[4] (up to one week after surgery) and not just following tracheal intubation. Thus, it seems that the utility of landiolol may be limited to those patients in whom the effect is required for brief periods without causing a decrease in arterial pressure.

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