REFERENCE

1 *Naguib M, Mohamed G.* Atropine-neostigmine mixture: a dose–response study. Can J Anaesth 1989; 36: 412–7.

REPLY

We welcome the opportunity to respond to the letter from Dr. Kopman, which expressed some concerns regarding our recent study.[1] We feel that his comments were based on a misunderstanding of the intent of our work. We would like to annotate his points of dispute.

First, we did not *advocate the definition of bradycardia, as stated by Dr. Kopman in his letter but used reduction in heart rate from control value as an end-point to evaluate the effect of different doses of atropine when administered with neostigmine. This approach is not unique and has been used before by different investigators.[2,3] In addition, the administration of neostigmine is associated with more profound bradycardia when given during halothane anaesthesia than, for example, during enflurane anaesthesia.[4] Halothane was used in our study as the background anaesthetic for the first ten minutes after the administration of the atropine-neostigmine mixture. Halothane is known to have negative chronotropic effects and to prolong A-V nodal conduction.[5] The magnitude of halothane interaction in our study was not known and was beyond the scope of the experiment. Therefore, we treated our data as dicotomous variables.*

Second, we did not suggest or imply that doses of atropine 0.05 to 0.06 mg · kg^{-1} should be employed clinically.

The calculated ED_{95} doses of atropine in our study were high. One of the reasons for this was related to the concomitant administration of halothane (as discussed before). In addition, one should keep in mind that the 95 per cent response falls on an almost horizontal portion of the curve, hence the precision with which one can express the ED_{95} is considerably less than that of the ED_{50}. Nevertheless, one of the advantages of the ED_{95} over the ED_{50} is its clinical utility – even though its uncertainty range is quite large.

We agree with Dr. Kopman's sensible statement regarding the central nervous system effects of 4 mg atropine in a 70 kg adult. However, we did not advocate or imply that such high doses be employed routinely in clinical practice in our study.

In conclusion, absence of evidence is not evidence of absence. As we explained in our report,[1] bradycardia was (and still is)[6] frequently observed with the commonly used neostigmine to atropine dose ratios and we maintain that a greater dose of atropine should be used in order to prevent the late bradycardic effect of neostigmine.

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REFERENCES

1 *Naguib M, Gomma M.* Atropine-neostigmine mixture: a dose response study. Can J Anaesth 1989; 36: 412–7.
2 *Gravenstein JS, Andersen TW, De Padua CB.* Effects of atropine and scopolamine on the cardiovascular system in man. Anesthesiology 1964; 25: 123–30.
3 *Gravenstein JS, Perkins HM.* The effect of neostigmine, atropine and ephedrine on heart rate in man. Anesthesiology 1966; 27: 298–303.
4 *Samra SK, Pandit UA, Pandit SK, Kothary SP.* Modification by halogenated anaesthetics of chronotropic response during reversal of neuromuscular blockade. Can Anaesth Soc J 1983; 30: 48–52.
5 *Atlee JL, Alexander SC.* Halothane effects on conductivity of the AV node and His-Purkinje system in the dog. Anesth Analg 1977; 56: 378–86.
6 *Kongsrud F, Sponhein S.* A comparison of atropine and glycopyrrolate in anaesthetic practice. Acta Anaesthesiol Scand 1982; 26: 620–5.

Hyperbaric oxygen and CO_2 embolism

To the Editor:

I read with interest the case report by McGrath *et al.* which described the treatment of massive carbon dioxide venous embolism with hyperbaric oxygen.[1] While I must compliment the authors on their prompt diagnosis and successful treatment, I question whether hyperbaric oxygen has a role in this situation.

The authors state that hyperbaric oxygen therapy (HBO) is the treatment of choice for cerebral gas embolism. This is true when the gas involved is nitrogen and may be the preferred treatment for air embolism, another situation in which the gas is comprised primarily of nitrogen. The rationale for HBO in these situations is threefold: to decrease bubble size as a direct effect of pressure, to improve tissue oxygenation in marginally perfused tissues, and to hasten the absorption of nitrogen bubbles into the blood.[2]

Under normal physiological circumstances nitrogen bubbles are poorly absorbed from tissues or blood vessels because of nitrogen's low solubility coefficient (approximately 0.013 in blood at 37 degrees)[3] and because of the low partial pressure gradient between the bubble (maximum PN_2 = 713 mmHg) and venous blood ($P\bar{v}N_2$ = 570 mmHg).[4] With HBO at three atmospheres, dissolved nitrogen is eliminated rapidly from the blood via the lungs with a corresponding decrease in the PvN_2, and at the same time the PN_2 of any gas bubbles is tripled. This greatly increased partial pressure gradient favouring bubble absorption is responsible for the rapid disappearance of nitrogen bubbles from the circulation during HBO.

In contrast carbon dioxide is highly soluble in the blood (solubility coefficient approximately 0.49),[3] and the partial pressure gradient between the blood and any CO_2 bubble will be in the order of 660 mmHg. (The PCO_2 of the bubble is approximately 713 and the $P\bar{v}CO_2$ is 46