J Anesth (1999) 13:240

Journal of
Anesthesia

Letters to the editor

Implications of the suppression of guanylate cyclase activity by halothane

Kumi Nakamura
Department of Anesthesia, Kyoto City Hospital, 1-2 Higashi-takadacho, Mibu, Nakakyo-ku, Kyoto 604-8845, Japan

To the editor: I read with interest the paper by Masaki and Kondo [1] and the subsequent discussion with Terasako [2,3]. Masaki and Kondo demonstrated clearly that halothane and sevoflurane (at concentrations greater than 0.222 and 0.812 mM, respectively) suppress the activity of soluble guanylate cyclase (GC) isolated from rat brain. In our study using isolated rat aorta [4], these anesthetics suppressed cGMP formation induced by nitric oxide (NO) or by an NO-donor drug (sodium nitroprusside, SNP), being consistent with the findings of Jing et al. [5]. In another study of ours using rat cerebellar slices [6], halothane, at concentrations that suppressed the formation of cGMP induced by *N*-methyl D-aspartate (NMDA) and D-aspartate, did not alter the effects induced by SNP. Masaki and Kondo suspected that the concentration of SNP we used (0.3 mM) was a supramaximal one [1], but under our experimental conditions, SNP continued to increase cGMP levels in a concentration-dependent manner at least up to 10 mM [7]. Moreover, both D-aspartate (1 mM) and SNP (0.3 mM) increased cGMP to similar levels, and halothane suppressed only the increase induced by D-aspartate [6]. I do not believe, however, that the results of Masaki and Kondo [1] or Jing et al. [5] conflict with ours [4,6]. Rather, when the findings of the above four papers are considered together, it is apparent that halothane suppresses GC activity, but that some site or mechanism between the glutamate receptor and NO formation is more susceptible to halothane than GC activity itself. The locus of action is possibly one of the mechanisms coupled to the glutamate receptor.

References

1. Masaki E, Kondo I (1998) Attenuation of nitric oxide-stimulated soluble guanylate cyclase from the rat brain by halogenated volatile anesthetics. J Anesth 12:81–86
2. Terasako K (1999) Does halothane or sevoflurane inhibit NO-stimulated soluble guanylate cyclase activity under physiological conditions? J Anesth 13:61
3. Masaki E (1999) Re: Terasako. Does halothane or sevoflurane inhibit NO-stimulated soluble guanylate cyclase activity under physiological conditions? J Anesth 13:62
4. Nakamura K, Terasako K, Toda H, Miyawaki I, Kakuyama M, Nishiwada M, Hatano Y, Mori K (1994) Mechanisms of inhibition of endothelium-dependent relaxation by halothane, isoflurane, and sevoflurane. Can J Anaesth 41:340–346
5. Jing M, Hart JL, Masaki E, Van Dyke RA, Bina S, Muldoon SM (1995) Vascular effects of halothane and isoflurane: cGMP dependent and independent actions. Life Sci 56:19–29
6. Terasako K, Nakamura K, Miyawaki I, Toda H, Kakuyama M, Mori K (1994) Inhibitory effects of anesthetics on cyclic guanosine monophosphate (cGMP) accumulation in rat cerebellar slices. Anesth Analg 79:921–926
7. Miyawaki I, Nakamura K, Yokubol B, Kitamura R, Mori K (1997) Suppression of cyclic guanosine monophosphate formation in rat cerebellar slices by propofol, ketamine and midazolam. Can J Anaesth 44:1301–1307

(Received for publication on March 18, 1999; accepted on May 12, 1999)