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Editorial

Oxygen sensing in the carotid body: inhibited hypoxic respiratory drive with muscle relaxant

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Because the discovery of the comprehensive mechanism from the sensing of oxygen to its intracellular fate is one of the major challenges in the field of anesthesiology and may be worth the Nobel Prize (in the phrase of Professor Lindahl at the 49th annual meeting of the Japanese Society of Anesthesiologists held in Fukuona, Japan), I have read with great interest the review in this journal by Shirahata [1]. Focusing in particular on how anesthetic agents, nondepolarizing muscle relaxants, and drugs used in anesthesia affect carotid body excitation by hypoxia, she clearly described the complex pathway of hypoxic signal transduction in the carotid body.

Currently the type I glomus cells are believed to be chemoreceptor cells that act as oxygen sensors, although the signal transduction is still an area of active research. The primary sensory cells, the type I glomus cells, respond to hypoxia or acidosis with depolarization, which initiates electrical activity, Ca^{2+} influx, and release of Ca^{2+} from the intracellular store and stimulates secretion of neurotransmitters. This depolarization appears to be mediated largely through the inhibition of the oxygen-sensitive background K^+ channel. The molecular nature of such background currents has long been a mystery; however, a new family of K^+ channels has recently been cloned [2–4]. These channels have a unique structure and little or no conventional voltage sensitivity, making them ideal candidates for generating background K^+ currents. Halothane augments the background K^+ current and then inhibits the oxygen-sensitive K^+ current of carotid body type I cells [5]. This suggests that endogenous background K^+ channels may play role in respiratory depression by general anesthetics.

Apart from a signal sensing process, neurochemicals released by stimulation of chemoreceptors also have a role. Acetylcholine (ACh) is known as a neurotransmitter at the neuromuscular junction, at preganglionic synapses, and at all postganglionic parasympathetic fibers. The role of ACh in respiratory control has been extensively studied, and it is thought to play a role in carotid body chemotransduction. Eriksson and colleagues [6] recently observed that vecuronium-induced partial neuromuscular block [corresponding to a train of four (TOF) ratio of 0.70] inhibits the respiratory response to hypoxia but not to hypercarbia, although resting ventilation is sustained during air breathing. This inhibitory effect on the hypoxic respiratory response has also been observed with other nondepolarizing muscle relaxants, such as atracurium and pancuronium [7]. A possible pathway has been suggested by blocking the nicotinic ACh receptors on type I glomus cells in the rat [8]. In addition, Wyon and colleagues [9] demonstrated that hypoxia-induced phrenic nerve activities were partially blocked by arterial injection of vecuronium near the carotid body in the anesthetized rabbit. However, the importance of cholinergic signal transmission during hypoxia in the carotid body is still controversial. It is well known that ACh is released during moderate hypoxemia [10], but ACh is not the sole neurotransmitter in the carotid body [11]. Furthermore, hypoxic respiratory control is not known to interact with muscle relaxants, and clinical adverse effects have been never reported. These considerations have stimulated further investigations of the interaction of neuromuscular blocking and the inhibition of neurochemical sensitivity with hypoxia in the carotid body.

If this inhibitory effect is confirmed in clinical situations and reversed by anticholinesterase (anti-ChE), anesthesiologists might be recommended to administer more anti-ChE (neostigmine, physostigmine, edrophonium etc) than necessary to restore the clinical findings of reversed muscle relaxant, such as head lift and hand grip, to reverse inhibition of the hypoxic respiratory drive. Furthermore, we might add another risk

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factor of postoperative hypoxemia to our textbooks: hypoxic respiratory drive inhibited by muscle relaxant.

References

1. Shirahata M (2002) Neurotransmission in the carotid body and anesthesia. J Anesth 16:298–309
2. Lesage F, Guillemare E, Fink M, Duprat F, Lazdunski M, Romey G, Barhanin J (1996) TWIK-1, a ubiquitous human weakly inward rectifying K^+ channel with a novel structure. Embo J 15:1004–1011
3. Pountney DJ, Gulkarov I, Vega-Saenz de Miera E, Holmes D, Saganich M, Rudy B, Artman M, Coetzee WA (1999) Identification and cloning of TWIK-originated similarity sequence (TOSS): a novel human 2-pore K^+ channel principal subunit. FEBS Lett 450:191–196
4. Chavez RA, Gray AT, Zhao BB, Kindler CH, Mazurek MJ, Mehta Y, Forsayeth JR, Yost CS (1999) TWIK-2, a new weak inward rectifying member of the tandem pore domain potassium channel family. J Biol Chem 274:7887–7892
5. Buckler KJ (1997) A novel oxygen-sensitive potassium current in rat carotid body type I cells. J Physiol 498:649–662
6. Eriksson LI, Lennmarken C, Wyon N, Johnson A (1992) Attenuated ventilatory response to hypoxaemia at vecuronium-induced partial neuromuscular block. Acta Anaesthesiol Scand 36:710–715
7. Eriksson LI (1996) Reduced hypoxic chemosensitivity in partially paralysed man. A new property of muscle relaxants? Acta Anaesthesiol Scand 40:520–523
8. Shirahata M, Ishizawa Y, Rudisill M, Schofield B, Fitzgerald RS (1998) Presence of nicotinic acetylcholine receptors in cat carotid body afferent system. Brain Res 814:213–217
9. Wyon N, Eriksson LI, Yamamoto Y, Lindahl SG (1996) Vecuronium-induced depression of phrenic nerve activity during hypoxia in the rabbit. Anesth Analg 82:1252–1256
10. Metz B (1969) Release of ACh from the carotid body by hypoxia and hypoxia plus hypercapnia. Respir Physiol 6:386–394
11. Lundberg JM, Hokfelt T, Fahrenkrug J, Nilsson G, Terenius L (1979) Peptides in the cat carotid body (glomus caroticum): VIP-, enkephalin-, and substance P-like immunoreactivity. Acta Physiol Scand 107:279–281