Propofol selectively modifies the arterial chemoreflex during severe hypoxia in the rabbit

A.W. Quail,[1,2] D.B. Cottee,[1,2] R. Roach[1] and S.W. White,[1,2] [1]Disciplines of Human Physiology, and Anaesthesia and Intensive Care, Faculty of Health, University of Newcastle, NSW 2308, Australia and [2]Cardiovascular Health Programme, Hunter Medical Research Institute, John Hunter Hospital, Newcastle, NSW 2305, Australia.

Propofol is an intravenous (i.v.) anaesthetic and sedative that is extensively used in modern clinical practice. *In vitro* and *in vivo* studies have shown that propofol mitigates carotid body (CB) chemotransduction (*e.g.* Ponte & Sadler; Johnsson *et al.*, 2005). The depressant effects of propofol depend on the intensity of the hypoxic stimulus activating the CB (Ponte & Sadler, 1989). Taken together, a general postulate that propofol exerts selective effects on reflex control patterns in initially awake mammals is justified, but the respective patterns and their functional significance in the integrated system of the whole organism is unknown.

Twelve female NZ White rabbits (3.3±0.07 kg) were studied to examine the hypothesis that propofol would produce selective effects on the integrated chemoreflex responses to hypoxia. On the day of the experiment the central ear artery and marginal ear vein were cannulated percutaneously with 24G cannulae under local anaesthesia (lignocaine 2%). The ear artery was used for mean arterial pressure (MAP) and blood gas analysis. Oxygen saturation (SpO_2) was monitored with a cutaneous probe attached to the non-cannulated ear. Minute ventilation (VE), respiratory rate (RR) and tidal volume (VT) were measured with a mask-pneumotachograph system. The protocol commenced with a 10 minute collection of control data with the rabbit breathing room air. Without removing the mask, a hypoxic gas mixture (7-8% O_2) was delivered for 15 min. The gas mixture was adjusted to maintain SpO_2 at 60%. At the conclusion of hypoxia, the animal again breathed room air through the mask. The rabbits recovered for 90 minutes between studies. Control data were again collected for 10 minutes breathing room air after which an i.v. infusion of propofol (0.2 $mg \cdot kg^{-1} \cdot min^{-1}$) was commenced. After 15 minutes of propofol infusion breathing room air, a hypoxic gas mixture was simultaneously administered through the mask for another 15 minutes. The rabbit then returned to breathing room air for 15 minutes while the propofol infusion was maintained. The infusion was then stopped and rabbits were awake and moving freely within 10 minutes.

In conscious rabbits during hypoxia VE and VT increased 161% and 171% ($P<0.01$) respectively from control levels, RR fell to 83% ($P<0.01$), MAP increased to 111% ($P<0.001$) and HR fell to 79% ($P<0.01$). After 15 minutes of propofol with rabbits breathing room air, RR and VE decreased to 75% ($P<0.01$) and 82% of control ($P<0.01$) respectively, while VT, HR and MAP were unchanged. During propofol and hypoxia, VE rose to 171% ($P<0.001$) due to an elevation in VT to 158% ($P<0.01$) while the RR and HR remained unchanged from propofol air values. The increase in MAP to 109% ($P<0.01$) did not differ significantly from the response in the conscious state.

It is concluded that propofol selectively modifies arterial chemoreflex evoked respiratory responses to hypoxia by inhibiting RR control but not VT. The decrease in HR observed with hypoxia in conscious rabbits was abolished by propofol while MAP, VE and VT responses remained intact. A new hypothesis is that propofol acts at multiple sites in the chemoreflex arc to selectively alter cardiorespiratory responses to severe hypoxia.

Ponte J, Sadler CL. (1989) Effect of thiopentone, etomidate and propofol on carotid body chemoreceptor activity in the rabbit and the cat. *British Journal of Anaesthesia* **62**: 41-45.

Jonsson MM, Lindahl SG, Eriksson LI. (2005) Effect of propofol on carotid body chemosensitivity and cholinergic chemotransduction. *Anesthesiology* **102**: 110-6.