effect of anesthetic depth on complications during ophthalmic artery chemosurgery.

We agree with the theory that catheter manipulation of the ophthalmic artery may stimulate trigeminal afferents and cause a trigeminal reflex, resulting in respiratory and cardiovascular complications. However, a few questions remain. Although all intracranial arteries are innervated by trigeminal afferents, there are few reports of trigeminal reflex during endovascular procedures involving other intracranial arteries.[9] Why does the trigeminal reflex occur particularly in the internal carotid artery and ophthalmic artery? What kind of trigger (*e.g.*, pain stimulus or stretching stimulus) causes these complications and at what threshold? Research focusing on the mechanism of these specific complications could help to prevent or reduce them.

Competing Interests

The authors declare no competing interests.

Marie-Claire Nghe, M.D., Anne Godier, M.D. Fondation Adolphe de Rothschild, Paris, France (M.-C.N.). mnghe@for.paris

References

1. Scharoun JH, Han JH, Gobin YP: Anesthesia for ophthalmic artery chemosurgery. Anesthesiology 2017; 126:165–72
2. Tanaka Y, Yamashita Y, Horinouchi T, Koike K: Adrenaline produces the relaxation of guinea-pig airway smooth muscle primarily through the mediation of beta(2)-adrenoceptors. J Smooth Muscle Res 2005; 41:153–61
3. Gallos G, Gleason NR, Virag L, Zhang Y, Mizuta K, Whittington RA, Emala CW: Endogenous gamma-aminobutyric acid modulates tonic guinea pig airway tone and propofol-induced airway smooth muscle relaxation. Anesthesiology 2009; 110:748–58
4. Jin Z, Choi MJ, Park CS, Park YS, Jin YH: Propofol facilitated excitatory postsynaptic currents frequency on nucleus tractus solitarii (NTS) neurons. Brain Res 2012; 1432:1–6
5. Meuwly C, Chowdhury T, Sandu N, Reck M, Erne P, Schaller B: Anesthetic influence on occurrence and treatment of the trigemino-cardiac reflex: A systematic literature review. Medicine (Baltimore) 2015; 94:e807
6. Yi C, Jee D: Influence of the anaesthetic depth on the inhibition of the oculocardiac reflex during sevoflurane anaesthesia for paediatric strabismus surgery. Br J Anaesth 2008; 101:234–8
7. Paques M, Vallée JN, Herbreteau D, Aymart A, Santiago PY, Campinchi-Tardy F, Payen D, Merlan JJ, Gaudric A, Massin P: Superselective ophthalmic artery fibrinolytic therapy for the treatment of central retinal vein occlusion. Br J Ophthalmol 2000; 84:1387–91
8. Goto M, Nagashima M, Baba R, Nagano Y, Yokota M, Nishibata K, Tsuji A: Analysis of heart rate variability demonstrates effects of development on vagal modulation of heart rate in healthy children. J Pediatr 1997; 130:725–9
9. Meuwly C, Golanov E, Chowdhury T, Erne P, Schaller B. Trigeminal cardiac reflex: New thinking model about the definition based on a literature review. Medicine (Baltimore) 2015; 94:484.

(Accepted for publication June 1, 2017.)

In Reply:

We thank Drs. Nghe and Godier for their constructive comments on our recent article[1] as they point toward a useful alternative approach to the anesthetic problems seen during ophthalmic artery chemosurgery. However, we disagree with their conclusions.

We advocate using low-dose (0.5 to 1.0 μg/kg) intravenous epinephrine at the first sign of respiratory compromise during cannulation of the internal carotid or ophthalmic artery.[1] The anesthetic is maintained using 1.0 to 1.2 minimum alveolar concentration (MAC) of sevoflurane during the cannulation process, which probably attenuates the hemodynamic changes one would otherwise expect from epinephrine. Typically, we see a 20 to 25% increase in heart rate and blood pressure lasting approximately 2 min, along with nearly instantaneous and complete correction of respiratory parameters. Most of these cases are performed in children aged 3 months to 6 yr. In the absence of underlying cardiac disease, we expect, and have found, this brief cardiovascular effect to be well tolerated. The duration of action of the single bolus of intravenous epinephrine neatly matches the expected duration of the respiratory compliance changes; both disappear simultaneously. We have found that since introducing early low-dose epinephrine to our protocol, the hypotension and bradycardia often seen during the ophthalmic artery cannulation process are rarely seen. It is possible that the epinephrine is treating both the respiratory and hemodynamic responses.

We agree that the literature supports the view that insufficient anesthesia can increase the likelihood of a trigeminocardiac reflex (TCR) occurring.[2,3] Meuwly *et al.*[2] defined deep anesthesia as an inhaled sevoflurane concentration that corresponded to 1 MAC for their population. Yi and Jee[3] likewise defined deep anesthesia as an inhaled anesthetic mixture corresponding with 1.2 MAC. We do in fact keep our patients deeply anesthetized with sevoflurane at 1.0 to 1.2 MAC. This has the advantage of maintaining immobility without having to administer neuromuscular blockers repeatedly during the case.

Given that our patients are already deeply anesthetized with sevoflurane, a potent bronchodilator, we feel that any additional benefit from adding propofol at this point is outweighed by the harm that it may cause. Giving an effective dose of propofol while under 1.0 to 1.2 MAC of anesthesia can reliably be expected to cause significant hypotension.[4]

In vitro, trigeminal afferent nerve stimulation eventually results in firing of the cardiac vagal neurons of the nucleus ambiguous.[5] This effect is blocked by isoflurane and ketamine, unaffected by propofol, and enhanced by fentanyl.[5]

Based on these findings there is a theoretical superiority of sevoflurane over propofol in preventing the TCR, and these findings are corroborated *in vivo*. Maintenance of anesthesia

during strabismus surgery with sevoflurane is more effective at blocking the TCR than propofol.[6,7] Patients undergoing strabismus surgery with a ketamine infusion have a lower incidence of TCR compared with those maintained with propofol, sevoflurane, or halothane.[8]

Extrapolating from clinical studies on strabismus surgery to ophthalmic artery chemosurgery, one may hypothesize that a bolus of ketamine, rather than propofol, would be more effective at blocking the hypotension and bradycardia seen during ophthalmic artery manipulation. We do not know whether these findings are applicable to the lung compliance changes also seen. Despite the theoretical advantages of ketamine, the undesired psychotropic side effects may preclude its usefulness.

What is the role of propofol then? It may be helpful if the patient is anesthetized with less than 1 MAC of volatile agent. There is a case report of the TCR occurring during a meningioma resection that responded well to propofol boluses. Of note, this patient was maintained with 0.5 MAC of desflurane, propofol infusion, and remifentanil.[9] In our limited experience, giving propofol during one of the respiratory events results in only partial recovery of compliance parameters along with prolonged hypotension (more than 15 min).

We await a randomized controlled trial comparing the impact of different anesthetic regimens on the incidence and severity of cardiorespiratory changes associated with ophthalmic artery chemosurgery. In the meantime, early, low-dose epinephrine will be available to rescue the patient who experiences severe respiratory compromise during one of these procedures.

Competing Interests

The author declares no competing interests.

Jacques H. Scharoun, M.D., Weill Cornell Medicine, New York, New York. jhs2001@med.cornell.edu

References

1. Scharoun JH, Han JH, Gobin YP: Anesthesia for ophthalmic artery chemosurgery. Anesthesiology 2017; 126:165–72
2. Meuwly C, Chowdhury T, Sandu N, Reck M, Erne P, Schaller B: Anesthetic influence on occurrence and treatment of the trigemino-cardiac reflex: A systematic literature review. Medicine (Baltimore) 2015; 94:e807
3. Yi C, Jee D: Influence of the anaesthetic depth on the inhibition of the oculocardiac reflex during sevoflurane anaesthesia for paediatric strabismus surgery. Br J Anaesth 2008; 101:234–8
4. Nafiu OO, Kheterpal S, Morris M, Reynolds PI, Malviya S, Tremper KK: Incidence and risk factors for preincision hypotension in a noncardiac pediatric surgical population. Paediatr Anaesth 2009; 19:232–9
5. Wang X, Gorini C, Sharp D, Bateman R, Mendelowitz D: Anaesthetics differentially modulate the trigeminocardiac reflex excitatory synaptic pathway in the brainstem. J Physiol 2011; 589(pt 22):5431–42
6. Choi SR, Park SW, Lee JH, Lee SC, Chung CJ: Effect of different anesthetic agents on oculocardiac reflex in pediatric strabismus surgery. J Anesth 2009; 23:489–93
7. Gürkan Y, Kiliçkan L, Toker K: Propofol-nitrous oxide *versus* sevoflurane-nitrous oxide for strabismus surgery in children. Paediatr Anaesth 1999; 9:495–9
8. Hahnenkamp K, Hönemann CW, Fischer LG, Durieux ME, Muehlendyck H, Braun U: Effect of different anaesthetic regimes on the oculocardiac reflex during paediatric strabismus surgery. Paediatr Anaesth 2000; 10:601–8
9. Chowdhury T, Ahuja N, Schaller B: Severe bradycardia during neurosurgical procedure: Depth of anesthesia matters and leads to a new surrogate model of the trigeminocardiac reflex: A case report. Medicine (Baltimore) 2015; 94:e2118

(Accepted for publication June 1, 2017.)