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doi:10.1093/bja/aes369

Differential effect of phenylephrine and ephedrine on cerebral haemodynamics before carotid cross-clamping during carotid endarterectomy

Editor—Internal carotid artery stenosis is often associated with impaired cerebral autoregulation, implying that cerebral blood flow depends on arterial pressure.1–3 To preserve cerebral perfusion and to prevent ‘watershed’ stroke during carotid endarterectomy (CEA), hypotension before and during cross-clamping needs to be avoided.4 Several short-acting agents, such as phenylephrine or ephedrine, are commonly used to correct intraoperative hypotension, but have different haemodynamic effects. Phenylephrine, an
α-agonist, increases arterial pressure by arterial vasoconstriction, whereas ephedrine, an α- and β-agonist, increases arterial pressure by arterial vasoconstriction combined with an increase in heart rate and cardiac output (CO). In healthy anaesthetized subjects with intact cerebral autoregulation, frontal lobe cerebral tissue oxygenation (rSO2) declined after phenylephrine while it was preserved after ephedrine.

To evaluate the effect of both ephedrine and phenylephrine on cerebral haemodynamics during CEA under general anaesthesia, we analysed the association between the increase in mean arterial pressure (MAP) induced by either ephedrine or phenylephrine and concurrent changes in cerebral haemodynamics using transcranial Doppler-derived mean middle cerebral artery blood velocity (Vmean) and near-infrared spectroscopy-derived rSO2. All patients were anaesthetised using the same anaesthetic regimen. In 11 patients undergoing CEA between February 2009 and June 2011, who all received either ephedrine (5–10 mg; n=7) or phenylephrine (50–100 μg; n=4) to correct relative hypotension (defined as >20% decrease in MAP when compared with preoperative MAP directly before cross-clamping).

Three minutes after ephedrine or phenylephrine administration, MAP increased from [mean (SD)] 79 (12) to 89(11) mm Hg or from 84 (6) to 102 (6) mm Hg (both P=0.025), respectively (Fig. 1). Ephedrine raised heart rate from 55 (12) to 65 (17) beats min⁻¹ (P=0.017), while phenylephrine declined heart rate from 74 (6) to 65 (5) beats min⁻¹ (P=0.005). After ephedrine administration, rSO2 increased from 70 (7)% to 73 (6)% (P=0.002); however, phenylephrine decreased rSO2 from 71 (7)% to 66 (9)% (P=0.076). The Vmean remained constant after ephedrine (46 (14) cm s⁻¹), but increased from 46 (13) to 49 (12) cm s⁻¹ (P=0.035) after phenylephrine. The linear regression analysis showed that the absolute change from baseline in rSO2 was positively related to the change in MAP with ephedrine [0.108% per mm Hg increase, 95% confidence interval (CI) 0.058–0.159]. However, for a phenylephrine-induced increase in MAP, an inversely related change in rSO2 compared with MAP (−0.202% per mm Hg increase, 95% CI −0.278 to 0.126) was found.

The mechanism of the reduction in rSO2 after phenylephrine and not after ephedrine is unclear. In patients with intact cerebral autoregulation, the decrease in rSO2 after phenylephrine was associated with concordant changes in CO, whereas rSO2 remained unchanged when CO remained constant after treatment with ephedrine. This observation confirms that changes in CO, even independently from arterial pressure, affect cerebral haemodynamics. Cerebral arteries are abundantly innervated by sympathetic fibres. Therefore, the decrease in rSO2 after phenylephrine could be explained by a direct α-receptor-mediated cerebral vasoconstriction, as a decrease in middle cerebral artery diameter might result in a decreased blood flow, while Vmean remains constant or even increases.

To our knowledge, this is the first report on the differential influence of phenylephrine and ephedrine on cerebral haemodynamics in patients undergoing CEA. Although the data are very limited, the observations were consistent, since no patients treated with phenylephrine showed an increase in cerebral oxygenation, and no patient in the ephedrine group showed a decrease. Therefore, based on this small case series, we conclude that the value of phenylephrine in terms of benefit for cerebral haemodynamics could be questioned. A controlled trial is warranted to clarify the effects of different vasoactive agents on cerebral oxygenation to determine the optimal agent to increase arterial pressure during CEA.

**Declaration of interest**

None declared.
The Invos Cerebral Oximeter (Somanetics Corporation, Troy, MI, USA) was provided free for the duration of the study by Coviden Nederland B.V., Zaltbommel, The Netherlands.

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**Ventrain** for ventilation of the lungs

Editor—Ventrain (Dolphys Medical, Eindhoven, The Netherlands) has been registered as an emergency ventilation device.1 We report its use in an elective ENT patient (Fig. 1).

A 60-yr-old man with an exophytic glottic tumour and significant inspiratory stridor presented for diagnostic laryngotracheo-bronchoscopy and possibly tracheostomy. Several options were considered for management of the airway.

First, high-frequency jet ventilation (HFJV) is the routine ventilation technique in our hospital for diagnostic laryngoscopies. Usually, a small-bore jet ventilation catheter is introduced via the nose into the trachea with the help of a Magill forceps, guided by routine direct laryngoscopy. The second option was routine (flexible) laryngoscopy and (awake) tracheal intubation with a wide-bore (≥4 mm ID) tube over a flexible bronchoscope, gum elastic bougie, or Aintree intubation catheter. However, both the options carry the risks of bleeding and swelling of the tumour, making an emergency tracheostomy more likely in a situation with pre-existing serious stridor. The third option would be an elective awake wide-bore tracheostomy, having a higher success rate than an emergency procedure, but this may be unnecessary and is not preferable from the oncological point of view. Fourthly, introducing a small-bore cannula through the crico-thyroid membrane into the trachea to apply HFJV is also a common procedure in our hospital. It creates a temporary, minimally invasive access to the airway below the level of the obstruction. However, any HFJ ventilator is a unidirectional device only providing inspiration, so expiration by the natural upper airway is mandatory. A large tumour might hinder expiration, leading to air trapping, with the risks of barotrauma and the inability to ventilate efficiently. In contrast, the Ventrain is capable of controlling both inspiration and expiration through a small-bore catheter and might thus reduce the risk of air trapping. We agreed on using this last option as it is minimally invasive and safe compared with the other techniques and leaves all therapeutic options intact.

It was explained to the patient that a cannula would be introduced in the neck in order to ventilate the lungs throughout the procedure. The patient consented and was quiet and cooperative all the time.

After local infiltration and injection of 3 ml 4% lidocaine into the trachea, a 2 mm ID, 75 mm long emergency tracheal airway catheter (ETAC; Cook Medical, Bloomington, IN, USA) was introduced via the cricothyroid membrane and its intratracheal position was confirmed by aspiration of air and by capnography. The Ventrain was then connected to the ETAC and to a 2 litre oxygen cylinder with a built-in pressure compensated flow regulator set to 15 litre min−1. General anaesthesia was provided by our standard procedure: initially, propofol and remifentanil boluses and subsequently continuous pump-driven infusion combined with boluses of cisatracurium, gauged by train-of-four monitoring. Ventilation with the Ventrain (2 s each for inspiration and expiration, thus a frequency of 15 min−1) produced moderate but clearly visible thoracic excursions with the chest always returning to its original shape. Temporarily closing nose and mouth led to greater excursions, but not to air trapping. Laryngoscopy by the ENT surgeon revealed left-sided vocal paralysis besides the large glottic tumour, explaining the inspiratory stridor at least in part. Laryngoscopy and biopsies lasted 15 min. SpO2 was 100% throughout. After the surgical procedure, the syringe drivers were stopped, the neuromuscular blocking agent was reversed, and ventilation was reduced by lowering the driving oxygen flow to 5 litre min−1 to raise the Pco2. Capnography was connected to the Ventrain and spontaneous ventilation started at an end-tidal Pco2 of 6.3 kPa. The patient woke up quietly. The