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Intraoperative pulmonary oedema in a child following systemic absorption of phenylephrine eyedrops

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Ophthalmic surgeons often apply phenylephrine topically to effect pupillary dilatation. We describe a paediatric patient in whom cardiac arrhythmias, severe hypertension and pulmonary oedema occurred following intraoperative ocular phenylephrine administration. We believe that systemic absorption of the drug was responsible and discuss ways in which this might be reduced when ocular phenylephrine is used in this context.

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Topical phenylephrine solutions are widely used in ophthalmic surgery, both for capillary decongestion and for pupillary dilatation. Phenylephrine is predominately an α-adrenoreceptor agonist and significant systemic absorption can occur after topical administration. Adverse consequences in adults have included hypertensive crisis,[1 2] tachycardia, reflex bradycardia and ventricular arrhythmias, [2] and myocardial infarction and cardiac arrest.[3] However, despite theoretical concerns about neonatal subarachnoid haemorrhage,[4] serious morbidity associated

with hypertension is uncommon in paediatric patients following systemic absorption of ocular phenylephrine. We describe intraoperative complications occurring in a paediatric patient that appear to have been caused in this way. Strategies for reducing systemic phenylephrine absorption and potentially reducing the risks of similar episodes are discussed.

Case report

An 8-year-old boy weighing 37.7 kg was admitted for right retinal detachment surgery. He had undergone previous uneventful ophthalmological surgery and had no significant past medical or family history. Topical local anaesthetic cream was applied to the dorsum of both hands on the ward but he failed to receive the preoperative ocular medication he had been prescribed, namely four drops of phenylephrine 2.5% and cyclopentolate 1% to each eye.

In the anaesthetic room, anaesthesia was induced with sevoflurane in oxygen. Following insertion of a 22-gauge cannula, the patient received propofol 40 mg, vecuronium 4 mg, alfentanil 250 μg and morphine 1.5 mg i.v. He was also given ondansetron 3.5 mg i.v., and diclofenac and paracetamol suppositories (37.5 mg and 500 mg, respectively). A size-3 laryngeal mask was inserted and manual ventilation commenced with 60% nitrous oxide and 1% isoflurane in oxygen. He was then transferred to the operating theatre and routine monitoring was applied. Mechanical ventilation was commenced via a circle circuit with carbon dioxide absorption and adjusted to maintain peak airway pressure below 20 cm H_2O. At all times intraoperatively, end-tidal carbon dioxide concentration was 5.3 kPa or less.

On the operating table, before incision, the operating surgeon noticed that the pupil was not dilated and between two and five drops of 10% aqueous phenylephrine (40–50 μl per drop) were administered topically to the right eye by the assistant surgeon, without the anaesthetist's knowledge. Five minutes into surgery, traction on the extra-ocular muscles precipitated a sinus bradycardia of 40 beats min^{-1}. Glycopyrrolate 0.2 mg was administered intravenously and the heart rate increased to 80 beats min^{-1}.

Several minutes later, non-invasive systolic arterial pressure rose from 95 to 211 mm Hg and the heart rate from 80 to 160 beats min^{-1}. The electrocardiogram showed frequent multifocal atrial and ventricular ectopic beats. The inspired isoflurane concentration was increased and the earlier administration of ocular phenylephrine was confirmed by the assistant surgeon on questioning. A diagnosis of hypertension and arrhythmias secondary to systemic absorption of ocular phenylephrine was made. Intravenous labetalol was given in 5 mg increments to a total of 25 mg over the next 10 min until the heart rate and blood pressure returned to normal.

A few minutes later, the monitors displayed a reduced tidal volume with unchanged airway pressures. With an inspired oxygen concentration ($F_{I_{O_2}}$) of 30%, oxygen saturation decreased to 88%. Auscultation of the chest revealed scant basal crepitations. Oxygen saturation returned to normal after a few minutes on increasing $F_{I_{O_2}}$ to 60% and ventilating manually. Mechanical ventilation was recommenced and $F_{I_{O_2}}$ gradually reduced back to 30% over 30 min with no further desaturation.

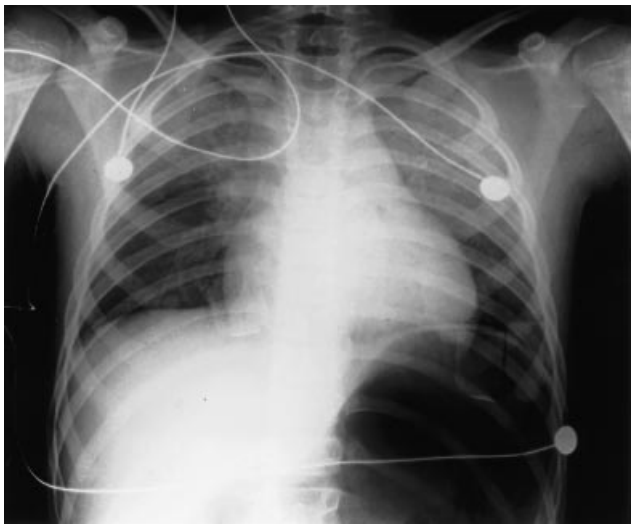

Fig 1 Anteroposterior chest radiograph revealing pulmonary oedema and a large gastric air bubble.

Auscultation was repeated after surgical closure. Crepitations were heard throughout the chest and 100 ml bloodstained fluid was aspirated from the trachea using a suction catheter passed via the laryngeal mask. Neuromuscular blockade was reversed and, on resuming spontaneous ventilation, the patient maintained satisfactory tidal volumes, respiratory rate and oxygen saturation. When the patient regained consciousness, the laryngeal mask was removed and he was transferred to the recovery room. Postoperative chest radiography revealed pulmonary oedema (Fig. 1). A postoperative 12-lead electrocardiogram was normal and cardiac enzymes were not raised. Oxygen 4 litre min^{-1} was administered through a face mask for 8 h postoperatively. The patient was discharged the next day with almost complete resolution of radiographic signs.

Discussion

The case described appears to be one of pulmonary oedema in a paediatric patient following an iatrogenic hypertensive crisis with cardiac arrhythmias. The drug most likely to have been responsible was ocular phenylephrine.

Other factors may have had a causative or contributory role in these complications, which have not been described before in similar circumstances. Although the intraoperative end-tidal carbon dioxide concentration was 5.3 kPa or less, it is possible that arterial carbon dioxide concentration was

supranormal. This may have predisposed the patient to cardiac arrythmias in the presence of a sympathomimetic agent.

An alternative explanation for the acute pulmonary oedema we observed might have been regurgitation and aspiration of stomach contents. The large gastric air bubble evident in Figure 1 suggests gastric insufflation as a result of ventilation via the laryngeal mask. If this occurred in the initial stages of anaesthesia, despite low airway pressures, it might have predisposed to later regurgitation. The laryngeal mask would not have protected the patient from subsequent pulmonary aspiration. However, this hypothesis disregards the haemodynamic events and the temporal relationship between them and the development of respiratory signs. We believe that gastric insufflation occurred after the development of pulmonary oedema, as a result of high airway pressures attained during manual ventilation of poorly compliant lungs via the laryngeal mask.

Although some regard the technique as controversial, intermittent positive-pressure ventilation via the laryngeal mask in children is widely practised.[5] The risk of clinically significant gastric insufflation is said to be small provided cautious ventilation, with modest tidal volumes and low airway pressures, is employed. Airway integrity, gas leak and abdominal distension should be closely monitored.[6] In our case, gastric insufflation would probably not have arisen had a tracheal tube been used. A tracheal tube would also have allowed us to ventilate at higher airway pressures during resuscitation, thereby potentially reducing the degree of pulmonary oedema (albeit at the risk of barotrauma).

It might be argued that a pure α-adrenergic antagonist should have been used to treat the hypertensive effect of absorbed phenylephrine. Labetalol's β-antagonist activity is between five and ten times greater than its α activity[7] and may have contributed to failure of the left ventricle. However, phenylephrine is known to have β-agonist actions at high doses.[7] The tachycardia and multifocal ventricular ectopics seen in our patient were suggestive of such an effect and represented the most immediate threat to life. In these particular circumstances, with no other indication of the relative predominance of phenylephrine's α and β effects, and in the knowledge that intravenous α-adrenergic antagonists like phentolamine may cause tachycardia,[7] labetolol's predominant β antagonism seemed to be therapeutically appropriate.

Phenylephrine solutions for ocular administration are available in 2.5% and 10% solutions. The 1% solution available for intravenous administration is usually diluted even further by anaesthetists, so doses used in the eye are high by systemic standards. Several techniques have been advocated for achieving effective mydriasis with ocular phenylephrine while reducing systemic absorption and associated haemodynamic effects. These include the use of 2.5% rather than 10% solutions,[8] 8–10 μl rather than 30–32 μl drops,[9–11] eyelid closure,[11] punctuate occlusion and blotting away excess drops after administration of the drug.[4]

From the case described above, we would also recommend that intraoperative administration of ocular drugs by the surgeon should be conducted only after consulting the anaesthetist. The risk of substantial systemic absorption may be increased if ocular incision is performed very soon after administration of such drugs, as in this case.

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