Severe hypertension and pulmonary edema associated with systemic absorption of topical phenylephrine in a child during retinal surgery

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ABSTRACT

Topical phenylephrine solutions are widely used in eye procedures to promote pupil dilation without cycloplegia. We report a case of intraoperative severe hypertension and acute pulmonary edema occurring in a child during retinal surgery after possible systemic absorption of topical phenylephrine eyedrops. Our objective is to discuss the proper treatment and preventive strategies for such a complication. A 4-year-old, male patient, 18.4 kg in weight, physical status ASA I was admitted for right retinal detachment surgery. Anesthesia was induced with sevoflurane in oxygen, followed by glycopyrrolate (5.0 μg/kg), propofol 25 mg, fentanyl 50 μg and cisatracurium 0.15 mg/kg given intravenously. Anesthesia was maintained with sevoflurane 2-2.5% in a mixture of nitrous oxide and oxygen (60%:40%). After incision, two drops of 10% aqueous phenylephrine were administered topically by the surgeon to the right eye for further pupil dilation. Few minutes later, the noninvasive blood pressure rose to 220/120 mmHg and the heart rate increased to 140 beats/min. Oxygen saturation (SpO_2) dropped from 99% (with an inspired oxygen concentration (FiO_2) of 0.4) to 82%. Auscultation revealed crepitations throughout the chest and a blood-stained frothy fluid was aspirated from the trachea with possible development of acute pulmonary edema. Hydralazine (5 mg) and furosemide (10 mg) were administered intravenously. Seven minutes later, the blood pressure returned to normal and the SpO_2 increased to 92% on FiO_2 of 1.0, with decreased intratracheal secretions. After approximately 20 minutes, the SpO_2 had improved to 99%, with a FiO_2 of 1.0 and the blood pressure was 109/63 mmHg and heart rate was 121 beats/min. The FiO_2 gradually reduced back to 0.4 over 30 min with no further desaturation. The patient was discharged from the post anesthesia care unit 5 h after surgery with adequate spontaneous breathing, SpO_2 99% on room air, normal blood pressure and pulmonary auscultation. Anesthesiologists and ophthalmologists should be aware of the possible cardiovascular side-effects of topical phenylephrine, and it should be used cautiously with appropriate intraoperative monitoring of hemodynamic variables. Moreover, preventive strategies to minimize systemic absorption of the drug should be taken.

Key words: *Acute pulmonary edema, child, hypertension, phenylephrine, retinal, surgery*

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INTRODUCTION

Phenylephrine is predominantly a direct selective α-1-adrenergic receptor agonist; at very high doses, β-activation does occur.[1] Topical phenylephrine is widely used as an eye drop to dilate the pupil in eye procedures to facilitate fundus examination. Reports have suggested that significant systemic absorption can occur after topical administration of ocular phenylephrine in the adult population, and it may cause side-effects such as hypertensive crisis,[2] tachycardia, reflex bradycardia, ventricular arrhythmias,[3] myocardial ischemia[4] and some evolving to death.[5,6] However, serious complications associated with hypertension were reported in pediatric patients following systemic absorption of topical phenylephrine.[7-9] We report a case of intraoperative severe hypertension and acute pulmonary edema occurring in a

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child submitted for retinal surgery after possible systemic absorption of topical phenylephrine eye drops.

CASE REPORT

A 4-year-old, male patient, 18.4 kg in weight, physical status I according to the classification system of the American Society of Anesthesiologists (ASA) was admitted to our institution for right retinal detachment surgery. On admission, there was no significant past or family history of medical diseases and no evidence of pulmonary or cardiac disease on physical examination. Preoperative vital signs were as such blood pressure of 100/65 mmHg, heart rate 92 and O_2 saturation (SpO_2) 100% on room air. The patient was premedicated with oral midazolam 0.5 mg/kg. In the operating room, standard intraoperative monitoring three-lead electrocardiogram (ECG), noninvasive blood pressure, end-tidal carbon dioxide ($EtCO_2$), peripheral nerve stimulator, temperature probe and pulse oximetry were applied. Anesthesia was induced with sevoflurane in oxygen. Following insertion of a 22-gauge cannula, he received glycopyrrolate (5.0 μg/kg), propofol 25 mg, fentanyl 50 mg and cis-atracurium 0.15 mg/kg intravenously. After induction of anesthesia, paracetamol suppositories 500 mg were given. Anesthesia was maintained with sevoflurane 2-2.5% in a mixture of nitrous oxide and oxygen (60%:40%). Intermittent doses of cis-atracurium (0.03 mg/kg) every 20-40 min were injected as needed to keep muscle relaxation based on neuromuscular stimulation. The patient was mechanically ventilated, and it was adjusted to provide an end tidal CO_2 concentration of 30–35 mmHg, maintain peak airway pressure below 15 cm H_2O and an oxygen saturation of ≥98% with 40% oxygen. Ringer's lactate solution was administered according to the standard fluid administration guidelines during anesthesia. Normothermia was maintained during the whole procedure by the use of a forced air warming device. Few minutes later, after start of surgery, the noninvasive blood pressure, which was around 90/55 mmHg, suddenly rose to 220/120 mmHg and the heart rate, previously around 75 beats/min, increased to 140 beats/min (sinus rhythm). Initially, the inspired sevoflurane concentration was increased to increase the depth of anesthesia. On questioning the surgeon, the earlier administration of two drops of 10% ocular phenylephrine to the right eye was confirmed for further dilation of inadequate dilated pupil. A diagnosis of severe hypertension secondary to systemic absorption of ocular phenylephrine was suspected. Subsequently, while preparing the antihypertensive medication, the monitors displayed increased airway pressure and oxygen saturation drop from 99% (with an inspired oxygen concentration (FiO_2) of 0.4) to 82%. Auscultation revealed crepitations throughout the chest and a blood-stained frothy fluid was aspirated from the trachea. There was neither clinical evidence of airway obstruction nor aspiration on examination and a diagnosis of pulmonary edema was justified at that time. Therefore, fluid administration was stopped, hydralazine (5 mg) and furosemide (10 mg) were administered intravenously, manual ventilation with 100% oxygen was commenced and suctioning via the tracheal tube was performed several times. Seven minutes later, the blood pressure returned to normal and SpO_2 increased to 92%, with decreased intratracheal secretions. After approximately 20 min, the SpO_2 had improved to 99% (with a FiO_2 of 1.0), the blood pressure was 109/63 mmHg and the heart rate was 121 beats/min. A Foley catheter was inserted and the urine output was 280 mL. Surgery was completed, mechanical ventilation was regained with a positive end expiratory pressure (PEEP) of 5 cm H_2O and FiO_2 gradually reduced back to 0.4 over 30 min with no further desaturation. After surgical closure, auscultation of the chest revealed no crepitations. Then, inhalational anesthetic was discontinued, the fresh gas rate was changed to 6 L/min of oxygen and neuromuscular block was reversed with neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg). Tracheal extubation was done when the train-of-four response was 90% and the patient demonstrated facial grimace and spontaneous opening of his eyes with adequate tidal volume and respiratory rate. The patient was transferred to the post anesthesia care unit (PACU) with oxygen via a face mask. A postoperative 12-lead ECG showed sinus rhythm and chest radiography revealed no evidence of pulmonary edema. Oxygen 3 L/min was administered through a face mask for 5 h postoperatively and then the patient was discharged from the PACU to the ward conscious and oriented, with a blood pressure of approximately 100/55 mmHg and O_2 saturation of 98% on room air and normal chest auscultation.

DISCUSSION

The present case report describe a pediatric patient who experienced acute pulmonary edema associated with severe hypertension and tachycardia, mostly related to a systemic effect, after the topical application of phenylephrine 10%. Although serious morbidity associated with hypertension may be uncommon in children following systemic absorption of ocular phenylephrine, the incidence of an iatrogenic hypertensive crisis, acute left ventricular failure and pulmonary edema following topical phenylephrine given intraoperatively in children has been reported.[7-9] Phenylephrine is a sympathomimetic direct α-agonist and it has a powerful arterial and

venous vasoconstrictor effect.[1] Induced hypertension by α-adrenergic stimulation can increase peripheral vascular resistance (increased afterload) and thus increase the left ventricular filling pressure. The increased systemic vascular resistance increases left ventricular ejection impedance and end-diastolic volumes and pressures. Alternatively, cardiac output may be further diminished, leading to left-sided heart failure and pulmonary edema.[1,6,10] Management of such complications is crucial. The key point is that the ability to increase heart rate and contractility are important compensatory mechanisms to preserve the cardiac output. A previous report recommended that if the increased pressure is severe, persistent or associated with complications like pulmonary edema or ECG changes, this should be treated immediately without reducing the ability of a stressed myocardium to increase contractility and heart rate. Thus, direct vasodilators and α-adrenergic antagonists are recommended to treat hypertension induced by systemic absorption of topical phenylephrine.[6] Therefore, we gave hydalazine as antihypertensive medication to reduce the peripheral vascular resistance in this case. We avoided beta-adrenergic antagonists as this may disturb the hemodynamic compensatory mechanisms.[1,6] Previous reports demonstrated that cardiac arrest occurs more frequently in patients who develop acute pulmonary edema and have received labetalol, rather than esmolol.[6,11] Our patient demonstrated tachycardia in response to severe hypertension, suggesting that the use of glycopyrrolate may further prevent a baroreceptor-mediated bradycardia. Furosemide was used in our study to control pulmonary edema by decreasing ventricular diastolic pressure. The common practice in response to intraoperative hypertension is deepening of anesthesia by increasing the inspired concentration of inhalational anesthetic to reduce the peripheral vascular resistance, but, unlikely, it may also impair cardiac performance that may already be compromised by a high after load.[6] Most systemic effects of topical ocular medications are dose related.[12,13] Phenylephrine solutions for ocular administration are available in 2.5% and 10% solutions. Even with the use of a lower concentration of ocular phenylephrine eye drops, caution is required during its application as it is still dangerous with unpredictable hypertensive response.[14] It may be preferable to assess adequacy of mydriasis before induction of general anesthesia to avoid administration of topical phenylephrine shortly after induction.[15] Several strategies have been suggested for decreasing the systemic absorption and associated hemodynamic effects of ophthalmic phenylephrine. These include digital pressure on the naso–lacrimal passage immediately for 60 s following topical administration of eye drops,[12,16] the use of 2.5% concentration of the topical phenylephrine rather than 10% solutions as both strengths of phenylephrine are equipotent mydriatrics in most patients,[14] avoiding of unnecessary repetition of doses and allowing adequate time for the pharmacologic effect to occur,[17] quick blotting away of excess drops after drug administration[12] and the use of micro drops in infants if possible.[18]

CONCLUSION

Anesthesiologists and ophthalmologists should be aware of the possible cardiovascular side-effects of topical phenylephrine, and it should be used cautiously with appropriate intraoperative monitoring of hemodynamic variables. Moreover, preventive strategies to minimize systemic absorption of the drug should be taken.

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