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Hypertension and Pulmonary Edema Associated with Subconjunctival Phenylephrine in a 2-month-old Child during Cataract Extraction

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OPHTHALMOLOGISTS commonly use locally applied mydriatic drugs preoperatively. Parasympatholytic substances, like cyclopentolate, or sympathomimetics, like phenylephrine, effectively cause the pupillary dilation necessary for many surgical procedures. Potential systemic side effects after absorption of these mydriatics,¹ especially in low-weight infants,^{2,3} have been known for a long time. Phenylephrine can provoke fatal hemodynamic changes.^{4,5} Nevertheless, there have been no reports of pulmonary edema so far, other than two cases wherein cocaine abuse⁶ or additional topically administered cocaine⁷ played a crucial role in pathogenesis. We report a case of acute pulmonary edema after ocular phenylephrine in a child undergoing congenital cataract extraction.

Case Report

A 2-month-old, 5-kg healthy female infant was scheduled for elective congenital cataract extraction of the right eye. Her medical history was unremarkable, with no allergies or genetic defects. Results

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of preoperative electrocardiograph (ECG) and blood analysis were normal apart from mild anemia (hemoglobin was 9.8 g/dl).

After premedication (midazolam, 1 mg/kg, rectally), anesthesia was induced with halothane (up to 2 vol%) by mask in a mixture of oxygen and nitrous oxide (FiO₂, 0.5). Routine monitoring included ECG (three-lead), blood pressure cuff, pulse oximetry, and rectal temperature probe. Initial heart rate was 140 beats/min, with a blood pressure of 60/30 mmHg. The child was normothermic. After cannulation of a peripheral vein, intubation with a 3.5-mm ID RAE-tube (Mallinckrodt Anaesthesiology Products, Inc., St. Louis, MO) was facilitated with propofol (3 mg/kg) and vecuronium bolus (0.1 mg/kg). Auscultation revealed regular bilateral breath sounds. Respirator-controlled ventilation was performed (N₂O:O₂, 2:1; I:E, 1:1.7; PEEP, 3 cm H₂O; CiceroD Dräger, Lübeck, Germany), which resulted in a SpO₂ of more than 94%, an end-tidal carbon dioxide of 32 mmHg, and a peak airway pressure of 18 cm H₂O. Halothane was discontinued, and anesthesia was maintained with propofol boluses. Within the first 20 min, the infant received 50 ml of lactated Ringer's solution. Thereafter, a continuous infusion of lactated Ringer's solution and 5% glucose (3:2, 5 ml·kg⁻¹·h⁻¹) was started.

Because early preoperative mydriatic instillation on the ward had been impossible because of the infant's agitation, the ophthalmologist now instilled four drops of cyclopentolate, 1%, (total, ≈1.3 mg) in the right eye of the anesthetized child. Ten minutes later, he additionally injected 0.2 ml of phenylephrine, 2.5%, (total, ≈5 mg) in the same eye *via* the subconjunctival route because of insufficient mydriasis.

The phenylephrine injection was followed almost immediately by incision. Fifteen minutes later, ventricular couplets occurred, the heart rate decreased to 95 beats/min, the blood pressure reading went off-scale after increasing, and SpO₂ decreased to 80% with FiO₂ of 0.33. The infant showed signs of intense peripheral vasoconstriction, with pale white skin and a strong pulse. Correct tube placement and patency were again confirmed; lung auscultation showed no abnormal findings. Manual hyperventilation with 100% oxygen improved peripheral O₂ saturation temporarily.

Epistaxis occurred 10 min later, and as foamy fluid appeared in the tube, the ophthalmologists were urged to bring the operation to an expeditious close. Intratracheal suctioning was performed several times until the end of surgery (overall surgical time, 30 min). The immediate postoperative chest radiograph showed bilateral pulmonary opacities in alveolar pattern particularly in the perihilar region (fig. 1).

Management of the pulmonary edema consisted of buccal application of nitroglycerin, 0.4 mg repeatedly; intravenous theophylline, 24 mg; mannitol 20%, 5 ml; and controlled fractionated infusion of

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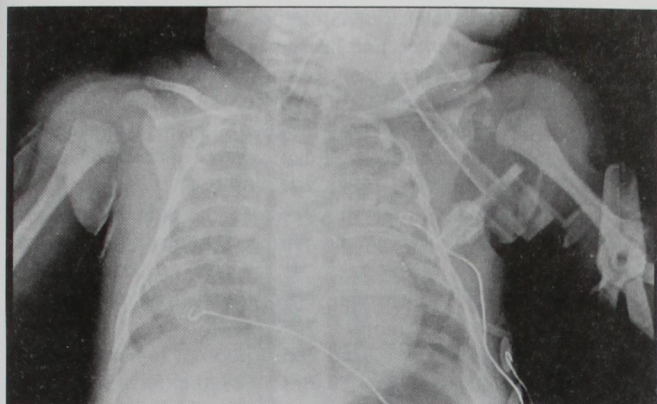


Fig. 1. Immediate postoperative chest radiograph with bilateral pulmonary opacities in alveolar pattern (acute cardiogenic pulmonary edema).

human albumin, 20% and sodium chloride under diuresis control (buccal nitroglycerin as a venous dilator immediately at hand in the OR; mannitol as a moderate diuretic).

Hemodynamics and saturation were consequently stabilized, and blood pressure gradually returned to normal. The infant was transferred to our intensive care unit, after which a chest radiograph confirmed the improved condition of the infant, showing opacities only of interstitial pattern with no more alveolar component. Extubation was possible within 3 h, and the further course was uneventful with complete restitution.

Discussion

Our case depicts a deleterious side effect of subconjunctival phenylephrine in combination with topical ocular cyclopentolate in an anesthetized infant.

Cyclopentolate, a muscarinic antagonist, is routinely used as a short-acting mydriatic and cycloplegic substance. Reported side effects in children include cardiorespiratory changes, disorientation, ataxia, and convulsions.²

Phenylephrine is a selective α_1 -agonist with β -activation only in very high dosage. The duration of action is relatively short (about 20 min, when administered intravenously), and it is metabolized in the liver by the monoamine oxidase. The maximum serum concentration occurs after 10 min, whereas a sufficient topical effect can be observed at the earliest in 30 min, as with all other mydriatics.

The systemic effects of ocular phenylephrine administration and resorption are blood pressure increase, cardiac arrhythmias, myocardial infarction, cyanosis, left ventricular failure, cardiac arrest, and subarachnoid hemorrhage.^{1,5} One study reports that, besides increas-

ing blood pressure, phenylephrine plays an additional role in the induction of pulmonary edema: Ferrari *et al.*⁸ found selective α_1 -adrenoceptor involvement causing pulmonary edema in rats. α_2 -Adrenoceptor agonists were unable to produce pulmonary edema, although they increased systemic arterial blood pressure to the same extent. Protection from pulmonary edema was only achieved with α_1 - and not with α_2 -adrenoceptor antagonists. Further, there are some reports of acute left ventricular failure associated with sympathomimetic substances in children that underline the potential risk under certain circumstances.^{9,10}

Ophthalmologists consider phenylephrine especially useful in infants, in whom pupillary diameters are tiny and the retinal periphery has to be accessed for diagnosis. Nevertheless, Rosales *et al.*³ could not find a statistically significant difference in mydriatic effect between tropicamide + phenylephrine *versus* tropicamide + cyclopentolate, but in the phenylephrine group there was significant blood pressure increase.

The systemic uptake of locally applied ocular drugs depends on a number of factors^{11,12}: Dosage, application route, aqueous or viscous characteristics, dilution by lacrimation, increased permeability of hyperemic conjunctival epithelium, and uptake through the lacrimal duct by the nasal mucosa, which is a major absorption site.

In this case, hypertension, left ventricular failure, and pulmonary edema seem to be primarily associated with the phenylephrine, but a cumulative effect related to the combination with cyclopentolate might also be possible. Phenylephrine, 2.5%, was instilled in a high dose without waiting long enough for the mydriatic effect of the previously administered cyclopentolate. Further, cyclopentolate drops, 0.5%, are recommended for infants rather than 1%. Additionally, manual occlusion of the lacrimal point after the application of eye drops could have helped to minimize systemic absorption.¹¹ The rapid recovery and *restitutio ad integrum* can be explained first by the pharmacokinetics of phenylephrine and second by the pharmacologic treatment.

In conclusion, great care needs to be taken in the local application of ocular drugs, which can produce such serious systemic side effects. The exact dosage of eye drops is hard to control in an agitated infant. Under these circumstances, it appears to be wiser to instill drops in sedation shortly before induction of anesthesia, even if this means slightly postponing the start of surgery while waiting for the local effect. In our opinion, the crucial step with regard to mydriatics is to wait 30-

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45 min for the pupillary dilation to take place. Microdrops could be used in infants to provide a lower risk of systemic action with comparable local effectiveness.^{13,14} All this would help to avoid an absolute overdosage of a substance whose systemic absorption is often underestimated and can never be predicted exactly.

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Endovascular Aortic Balloon Clamp Malposition during Minimally Invasive Cardiac Surgery: Detection by Transcranial Doppler Monitoring

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MINIMALLY invasive cardiac surgery for coronary artery bypass grafting (CABG) and cardiac valve repair or replacement is a rapidly expanding field in cardiothoracic surgery.¹⁻³ Although it offers potential advantages to the patient and the health-care system, including improved

cosmetic results, reduced pain, shorter hospital stays, and an earlier return to normal activity,⁴ it is not without its own risks.

We report a case of a temporary reduction in cerebral perfusion, detected by transcranial Doppler (TCD), resulting from endovascular aortic balloon clamp malposition during minimally invasive mitral valve surgery. Monitoring strategies to detect endoaortic clamp malposition are discussed.

Case Report

A 51-yr-old man, with preserved left ventricular function and severe mitral regurgitation resulting from myxomatous degeneration, was scheduled to undergo mitral valve repair using a minimally invasive port-access system.

The use of a catheter-based endovascular cardiopulmonary bypass (CPB) system (EndoCPB system; Heartport Inc., Redwood City, CA)

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