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CASE REPORT

Cyclomydril® eye drops: An unusual contributing factor to postoperative apnoea in a neonate – A case report

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Premature neonates presenting for surgery are at risk for postoperative apnoeas for various reasons, including their immature physiology, general anaesthesia, opiates and other drugs administered during a procedure.
An ex-premature baby presented for a laparotomy following a complication of necrotising enterocolitis (NEC) at 39 weeks postconceptual age. An opthalmological procedure was planned to follow the laparotomy under general anaesthetic. Postoperatively the neonate remained apnoeic and the anaesthetists were unable to safely extubate her. She required ventilation in the intensive care unit (ICU) overnight. After considering all causes of postoperative apnoea in this neonate, an overdose of Cyclomydril® eye drops was thought to be a significant contributing factor.
Cyclomydril® eye drops consist of cyclopentolate, an anticholinergic, and phenylephrine, an adrenergic drug. The combination produces mydriasis of short duration that is superior to that of either drug alone at the same concentration, with little or no cycloplegia.
Infants are especially sensitive to cardiopulmonary and neurological side-effects of cyclopentolate due to their immature cardiovascular and neurological systems, and their immature metabolic pathways. Although very rare, Cyclomydril® drops have been known to cause apnoea, and even hypoxic arrest, in outpatient ophthalmology clinics at routine screening for retinopathy of prematurity.
Anaesthetists should be aware of the potential dangers of Cyclomydril® drops and plan accordingly. It is the authors' recommendation that neonates receiving Cyclomydril® during the course of a procedure should be admitted to a high care unit or ICU for 24 hours postoperatively for observation and apnoea monitoring.

Keywords: premature neonates, atypical apnoea, post-anaesthesia apnoea, cyclopentolate, Cyclomydril®

Introduction

It is well known that premature infants have immature respiratory control that may result in apnoea, with or without bradycardia.[1] These apnoeas can be spontaneous or provoked by several insults, namely:

- Gastro-oesophageal reflux
- Central nervous system lesions: intracranial haemorrhages, seizures
- Infection: systemic or localised, NEC, meningitis
- Cardiac abnormalities: patent ductus arteriosus, heart failure
- Abdominal distension: NEC
- Chronic lung disease of prematurity
- Post immunisation
- Metabolic derangements: glucose and electrolyte imbalances
- Drugs: opioids, prostaglandin E1, magnesium, general anaesthesia
- Anaemia
- Upper airway obstruction: macroglossia, micrognathia, choanal atresia

Premature neonates are a group of patients that might present for surgery for various reasons, and as such, it is important that anaesthetists are aware of the potential adverse effects that their anaesthetic techniques and drugs could provoke, as well as the effects of other drugs that the surgeon may request or administer. In particular, the risk of postoperative apnoeas and the potential for hypoxic arrest.

The authors present an unusual contributing factor to postoperative apnoea in a neonate.

Case report

An ex-premature baby born at 25^{+5} weeks post-conceptual age (PCA) presented for a laparotomy following a complication of necrotising enterocolitis (NEC) at 39 weeks PCA. Bilateral Avastin® (bevacizumab) injection of the eyes as part of the management of retinopathy of prematurity (ROP) was planned to follow the laparotomy under general anaesthetic.

The patient was induced using sevoflurane, oxygen and air. The vocal cords were sprayed with lignocaine and the patient was subsequently intubated. Maintenance was obtained with isoflurane, oxygen and air at a MAC of around 0.9. Cisatracurium was used as a muscle relaxant at a dose of 0.15 mg/kg at the start of the procedure. Analgesia was provided at the start of the procedure with fentanyl 2 mcg/kg, clonidine 1 mcg/kg and intravenous paracetamol 10 mg/kg. The neonate's temperature was maintained between 35.6–36.9 degrees Celsius using an under body forced air warmer. The muscle relaxant was reversed with neostigmine and glycopyrrolate approximately

three hours after the induction of anaesthetic. Cyclomydril® eye drops were administered four times by the anaesthetist, half an hour after induction, at half-hourly intervals as a courtesy to the ophthalmologist, in preparation for the ophthalmology procedure to follow. The anaesthetist had no prior experience with administering the drops and unknowingly gave an extra dose.

Postoperatively the neonate remained apnoeic for over an hour and the anaesthetists were unable to safely extubate her. She required ventilation in the intensive care unit (ICU) overnight and was successfully extubated the following day. Although a short-acting opiate (fentanyl) had been used which can also contribute to apnoea in neonates, it was thought that enough time had passed for its effects to have lessened. Similarly, the muscle relaxant had been reversed appropriately. A venous blood gas sample was taken to rule out other causes (see Table I).

Table I. Venous blood gas

ph: 7.22
pCO_2: 8.3 kPa
pO_2: 2.7 kPa
HCO_3^-: 21.1 mmol/L
Base excess: -2.3 mmol/L
Na^+: 136 mmol/L
K^+: 4.1mmol/L
Glucose: 9.0 mmol/L
Lactate: 1.3
Hct: 30%
Hb: 10.2 g/dL

This was deemed to be a respiratory acidosis secondary to poor respiratory effort, with a normal blood glucose and Hb above 10 g/dL. After reviewing the anaesthetic chart and considering all possible causes of postoperative apnoea in this neonate, an overdose of Cyclomydril® eye drops was thought to be a significant contributing factor.

Discussion

Cyclomydril® eye drops consist of cyclopentolate, an anticholinergic, and phenylephrine, an adrenergic drug.[2-4] The combination produces mydriasis of short duration that is superior to that of either drug alone at the same concentration, with little or no cycloplegia. The recommended dose is one drop in each eye, every 5–10 minutes, not to exceed three drops per eye.[3-5] It is recommended that when instilling the drops, the lacrimal sac should be compressed to minimise systemic absorption.

Infants are especially sensitive to cardiopulmonary and neurological side-effects of cyclopentolate due to their immature cardiovascular and neurological systems, and their immature metabolic pathways.[2] Side-effects include tachycardia, hypertension, urinary retention and reduced gut motility. Severe toxicity can result in coma, medullary paralysis, and even death.[3-5]

Although very rare, Cyclomydril® eye drops have been known to cause apnoea, and even hypoxic arrest, in outpatient ophthalmology clinics at routine screening for retinopathy of prematurity.[2] Adverse events such as apnoeas and bradycardias have been documented to occur up to 24 hours following instillation of the eye drops.[6]

Retinopathy of prematurity is one of the leading causes of childhood blindness worldwide.[7] The pathogenesis is related to neovascularisation of the retinal surface and eventually leads to macular dragging and retinal detachment. Intravitreal injection of Avastin® has been shown to reduce neovascularisation in this disease. Neonates receiving Avastin® injections will require a general anaesthetic, as well as pupillary mydriasis. Thus it is important for anaesthetists to be aware of the potential adverse consequences of the installation of Cyclomydril® eye drops.[2]

Authors' recommendations

Neonates presenting for intravitreal injection for the management of retinopathy of prematurity under general anaesthesia requiring Cyclomydril® eye drops should:

1. Have the drops instilled by an ophthalmologist.
2. Not receive a dose exceeding the recommended dose of three drops per eye administered five to ten minutes apart.
3. Receive appropriate postoperative placement ensuring apnoea monitoring for 24 hours (a high care bed or ICU bed is recommended).[2,6]

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