

Case reports

Nebulised Ipratropium Causing a Unilateral Fixed Dilated Pupil in the Critically Ill Patient: A Report of Two Cases

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ABSTRACT

We describe two cases of a unilateral fixed dilated pupil secondary to the ocular instillation of nebulised ipratropium bromide. In one patient there was no other neurological abnormality. The second patient was unconscious following a cardiac arrest.

While a fixed dilated pupil is an alarming sign, if it is caused by ocular instillation of ipratropium bromide the condition will resolve, although it may take up to 24 hours. The differential diagnosis of a unilateral dilated pupil includes partial third nerve palsy, tonic pupil, direct trauma to the eye and pharmacological mydriasis. The diagnosis can often be determined using pilocarpine eye drops. (Critical Care and Resuscitation 2004; 6: 268-270)

Key words: Unilateral fixed dilated pupil, anisocoria, unilateral mydriasis

Many patients admitted to the intensive care unit are commenced on nebulised salbutamol and ipratropium bromide to treat bronchospasm. Reported side effects of this treatment include arrhythmias and tremor. An ocular effect of ipratropium, when inadvertently instilled directly into the eye, is mydriasis and cycloplegia. Other possible causes of mydriasis include trauma to the eye, third nerve palsy (partial or complete), hypothermia, Adie's pupil and seizure activity in an unconscious patient.

We report two cases of a unilateral fixed dilated pupil caused by ocular instillation of nebulised ipratropium bromide.

CASE REPORTS

Patient 1

A 62-year-old man was admitted to the intensive

care unit following an elective mitral valve replacement. His postoperative course was complicated by bleeding which required operative re-exploration twice in the immediate postoperative period. On day three he developed respiratory failure secondary to right middle and lower lobe consolidation. This was treated with intravenous piptazobactam/piperacillin, vancomycin, chest physiotherapy and nebulised ipratropium and salbutamol. Despite treatment he became increasingly hypoxic and was commenced on continuous positive airway pressure (CPAP) using a face mask. On day five a 'fixed' dilated pupil of the patient's left eye was reported, although he did not complain of any visual disturbance. Examination confirmed a dilated pupil in the left eye which was non responsive to light and measured 8 mm in diameter. Eye movements were normal and there was no visual deficit found on clinical testing. The differential diagnosis included partial or

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complete third nerve palsy, Adie's pupil or pharmacological mydriasis. Pilocarpine 0.1% was placed in both eyes; the right and left pupils were unreactive. Thirty minutes later pilocarpine 1% was given; again there was no change in the left pupil but the right pupil constricted confirming a local pharmacological cause of the fixed dilated left pupil. The dilated pupil recovered after 24 hours.

Patient 2

A 68 year old man was resuscitated following a cardiac arrest. He was admitted to the intensive care unit with a Glasgow coma scale score of 3. Three days following his admission he was noted to have an isolated dilated unreactive pupil. A cerebral computer tomography (CT) scan was ordered to rule out an intracerebral lesion. While waiting for the CT scan it was noted that the pupil dilated following a previous dose of nebulised ipratropium and salbutamol. The CT scan was unremarkable and the pupil subsequently returned to normal.

DISCUSSION

Anisocoria (different size pupils) may be due to an abnormally small pupil (e.g. Horner's syndrome, where there is a normal light reaction in both eyes) or an abnormally large pupil (usually associated with an abnormal light reaction in the dilated eye).¹ A fixed dilated pupil is often considered to be an ominous sign, particularly in a comatose patient, although in some circumstances it may be a benign sign. For example, it has been described in patients receiving nebulised ipratropium and salbutamol.²⁻⁴ A case was also reported in a child where the ipratropium bromide was witnessed splashing into the eye.⁵ Hand-to-eye contamination in patients using scopolamine patches for motion sickness have also been reported to cause a fixed dilated pupil.^{6,7} A dilated pupil can also be caused from a direct ocular instillation of an alpha adrenergic agent (e.g. ephedrine,⁸ phenylephrine,⁹ cocaine¹⁰).

Ipratropium bromide is a useful bronchodilator which is often used in combination with salbutamol in intensive care patients.¹¹ It is an antimuscarinic agent and, like atropine, causes mydriasis, an effect noted since the middle ages from ocular administration of extracts from the plant *Atropa belladonna*. Its effect on the eye may last up to 24 hours.

Pilocarpine is a direct acting parasympathomimetic agent which duplicates the actions of acetylcholine causing constriction of the pupil by stimulating the sphincter pupillae and altering accommodation by contracting the ciliary muscles. It also reduces intra ocular pressure. Its duration of action is 4 to 6 hours. Instillation of pilocarpine drops can also be used to

localise the cause of a fixed dilated pupil, the differential diagnosis of which includes,

- a. Trauma to the eye, which is associated with small radial splits in the iris (the red reflex using plus 10 on the ophthalmoscope highlights these tears and there are usually other signs of contusion to the eye and orbit)
- b. Adie's pupil or any other causes of a tonic pupil, which includes autonomic neuropathies from other causes
- c. Partial or complete third nerve palsy
- d. Pharmacological mydriasis after instillation of mydriatic agents inadvertently or intentionally to examine the fundus or treat a perforating eye injury and,
- e. A prosthetic eye.

A tonic pupil occurs following damage or disease of the ciliary ganglion which causes post ganglionic denervation hypersensitivity. This is demonstrated by pupillary constriction to dilute pilocarpine (Figure 1).

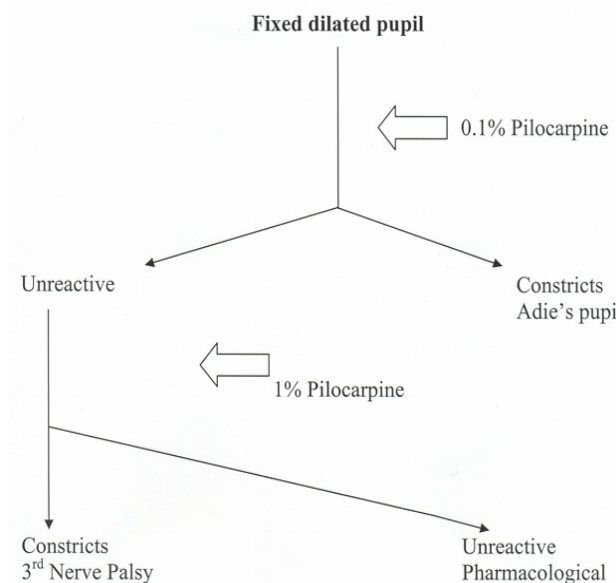


Figure 1. A flow diagram using topical pilocarpine to confirm the aetiology of a fixed dilated pupil.

Since pilocarpine is water soluble it is a simple matter to dilute 1% pilocarpine to a 1/10 solution. While a tonic pupil constricts to a 1/10 solution of pilocarpine, a normal pupil remains unaffected. However, if 1% pilocarpine is instilled, this will constrict a normal pupil or a dilated pupil secondary to a third nerve palsy. If there is no constriction to undiluted pilocarpine 1% the diagnosis is consistent with ocular instillation of a mydriatic agent such as ipratropium bromide,¹² as it blocks the response of the sphincter muscle to cholinergic stimulation.¹³

The Adie pupil may present as a dilated pupil that only slowly reacts to light. The aetiology of this condition is unknown. Initially, it is unilateral in 80% of patients. As outlined earlier the pupil will constrict in response to pilocarpine 0.1% eye drops.¹²

Complications of pharmacological mydriasis include blurred vision and acute angle closure glaucoma.¹⁴ A conscious patient with acute angle closure glaucoma will usually complain of pain and visual loss. This complication is difficult to detect in the unconscious patient and there are reports of permanent visual loss resulting from inadvertent ocular instillation of ipratropium bromide.^{14,15}

In summary, instillation of ipratropium bromide should be considered as a possible cause of a unilateral fixed dilated pupil. Pilocarpine 1/10 solution will constrict the dilated Adie pupil. A third nerve palsy will constrict with Pilocarpine 1% drops, while a local pharmacological cause will be unresponsive.

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