Reminder of important clinical lesson

Transdermal hyoscine induced unilateral mydriasis

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Correspondence to Dr Breffni Hannon, breffnihannon@yahoo.co.uk**Summary**

The authors present a case of unilateral mydriasis in a teenager prescribed transdermal hyoscine hydrobromide (scopolamine) for chemotherapy induced nausea and vomiting. The authors discuss the ocular side-effects associated with this particular drug and delivery system and the potential use of transdermal hyoscine as an antiemetic agent in this group.

BACKGROUND

The development of unilateral mydriasis in a patient with cancer raises concerns for intracranial metastatic disease. We present a recognised but often overlooked cause of mydriasis caused by transdermal hyoscine hydrobromide.

CASE PRESENTATION

A teenager with a diagnosis of Ewing's sarcoma of her right first rib with metastases to right iliac bone was commenced on a scopolamine patch (transdermal hyoscine) for cyclical nausea and vomiting related to chemotherapy (topotecan and cyclophosphamide). Previous trials of more conventional antiemetics (ondansetron and cyclizine) were unsuccessful largely due to tablet phobia and resultant non-compliance with oral medications. She was advised to apply a single patch behind her ear and replace every 72 h in keeping with the manufacturer's guidelines. Her symptoms improved rapidly and she was able to reduce the dose to a half patch within a month of commencing.

She presented to the oncology day ward 2 months later with acute onset visual disturbance. In particular she reported a 2-day history of an inability to focus up close which affected the right eye only. Distance vision was unaffected. She did not describe any pain, photophobia or diplopia. Examination of the eye revealed a unilateral dilated pupil which was reactive to light but sluggish compared with the left pupil. A complete clinical neurological examination revealed no other findings. There were no other antimuscarinic effects reported (including dry mouth, constipation, urinary retention, flushing or cardiac effects).

DIFFERENTIAL DIAGNOSIS

The patient refused the oncology team's proposal of a CT brain to outrule metastases.

TREATMENT

Patch removal was advised, which led to symptom resolution after several days.

OUTCOME AND FOLLOW-UP

Nausea did not re-occur, as chemotherapy was subsequently discontinued due to progression of disease locally,

and she remained symptom free until death 2 months later.

DISCUSSION

Hyoscine hydrobromide is a belladonna alkaloid and antimuscarinic agent which has similar actions to atropine.¹ Its action on the iris, ciliary body and certain secretory glands is more potent than atropine while its actions on cardiac, intestinal and bronchial smooth muscle are less potent.

Transdermal hyoscine is applied to the postauricular area and contains a drug reservoir of 1.5 mg of hyoscine. This is programmed to deliver 0.5 mg of hyoscine per day over a 3-day period. A priming dose of 140 mcg is incorporated into the adhesive layer to saturate binding sites within the skin and to accelerate achievement of steady state levels. Absorption leads to blood levels equivalent to those obtained by intravenous infusion. The postauricular area has been shown in both cadaveric and in vitro studies to be more permeable than other areas, including the back, chest, abdomen, forearm and thigh. Changes in skin temperature have been shown to be of limited significance on skin permeation.^{2 3}

Transdermal hyoscine is most frequently used in the management of motion sickness. It has also been successfully used in the management of acute vertigo, in reducing nocturnal acid secretion in patients with duodenal ulcers, and as a premedication prior to surgery.²

Hyoscine as an antiemetic

Hyoscine is not currently indicated for use in chemotherapy induced nausea and vomiting, however it does have some unique features which make it worthy of consideration as an off-label agent in select cases. The transdermal route of administration may prove a more acceptable option for patients overwhelmed by tablet burden, severe vomiting with resultant concerns regarding absorption of oral medications, or whose compliance with oral medications is suboptimal, as in our case. The relatively long duration of action of hyoscine may also be beneficial in cancer settings.

A small number of trials have explored the use of hyoscine for chemotherapy induced nausea and vomiting,

with mixed results. One randomised double blind crossover trial compared transdermal hyoscine with placebo in patients receiving cisplatin. However, no significant differences were noted between the two groups.⁴ More positive results were seen in a placebo controlled pilot study in 12 children receiving methotrexate. In eight of the 12 cases, marked differences were noted between the two groups, and a subsequent 19 out of 23 courses of treatment using transdermal hyoscine were free of vomiting.⁵

In recent years, interest in hyoscine as an antiemetic has been largely superseded by newer agents. In times of greater budgetary constraints however, it is worth noting that transdermal hyoscine is significantly cheaper at approximately £2 per patch compared with many alternative agents.^{2 5 6}

Hyoscine induced mydriasis

Antimuscarinic agents have potent mydriatic and cycloplegic effects by blocking the responses of the sphincter muscle of the iris and ciliary muscle of the lens to cholinergic stimulation.² In some cases, these effects have been reported in response to high systemic levels of scopolamine released directly from the patch. Bilateral mydriasis and coma secondary to transdermal hyoscine has been reported in an intensive care unit setting in a patient with head injury and hydrocephalus, which was associated with significant improvement upon removal of the patch.⁷

A small number of case reports in the literature discuss unilateral mydriasis, hypothesised as being caused by accidental direct contamination of the eye (such as rubbing the eye immediately after applying or adjusting the patch).⁸ This is the most likely cause in our case as the patch was placed behind her right ear, also the side of her mydriasis, particularly given the absence of pre-existing ocular or visual problems.

Several cases of long duration have been reported where patients accidentally handled contact lenses following application of the patch. Patients with narrow angle glaucoma may develop acute attacks of primary angle closure related to transdermal hyoscine.⁹

Pharmacological blockade can be simply distinguished from neurogenic papillary dilatation using the pilocarpine test. One to two drops of 0.5 to 1.0% pilocarpine hydrochloride should be instilled into both eyes. In the absence of traumatic injury to the eye, and normal intraocular pressure, failure of the dilated pupil to constrict within 30 min is proof of chemical blockage of the iris muscles.⁹

Neurogenic dilatation of the pupil as a result of injury to the oculomotor nerve does not directly affect the integrity of the cholinergic receptor function of the pupil sphincter; therefore the pupil should be capable of constriction when a parasympathetic agent such as pilocarpine is instilled into the eye.⁸ Atropinic drugs, in contrast, will decrease pilocarpine miosis. Other potential causes of a failure to

response to pilocarpine would include traumatic damage to the sphincter muscle or increased intraocular pressure, which can easily be ruled out by history and clinical examination.¹

Learning points

- The potential mydriatic and cycloplegic effects of transdermal hyoscine are often overlooked and should be considered in patients presenting with new-onset visual disturbance and ocular symptoms.
- Patients should be counselled regarding the potential side-effects of the drug, and careful hand hygiene following application of the patch.
- The pilocarpine test is an easily reproducible test for distinguishing this adverse effect from potential central nervous system involvement in patients with cancer, and may prevent unnecessary investigations.
- Transdermal hyoscine is a potentially useful antiemetic with a novel route of administration which could be considered in selected patients with chemotherapy induced nausea and vomiting. Further large scale clinical trials are needed to compare this drug with other antiemetics.
- Its cost-effectiveness compared with alternative agents is a further advantage which is particularly relevant in the current climate of drug budget constraints.

Competing interests None.

Patient consent Not obtained.

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