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Transdermal scopolamine (Hyoscine): visual side-effects

ALISON Y. FIRTH MSc DBO(T)

Academic Unit of Ophthalmology and Orthoptics, University of Sheffield, Sheffield

Abstract

***Aim*: To highlight the side-effects of transdermal scopolamine.**
***Method*: Evidence from the literature is presented concerning the use of this drug and visual side-effects.**
***Results*: The main side-effects are pupillary dilation and blurring of vision. These appear to be more frequently encountered with repeated use of patches and where there is local contamination between the patch and the eye.**
***Conclusions*: Awareness of the visual side-effects of transdermal scopolamine may help the clinician recognise symptomatic conditions presenting in adults; and especially in children with special needs who are unable to communicate problems.**

Key words: Blurred vision, Mydriasis, Scopolamine

Introduction

Scopolamine (Hyoscine) is a parasympatholytic drug obtained from the belladonna plant. It prevents the action of acetylcholine on the muscle cell. The drug may be used topically, orally, by injection or transdermally.

The various forms of the drug are used for motion sickness (commercially available), other forms of nausea and vomiting, as a premedicant for anaesthesia, and to produce cycloplegia and mydriasis. Severe central nervous system side-effects of confusion, restlessness or hallucinations have been reported with transdermal use.[1,2] Other side-effects include tachycardia, blurred vision and suppression of salivation. The latter is utilised in several clinical conditions to control drooling. This review considers the side-effects which have been reported in adults using transdermal scopolamine and highlights problems that may occur due to side-effects where transdermal scopolamine is used to reduce drooling in the child with special needs.

Transdermal delivery

A transdermal therapeutic system for scopolamine (TTS-S) was developed due to scopolamine being absorbed well through the skin. Transdermal administration may be used to avoid the side-effects of administration orally or by injection.[3,4] Application consists of a circular film-like patch 1.5 cm in diameter and 0.2 mm thick with a backing layer, a drug reservoir separated from the skin by a microporous rate-controlling membrane, and an adhesive that provides contact between the membrane and the skin. The drug is dispensed over a 72 hour period. An effective drug concentration is obtained after 6 to 8 hours. Schmitt and Shaw[5] found that drug concentrations were similar over 24 to 72 hours after applying the patch, but were higher between 12 and 24 hours. After removal of the patch, the drug concentration remained significantly elevated for 48 hours. They concluded that this may lead to increased serum levels following successive patch applications.

Correspondence and offprint requests to: Alison Y. Firth MSc DBO(T), Academic Unit of Ophthalmology and Orthoptics, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF. Tel: 0114 2712064. e-mail: a.firth@sheffield.ac.uk

Side-effects in the adult

Many individual cases of visual side-effects from the transdermal use of medication containing scopolamine for travel (motion) sickness (Transderm) have been reported. These include unilateral mydriasis on the side to which the patch was applied, which may be due to contaminating the finger on placement of the patch and then rubbing the eye. Mydriasis can last 72 hours.[6] Local contamination was thought to be responsible in one subject with unilateral mydriasis who removed the patch and then applied a contact lens.[7] If the patch has been irritating, finger contact in rubbing is increased, and this was the proposed reason in another patient who presented with an unilateral, fixed dilated pupil.[8] Arnold *et al.*[9] reported a case where diplopia occurred after use of a scopolamine patch in a patient with previously operated infantile esotropia. The angle was presumed to increase following contamination of the patient's dominant eye, in which a contact lens was worn. The mydriasis can also precipitate an acute attack in acute angle closure glaucoma. Four days following the first application of a patch, which had not been removed, acute angle closure glaucoma occurred in a previously undiagnosed 58-year-old woman.[10]

Persistent mydriasis is more typical of local instillation and bilateral dilation is more often observed as a side-effect of transdermal administration.[11]

McCrary and Webb[12] highlighted the importance of using 1% pilocarpine in an attempt to constrict the pupil where anisocoria is present, to differentiate between a neurological cause or drug-induced change if the pupil is non-reactive. Where scopolamine is the cause, no constriction will occur. They reported two cases to illustrate this.

Gordon *et al.*[3] investigated the effect of transdermal scopolamine (Scopoderm TTS, concentration not given) on human performance in navy personnel, aged 18–20 years, by a double-masked cross-over trial. No significant difference was found in performance tests. Side-

effects which may have affected visual acuity, accommodation, salivation and mood state were evaluated. No differences were found in visual acuity or accommodation. Salivation was reduced and there was higher reporting of fatigue and drowsiness in the medication group. Even when combining transdermal use with oral tablets (single dose of 0.6 mg or 0.3 mg or placebo) to achieve a quicker effect, no differences were found in side-effects reported between the groups.[13] Although Price *et al.*[14] mention blurred vision as a side-effect in a study where the drug was used for motion sickness, the number affected was not statistically significant when compared with placebo groups. These studies involved a single dose.

With repeated doses visual problems have been reported.[15–17] In a letter to the *New England Journal of Medicine* Johnson *et al.*[1] wrote on behalf of the medical team aboard a large cruise ship stating that over the past 2 years many passengers using 'Transderm Scop' patches for sea sickness were presenting with blurred vision, sore throat, dry mouth and confusion. Bilateral dilatation of pupils was seen on examination, increased on the side the patch was worn. Although the side-effects are listed, the authors warn that the frequency of these side-effects should be noted.

Parrott and Jones[18] found that although 22 subjects of 28 with scopolamine patches reported blurred vision, only 5 were unable to undertake psychological performance tests due to blurring of print; of these, one subject was on their first patch and 4 were on their second patch. Parrott[19] measured near point of accommodation using the RAF rule in 12 males aged 18–27 years. Standard patches were applied behind the ear on alternate days, with subjects being on the drug or placebo on any one day. No reports of blurred vision occurred after the first scopolamine patch, one after the second, four after third and six after the fourth. Those reporting blurred vision showed a decrease in near point of accommodation (tested monocularly) to 28.8 cm by the fourth patch; those who did not report blurring showed minimally reduced accommodation from 11.5 cm to 12.7 cm by the fourth patch. Subjects who developed blurred vision had initial near points which were longer (mean 16.3 cm) and the authors interpreted this as meaning the subjects were hypermetropic, although no refraction was performed. During placebo days the near point of accommodation again shortened. Performance impairments were also found with repeated doses.[20]

Diplopia and blurred vision were listed as side-effects of a single dose of scopolamine by van Marion *et al.*[21] Here a patch was applied 4 hours before sailing in 49 healthy sailors with a history of motion sickness, and removed 72 hours later during a 7 day period at sea. Seven subjects reported diplopia and blurred vision during days 2–3 and 3 during days 4–6. No detail is given, but pupil size was assessed and 'no cycloplegia observed'. One-third experienced a dry mouth and this was still present 1 day after removal of the patch. This led the authors to recommend that a new patch should not be applied within 24 hours of removal of the previous patch.

Visual disturbances have also been reported after use of transdermal scopolamine (Scopoderm TTS CIBA) for prevention of post-surgical nausea and vomiting in adults.[22–24] However, no detail of the exact nature of the 'visual disturbance' is given, although it is reported as occurring more frequently (8 of 42 patients) 24–48 hours post-operatively.[23]

Transdermal scopolamine for sialorrhoea

Sialorrhoea (drooling) can be a problem in many patient groups: those with Parkinson's disease, motor neurone disease, head injury, oral cancers[25] and cerebral palsy. Scopolamine is a more powerful suppressant of salivation than atropine and this significant reduction of salivary flow[3,26] has led to its use in sialorrhoea.

Rogawski[27] suggested that the transdermal method of delivery of scopolamine had advantages over oral atropine after using a patch for drooling in a 57-year-old with motor neurone disease. Avoidance of pills in patient groups who have difficulty swallowing was given as a benefit, although the author acknowledged that side-effects could still occur with the transdermal system of delivery. In a 40-year-old head-injured patient no side-effects were reported over a 4 month period; initially one patch was used but subsequently two patches were applied at a time (the patches being renewed every 72 hours). The scopolamine TTS has been used, for up to 24 days, for several conditions where hypersalivation or swallowing problems were present as a result of various oral and upper aerodigestive tract pathologies.[28] Despite blurred vision being reported in 7 of 109 patients, after seeing an ophthalmologist (no clinical details given) the patch was continued in 6.

Special needs

Brodtkorb *et al.*[29] reported findings during a single-dose double-masked placebo-controlled cross-over study in 18 mentally retarded patients aged 20–62 years. Response was variable but the effect generally good and a significant reduction in drooling was found during the 24–72 hours after application of the patch. Although side-effects of mouth dryness, tiredness, conjunctival irritation and thirst were reported, they were equally reported in the scopolamine and placebo periods. The authors do state 'The registration of side-effects was difficult in this study as the patients had little or no speech'. The use of scopolamine is suggested on special occasions, to cure peri-oral skin lesions, or during dentistry work.

Siegel and Klingbeil[30] reported the use of a scopoderm patch in a 4-year-old child with severe spastic quadriplegia and developmental delay and extremely limited cognitive function. The patch had been used over a 2 year period, a new patch being applied every 72 hours. No mydriasis or other side-effects were observed. The authors do mention sensitivity to heat as being observed in other patients in whom the patch has been used and so suggest that they may be discontinued during hot weather.

Following this case report and a report of short-term safety in children (aged 1–11 years) in whom scopolamine has been used prophylactically as an anti-emetic following strabismus surgery,[31] Lewis *et al.*[32] investigated the effects of its short-term wear in developmen-

tally delayed children aged 5–18 years. Transdermal scopolamine (full patch) was used for 2 weeks, followed by a 1 week 'wash-out' period and placebo patch for 2 weeks (or vice versa). Patches were applied on the child's back to avoid tampering. Eight of the 10 children had epilepsy. One had a cluster of simple partial seizures during the active patch phase. Two-thirds of the patients were noted to have pupillary dilation. Horimoto *et al.*[31], however, state that the size of the existing patches should be reduced for children and in their study a quarter-patch was used for children under 2 years of age, and a half-patch in the others.

One case is reported of a 4-year-old boy with spastic quadriplegia prescribed one-quarter of a patch to give 0.15 mg of scopolamine over a 3 day period.[33] After 5 days a 40$^{\Delta}$ esotropia developed, no significant hypermetropia was present and pupils were round and reactive to light. Seven days after cessation of the patch, the deviation had resolved. The authors suggest that the effect on accommodation led to the esotropia.

Two children (aged 7½ years and 5 years 8 months) who were wearing a full patch showed reduced near visual acuity compared with visual acuity measurements after removal of the patch.[34] The pupils were dilated and the authors point out effects of this such as increased sensitivity to light and flicker.

Comment

Other drugs are available for drooling. Tscheng[35] in a review suggests that glycopyrrolate (anticholinergic) may have an advantage over other agents due to fewer adverse effects. Other options are antireflux agents; benztropine; beta blockers; propantheline (anticholinergic); or botulinum toxin A into the parotid gland(s). Jongerius *et al.*[36] found that the anticholinergic effect of intraglandular botulinum toxin exceeded that of scopolamine and that it does offer an alternative treatment.

Conclusion

Visual side-effects of transdermal scopolamine can include pupillary dilation and reduction in accommodation. Local contamination should always be considered, particularly where pupillary dilation is unilateral. The non-visual side-effect of suppression of salivation may be used in patients who suffer drooling. However, amongst this group are those with special needs who may not be able to communicate disturbing side-effects, and some may experience a blurring of near visual acuity.

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