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**Published paper**

Transdermal Scopolamine (Hyoscine): visual side effects.

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Abstract

**Aims:** To highlight the side effects of transdermal scopolamine.

**Methods:** 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.

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 CNS side effects of confusion, restlessness or hallucinations with transdermal use have been reported. 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 when administered orally or by injection.\(^3,4\) Application consists of a circular film like patch of 1.5cm diameter and 0.2 mm thickness 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 et al\(^5\) 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, the drug concentration remained significantly elevated for 48 hours. They concluded that this may lead to increased serum levels following successive patch applications.

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. This can last 72 hours.\(^6\) Local contamination was also 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 case who presented with an unilateral, fixed dilated pupil.\textsuperscript{8} Arnold et al\textsuperscript{9} report 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.\textsuperscript{10}

Persistent mydriasis is more typical of local instillation and bilateral dilation is more often observed as a side effect of transdermal administration.\textsuperscript{11}

McCrary and Webb\textsuperscript{12} highlight 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. Two cases are reported to illustrate this.

Gordon et al\textsuperscript{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 blind 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 0.6mg or 0.3mg or placebo) to achieve a quicker effect, no differences were found in side effects reported between the groups.\textsuperscript{13} Although Price et al\textsuperscript{14} mention blurred vision as a side effect in a study where the drug was used for motion sickness, the number was not statistically significant when compared with placebo groups. These studies involved a single dose.

With repeated doses visual problems have been reported.\textsuperscript{15-17} In a letter to the New England Medical Journal Johnson et al\textsuperscript{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\textsuperscript{18} found that although 22 subjects of 28 with scopolamine patches reported blurred vision, only 5 subjects were unable to undertake psychological performance tests due to blurring of print, of these one on their first patch and 4 on the second patch. Parrott\textsuperscript{19} measured near point of accommodation using the RAF rule in 12 males aged 18 to 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, 4 after third and 6 after the fourth. Those reporting blurred vision showed a decrease in near point of accommodation (tested monocularly) to 28.8cm by fourth patch; those who did not report blurring showed minimally reduced accommodation from 11.5 cm to 12.7cm by the fourth patch. Subjects who developed blurred vision had initial near
points which were longer (mean 16.3cm) and the authors interpret this as being subjects who 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 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 these problems during days 2 to 3 and 3 during days 4 to 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 one day after removal of the patch. This leads 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 nausea and vomiting post surgery 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 to 48 hours post-operatively.²³

**Transdermal scopolamine for sialorrhea (drooling)**

Sialorrhea can be a problem in many patient groups: Parkinson’s disease, motor neurone disease, head injured patients, patients with oral cancers²⁵ and cerebral palsy. Scopolamine is a more powerful suppressant of salivation than atropine and this significant reduction of salivary flow³,²⁶ has led to its use in ‘drooling’ (sialorrhea).
Rogawski\textsuperscript{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 having to swallow 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 being used but subsequently 2 patches 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 resulting from various oral and upper aerodigestive tract pathologies\textsuperscript{28} and despite blurred vision being reported in 7 of 109 patients, after seeing an ophthalmologist (no clinical details given) the patch was continued in 6.

\textit{Special needs}

Brodtkorb et al\textsuperscript{29} reported findings during a single dose double blind 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 Klingbiel\textsuperscript{30} reported the use of a scopoderm patch in a four 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 where 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 to 11 years) where scopolamine has been used prophylactically as an anti-emetic following strabismus surgery,\textsuperscript{31} Lewis et al\textsuperscript{32} investigated the effects of short term wear in developmentally delayed children aged 5 to 18 years. Transdermal scopolamine (full patch) was used for 2 weeks, followed by a one 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\textsuperscript{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 to one half in the others.

One case is reported of a 4 year old boy with spastic quadriplegia prescribed one quarter of a patch to give 0.15mg of scopolamine over a 3 day period.\textsuperscript{33} After 5 days a 40PD 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 cases (aged 7½ years and 5 years 8 months) in which a full patch was being worn both showed reduced near visual acuity compared with visual acuity measurements after cessation of the patch.\textsuperscript{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\textsuperscript{34} in a review suggests that glycopyrrrolate (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 the parotid gland(s). Jongerius et al\textsuperscript{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.
References


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