The efficacy and safety of transdermal scopolamine for the prevention of postoperative nausea and vomiting: a quantitative systematic review

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Authors' objectives
To assess the role of transdermal scopolamine in the prevention of post-operative vomiting, nausea, and nausea and vomiting.

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched up to September 2001, using the following free textwords and alternative spellings: 'postoperative', 'postanaesthetic', or 'surgical', 'nausea', 'emesis', 'vomiting', or 'retching' and 'scopolamine' or 'hyoscine'. The German manufacturer of transdermal scopolamine was contacted for additional information including unpublished data. Only full reports were included.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Comparisons of transdermal scopolamine with placebo or no treatment were eligible. Where reported, the included studies all used the Ciba-Geigy-Patch. Patches were applied the night before, 1 to 2 hours before, at induction or at the end of surgery. In most studies the patches were applied behind the ear, overlying the mastoid process.

Participants included in the review
Patients undergoing regional or general anaesthesia were eligible for inclusion. The age of the patients, where stated, ranged from 1 to 83 years, and patients of both genders were included. Several studies enrolled only women. The participants underwent the following types of surgery: laparoscopic; gynaecological, both major and minor; orthopaedic; general; ear, nose and throat; eye; oral; abdominal; thyroid; breast; Caesarean section; and plastic. The patients received various types of anaesthesia: balanced, total intravenous anaesthesia, neuro lepataesthesia, inhaled, spinal and epidural.

Outcomes assessed in the review
Studies that assessed the prevention of post-operative nausea and vomiting (PONV) were eligible. The review assessed the frequency of post-operative vomiting (PV), post-operative nausea (PN), PONV, rescue treatment and adverse effects.

How were decisions on the relevance of primary studies made?
Each of the four authors independently assessed potentially relevant studies according to the inclusion criteria, and any disagreements were resolved by consensus (see Other Publications of Related Interest).

Assessment of study quality
Validity was assessed using the 5-point Oxford scale that assesses randomisation, blinding and drop-outs. The sponsorship of studies by pharmaceutical companies was also assessed. Each of the four authors independently assessed validity and any disagreements were resolved by consensus (see Other Publications of Related Interest).

Data extraction
More than one author appears to have extracted data, but the actual number was not specified. The following information were tabulated in the review: the number of patients per treatment group; outcomes; details of the
intervention, including the time of application; characteristics of the patients such as age, gender and type of operation; type of anaesthesia and duration of surgery; and whether a pharmaceutical company sponsored the study or provided the drugs. Dichotomous data were extracted for distinct time intervals (0 to 6 hours and 0 to 24 hours).

**Methods of synthesis**

**How were the studies combined?**

Pooled relative risks (RRs) and 95% confidence intervals (CIs) were calculated using a random-effects model for two observation periods (0 to 6 hours and 0 to 24 hours). The numbers-needed-to-treat (NNT) or harm (NNH) were also calculated, along with 95% CIs.

**How were differences between studies investigated?**

Statistical heterogeneity was tested using the chi-squared test and explored graphically using forest plots and L'Abbe plots. The data were re-analysed according to the type of anaesthesia (general versus any kind of regional anaesthesia), the timing of when the scopolamine patch was applied (night before surgery versus before induction or during the operation), and according to the size of the treatment group (studies with at least one group of less than 30 patients versus all other studies) and after excluding children. A sensitivity analysis was performed by restricting the analysis to a subset of studies with a predefined control event rate of 40 to 80% for PV, PN and PONV, and of 20 to 60% for rescue treatment.

**Results of the review**

Twenty-three RCTs (1,963 patients) were included.

The validity scores ranged from 1 to 5 out of a possible 5 points. One RCT scored 1 point, one RCT scored 2, ten RCTs scored 3, nine RCTs scored 4 and two RCTs scored 5.

0 to 6 hours: transdermal scopolamine significantly reduced emetic symptoms at 0 to 6 hours, but considerable statistical heterogeneity was found (no details were given). For PV (9 RCTs), the RR was 0.65 (95% CI: 0.45, 0.94) and the NNT was 12.5 (95% CI: 6.7, infinity). For PN (8 RCTs), the RR was 0.63 (95% CI: 0.45, 0.89) and the NNT was 6.3 (95% CI: 3.7, 25.0). For PONV (10 RCTs), the RR was 0.68 (95% CI: 0.51, 0.92) and the NNT was 6.3 (95% CI: 3.7, 25.0). For rescue (3 RCTs), the RR was 1.16 (95% CI: 0.74, 1.82) and the NNT was 33.3 (95% CI: 10.0, infinity).

0 to 24 hours: transdermal scopolamine significantly reduced emetic symptoms at 0 to 24 hours. For PV (15 RCTs), the RR was 0.63 (95% CI: 0.55, 0.73) and the NNT was 5.6 (95% CI: 4.0, 9.1); no significant heterogeneity was detected (P=0.49). For PN (13 RCTs), the RR was 0.64 (95% CI: 0.51, 0.80) and the NNT was 4.3 (95% CI: 2.9, 8.3). For PONV (20 RCTs), the RR was 0.66 (95% CI: 0.57, 0.76) and the NNT was 3.8 (95% CI: 2.9, 5.6). For rescue (10 RCTs), the RR was 0.77 (95% CI: 0.66, 0.90) and the NNT was 11.1 (95% CI: 7.7, 25.0).

There was no significant difference according to the type of anaesthesia or the timing of when the scopolamine patch was applied, and after excluding children. The results suggested that better results were reported by smaller trials (results were presented).

Adverse events: the studies reported several side-effects. These included the following: visual disturbances (mydriasis, blurred vision and amblyopia), dry mouth, agitation/confusion, dizziness, urinary retention, local skin irritation, sedation/somnolence/drowsiness, headache, anxiety and problems with orthostatism. Visual disturbances and dry mouth were significantly more common with scopolamine compared with no scopolamine. The RR for visual disturbances (14 RCTs) was 2.15 (95% CI: 1.46, 3.16) and the NNH was 12.5 (95% CI: 7.3, 33.3). For dry mouth (12 RCTs), the RR was 1.49 (95% CI: 1.13, 1.96) and the NNH was 5.6 (95% CI: 3.1, 33.3). There was no significant difference between scopolamine and control in terms of dizziness, agitation or sedation. The RR was 1.13 (95% CI: 0.71, 1.79) for dizziness, 2.15 (95% CI: 0.78, 5.92) for agitation and 2.01 (95% CI: 0.59, 6.84) for sedation.

Problems in the use of scopolamine patches occurred in 4.7% (range: 1.2 to 12.6) across 7 RCTs.

**Authors’ conclusions**
Transdermal scopolamine had a greater anti-emetic effect than placebo, but it was associated with a greater risk of side-effects.

**CRD commentary**
The review question was clear in terms of the study design, participants, intervention and outcomes. Several relevant sources were searched and attempts were made to locate unpublished material. The study selection, validity assessment and data extraction processes were carried out by at least two authors, thus reducing the potential for bias and errors. Validity was assessed using validated criteria, and results of the validity assessment and other relevant information on the included studies were tabulated. The studies were pooled in a meta-analysis and the influence of various factors on the results was explored. However, statistical heterogeneity was not consistently reported for all analyses, and it is unclear whether homogeneity was achieved by restricting the analyses to any subgroups of studies. In view of this, it is not possible to state that results from the meta-analyses apply to all situations where scopolamine is used in the prevention of PONV.

**Implications of the review for practice and research**
The authors did not state any implications for further research and practice.

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