Transdermal Scopolamine Reduces Nausea and Vomiting
After Outpatient Laparoscopy

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The authors evaluated the effect of transdermal scopolamine on the incidence of postoperative nausea, retching, and vomiting after outpatient laparoscopy in a double-blind, placebo-controlled study. A Band-Aid®-like patch containing either scopolamine or placebo was placed behind the ear the night before surgery. Anesthesia was induced with fentanyl (0.5–2 μg/kg iv), thiopental (3–5 mg/kg iv), and succinylcholine (1–1.5 mg/kg iv) and maintained with isoflurane (0.2–2%) and nitrous oxide (60%) in oxygen. Scopolamine-treated patients had less nausea, retching, and vomiting compared with placebo-treated patients (P = 0.0029). Severe nausea and/or vomiting was present in 62% of the placebo group but only 37% of those getting the scopolamine patch. Repeated episodes of retching and vomiting were also less frequent in the scopolamine group compared with the placebo group (23% vs. 41%; P = 0.0213) as was the need for additional antiemetic therapy (13% vs. 32%; P = 0.0013). Patients in the scopolamine group were also discharged from the hospital sooner (4 ± 1.3 vs. 4.5 ± 1.5 h; P = 0.0487). Side effects were more frequent among those patients treated with the scopolamine patch (91% vs. 45%; P < 0.05) but were not troublesome. The authors conclude that transdermal scopolamine is a safe and effective antiemetic for outpatients undergoing laparoscopy. (Key words: Antiemetics: scopolamine. Delivery systems: transdermal scopolamine. Side effects: nausea; vomiting.)

Despite advances in antiemetic therapy, nausea and vomiting continue to be among the most common side effects following general anesthesia.1 Associated complications range in severity from mild discomfort to hospital admission for dehydration or pulmonary aspiration.1

Although scopolamine is an effective antiemetic, it is used sparingly because parenteral administration frequently results in undesirable side effects.2,3 Furthermore, the duration of antiemetic action of parenterally administered scopolamine is short.5 A transdermal delivery system (skin patch) has been recently developed that continuously releases scopolamine for up to 3 days. This system produces low steady plasma concentrations of scopolamine and may provide more consistent antiemetic action with fewer side effects.4 The goal of this study was to determine if placement of a transdermal scopolamine patch prior to surgery can safely reduce the incidence and severity of postoperative nausea and vomiting in patients undergoing outpatient laparoscopy.

Methods

The transdermal scopolamine patch (Transderm Scop, Ciba Pharmaceuticals, Edison, NJ) consists of a reservoir containing the drug in a mixture of mineral oil and polysorbate 80 held between an impermeable backing layer and a rate-controlling microporous membrane (fig. 1). An adhesive layer containing a priming dose of 140 μg of scopolamine is attached to the side of the unit in direct contact with the skin. The entire unit is 0.2-mm thick, contains 1.5 mg of scopolamine, and is designed to deliver 5 μg/h at a constant rate over a 3-day period. Placebo patches produced for the study were identical in appearance but did not contain scopolamine.

Following approval from the University of Utah Health Sciences Center Institutional Review Board, 191 ASA physical status 1 or 2 women scheduled for outpatient laparoscopy under general anesthesia gave oral and written informed consent for our study. Patients who were pregnant, nursing, had a medical history of narrow-angle glaucoma, gastrointestinal obstruction, urinary tract obstruction, or were using antiemetics, anticholinergics, or antihistamines were excluded from the study. Subjects were assigned to receive, in a double-blind, randomized fashion, a Band-Aid®-like circular patch containing scopolamine or an identical placebo patch. Patients were instructed to apply the patch on the skin behind either ear (overlying the mastoid process) the night before surgery, or at least 8 h prior to the scheduled starting time of surgery as is currently recommended.4 Patients were reminded by phone call the night before surgery to apply the patch.

The morning of surgery a catheter was inserted into a peripheral arm vein after which an iv infusion was begun with lactated Ringer’s solution. Patients were brought to the operating room and monitored with an automatic blood pressure cuff, three-lead electrocardiogram, precordial stethoscope, and pulse oximeter. Fentanyl, 0.5–2 μg/kg, and curare (3 mg) or pancuronium (1 mg) were then administered intravenously and anesthesia was induced with thiopental (3–5 mg/kg iv). Tracheal intubation was facilitated with succinylcholine (1–1.5 mg/kg

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iv). Anesthesia was maintained with isoflurane (0.2–2%) and nitrous oxide (60%) in oxygen. Additional muscle relaxation was achieved with either atracurium or vecuronium when necessary. Reversal of residual muscle relaxation at the end of surgery was achieved with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). No antiemetics, centrally active anticholinergics, or antihistamines were administered during the procedure or for the first 2 h in the postanesthesia care unit (PACU).

Starting immediately after surgery, the presence, severity, and duration of nausea, retching, and vomiting were elicited from both the patient and the nurse taking care of the patient on an hourly basis until discharge from the hospital. During recovery, if nausea persisted for 2 h (severe nausea) or the patient had two episodes of retching or vomiting, 0.625 mg of droperidol was administered intravenously. Additional droperidol, 0.625 mg iv, was given if the patient continued to complain of nausea or if vomiting or retching persisted. Nausea lasting less than 2 h without vomiting or retching (mild nausea) was not treated.

The patients were asked about possible side effects related to scopolamine during the postoperative period and any complaints were documented. Upon discharge from the hospital, subjects were given an addressed, stamped diary card (to be returned to the investigators) on which they were instructed to record the time of patch removal, further episodes of nausea, retching, and vomiting, and any possible side effects. In addition, the patient was interviewed by telephone 48 h postoperatively to enhance diary card documentation.

**Statistical Analysis**

SAS software (SAS Institute Inc., Cary, NC) was used for statistical calculations. Comparison of group demographics were made using Student’s t tests and chi-square test statistics. Analyses of drug efficacy (patient discomfort and need for antiemetic therapy) were made using ranked categorical frequency analysis; in particular, the SAS Procedure CATMOD was employed. The incidence of side effects was compared with chi-square test statistics.

**Results**

One hundred ninety-one patients were enrolled into the study; 53 patients were excluded from analysis because of a breach in the study protocol. Reasons for the removal of these subjects from evaluation included failure to apply the patch (n = 17), patch removal either before surgery (n = 5) or within 6 h after surgery (n = 2), drugs with potential antiemetic effects given intraoperatively (n = 21), epidural instead of general anesthesia (n = 1), nonabdominal surgery (n = 3), and cancellation of surgery (n = 3). In addition, one patient received no fentanyl. There was no difference between active (n = 27) and placebo (n = 26) groups with respect to subject removal from analysis. When appropriate, data from these patients were included in the analysis of side effects.

Age, ASA physical status classification, hours from patch placement to the start of anesthesia, duration of anesthesia, and total hours the patch was in place were similar between the active (n = 70) and placebo (n = 68) groups (table 1). Furthermore, there were no differences between the scopolamine and placebo groups with respect to medical history, physical examination, or concomitant medications.

A comparison of the distributions of no discomfort, mild nausea only, and severe nausea, retching, or vomiting revealed significantly less nausea, retching, and vomiting in the scopolamine-treated group (table 2). Severe nausea, retching, or vomiting was experienced by only 26 of 70 (37%) scopolamine-treated patients compared with 42 of 68 (62%) of patients in the placebo group (table 2). In addition, repeated episodes of retching or vomiting were more frequent in the placebo-treated patients (28 of 68; 41%) than in scopolamine-treated patients (16 of 70; 23%) ($X^2_1 = 5.30; P = 0.0213$). Antiemetic therapy was required in only nine (13%) of scopolamine-treated patients compared with 22 (32%) of the placebo-treated patients (table 3). No scopolamine-treated patients required more than one dose of droperidol whereas six placebo patients needed two or more doses (table 3).

Discharge time (time from arrival in the PACU until discharge from the hospital) was reduced from an average of 4.5 ± 1.5 h in the placebo group to 4 ± 1.3 h in the

**Table 1. Demographics and Times of Patch Application**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Placebo (n = 68)</th>
<th>Scopolamine (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>32.1 ± 5.7</td>
<td>32 ± 5.4</td>
</tr>
<tr>
<td>ASA physical status 1</td>
<td>61</td>
<td>62</td>
</tr>
<tr>
<td>ASA physical status 2</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Patch to anesthesia (h:min)</td>
<td>11:17 ± 2:15</td>
<td>11:12 ± 1:59</td>
</tr>
<tr>
<td>Duration anesthesia (h:min)</td>
<td>1:12 ± 0:18</td>
<td>1:13 ± 0:20</td>
</tr>
<tr>
<td>Patch in place (h:min)</td>
<td>37:31 ± 7:08</td>
<td>36:55 ± 7:49</td>
</tr>
</tbody>
</table>

All values are mean ± SD.
TRANSDERMAL SCOPOLAMINE REDUCES NAUSEA AND VOMITING

TABLE 2. Postoperative Nausea, Retching, and Vomiting

<table>
<thead>
<tr>
<th>Response</th>
<th>Placebo</th>
<th>Scopolamine*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>No discomfort</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>Mild nausea only</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Severe N, R &amp; V</td>
<td>42</td>
<td>62</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>100</td>
</tr>
</tbody>
</table>

* Test for linear trend. $X^2 = 8.87; P = 0.0029.$

scopolamine-treated group ($t = 1.99; P = 0.0487$). Following discharge from the hospital, ten patients (six having scopolamine and four placebo) experienced episodes of nausea, retching or vomiting with no significant difference between groups.

While 53 patients enrolled in the study were not included in the analysis of nausea, retching, and vomiting because of a breach in protocol, all patients except those who failed to apply the patch were included in the analysis of side effects. While no serious side effects were noted during the study, side effects occurred more frequently in patients treated with the scopolamine patch (91% vs. 45%; $P < 0.05$). The most commonly reported side effects are reported in Table 4. These side effects usually occurred after surgery, although a significant number of patients experienced either a dry mouth or dizziness prior to anesthesia and surgery. The patch was deemed acceptable by all patients except one. In that patient (scopolamine group) the patch was removed due to dizziness.

Discussion

Scopolamine crosses the blood-brain barrier and blocks cholinergic stimulation of the vomiting center from both the gastrointestinal tract and the vestibular center. Although scopolamine has effective antiemetic action, clinical utility of this benefit in the perioperative period has been limited. The principal reason is that im or iv scopolamine produces relatively high plasma concentrations and is associated with a high incidence of undesirable side effects including excessive sedation, agitation, and hallucinations. In addition, the short elimination half-life (approximately 1 h) of scopolamine limits its antiemetic efficacy when administered parenterally.

TABLE 3. Antiemetic Therapy

<table>
<thead>
<tr>
<th>Number of doses required</th>
<th>Placebo*</th>
<th>Scopolamine*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>None</td>
<td>46</td>
<td>67.7</td>
</tr>
<tr>
<td>One</td>
<td>16</td>
<td>23.5</td>
</tr>
<tr>
<td>Two or more</td>
<td>2</td>
<td>8.8</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>100</td>
</tr>
</tbody>
</table>

* Test for linear trend. $X^2 = 10.324; P = 0.0013.$

Our data confirm the safety and efficacy of transdermal scopolamine as an antiemetic following outpatient laparoscopy. Although the scopolamine transdermal delivery system clearly reduces motion sickness, published reports documenting the efficacy of prophylactic transdermal scopolamine (TDS) for reduction of nausea and vomiting during the perioperative period have been limited. Uppington et al. found that TDS decreases the incidence of postoperative nausea and vomiting in patients undergoing major gynecologic surgery. In patients receiving epidural morphine for postoperative analgesia, prophylactic placement of TDS has also been shown to reduce postoperative nausea and vomiting and decrease the need for alternative antiemetic therapy. However, when TDS was administered to children prior to strabismus surgery, no significant difference in postoperative nausea and vomiting could be detected.

The etiology of postoperative nausea and vomiting is multifactorial and complex. Patient-related factors (anxiety, obesity) as well as other causes (anesthetic agents, technique, hypotension, hypoxemia, pain) can contribute to or result in nausea and vomiting. We attempted to produce similar conditions while comparing treatment and placebo groups in order to control for some of the many possible causes of nausea and vomiting. While the incidence of nausea and vomiting experienced by our patients appears high, others have also reported similar findings. We employed our usual anesthetic technique for laparoscopy to evaluate the impact of transdermal scopolamine in this setting. Eliminating fentanyl and nitrous oxide from our anesthetic technique may have reduced our incidence of postoperative nausea and vomiting, although the influence of nitrous oxide remains controversial. In addition, the prophylactic administration of other antiemetic agents, such as droperidol, as well as eliminating agents that may increase nausea and vomiting, may be as effective as transdermal scopolamine. It is unlikely, however, that any parenterally administered agent will provide relief as long lasting as...
transdermal scopolamine. Additional clinical studies comparing different antiemetic agents in a variety of clinical settings are needed to determine the most efficacious therapies.

Despite an increase in side effects, patient acceptance of the transdermal patch was high and only one patient removed it. However, Gibbons reported the need to remove the patch in five of 21 children due to hallucinations or extreme agitation. Similar instances of agitation and hallucinations have been reported in the elderly with the use of transdermal scopolamine for motion sickness. Thus, the propensity for nausea and vomiting to occur with certain patients, anesthetics, and operations must be weighed against the potential for troublesome side effects if transdermal scopolamine is to be optimally applied. In addition, transdermal scopolamine is contraindicated in some patients with glaucoma or urinary bladder obstruction.

In conclusion, prophylactic transdermal scopolamine is a safe and effective antiemetic for the prevention of postoperative nausea and vomiting in patients undergoing outpatient laparoscopy. Selective application of transdermal scopolamine at least several hours prior to operation may bring most benefit to those patients with a predisposition toward nausea and vomiting, a history of significant postoperative nausea and vomiting, or to patients undergoing surgical procedures known to produce a high incidence of this problem.

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References