Title: TRANSDERMAL SCOPOLAMINE AS A PREANESTHETIC DRUG AND POSTOPERATIVE ANTIANUSELECTANT AND ANTIEMETIC

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Introduction. Nausea and vomiting are considered to be major elements of postoperative morbidity. Scopolamine, a frequently used anesthetic premedicant, is the most effective prophylactic antemetic available for motion sickness.1 A transdermal delivery system (Transderm-Escobal CIBA) has been developed to deliver scopolamine in small doses to the systemic circulation at a controlled rate. It protects against motion sickness during a 72 hour period while inducing few of the unpleasant pharmacological effects of scopolamine. The study examines the effectiveness of scopolamine administered transdermally to the surgical patient with respect to its premedicant sedative-antismologi- gogue and postoperative antiemetic properties.

Methods. A double-blind study was approved by the Research and Human Subject Review Committee of the Institute for Medical Research, and an approved informed consent was signed by each patient. Thirty healthy adults having gynecologic, gall bladder or orthopedic surgery comprised each of three groups: 1) Transdermal Scopolamine (TDS) in which scopolamine was applied to the posterior auricular skin as a circular unit (0.04 cm2/kg-1) 12 hours prior to surgery and removed 48 hours following surgery. The iv in vivo release rate is 2 ug/cm2·hr. Patients also received 0.2 ml normal saline IM 90 minutes prior to surgery; 2) Active Treatment Control (ATC) in which 0.0035 mg/kg-1 scopolamine IM was given 90 min prior to surgery and a placebo transdermal disc 12 hours earlier; 3) Placebo Control in which transdermal and IM placebos were given. Double-blind technique was employed. A standardized anesthetic regimen was employed: thiopental, succinylcholine, N2O-O2-enflurane-metocurine, with atropine-neostigmine reversal. Postoperative analgesia was established with morphine or meperidine IV in the recovery room and IM on the ward. Clinically significant vomiting was treated with promethazine 0.4 mg/kg-1 IM. IV fluids were regulated by protocol. A double-blinded nurse monitor-coordinator was employed. Patients were evaluated subjectively and objectively 1) at the time of IM premedicant and 30 and 60 min later for amount (none, mild, moderate, severe) of anxiety, sedation, restlessness, confusion, cycloplegia, dryness of mouth, nausea and vomiting; 2) on emergence; 3) in recovery room; 4) on ward at 4, 8, 20, 24, 28, 32 and 44 hours following surgery (appetite also noted). Data were analyzed using analysis of variance to determine if statistical differences (p<0.05) existed amongst the 3 groups.

Results. 1) Preop sedation: ATC>TDS and PC at 30 (p<0.01/0.05) and 60 (p<0.01/0.05) min. TDS>PC at 60 min (p<0.05). ATC and TDS>PC (p<0.01/0.05) for maximal sedation. Preop dry mouth: ATC>PC at 60 min (p<0.01). TDS>PC at 30 min (p<0.01). ATC and TDS>PC (p<0.01/0.05) for maximal dry mouth. 2) Anesthesia emergence: Dry mouth: ATC and TDS>PC (p<0.01/0.05). 3) Postop nausea and vomiting: ATC<PC at 8 (p<0.05), 20 (p<0.05) and 24 (p<0.05) hrs. TDS<PC at 20 hours (p<0.05) and was accompanied by increased appetite (p<0.05). Maximal postop nausea: TDS<PC and ATC (p<0.01/0.05). Maximal postop vomiting: TDS and PC (p<0.01/0.01). Postop dry mouth; TDS>ATC and PC (p<0.05/0.05) at 44 hours.

Discussion. This study demonstrated the effectiveness of scopolamine delivered transdermally as a premedicant sedative and antiemetic. The antiemetic effect persisted through anesthesia emergence and into the second postoperative day. The overall incidences of postoperative nausea and vomiting were low (gynecologic) gall bladder surgery) and made statistical differences of drug effects difficult to demonstrate; hence the inclusion of analysis of maximal degree of recorded nausea and vomiting. The observed low incidence may be attributed to the humanistic approach to study-patient care as well as utilization of modern anesthetic techniques. At specific times during the first postoperative day both injectable and transdermal scopolamine affected a lower incidence of vomiting than that recorded for the placebo control. Both forms of scopolamine decreased the maximal degree of vomiting but only the transdermal form reduced the maximal degree of nausea. The transdermal therapeutic system utilized in this study is the first rate-controlled transdermal pharmaceutical product and functionally is the equivalent of a carefully administered IV infusion. It was designed to separate the therapeutic (antiemetic) effect of scopolamine from its undesirable CNS side actions. It is concluded that the 72 hour application of transdermal scopolamine is an effective means for the utilization of scopolamine as both an anesthetic premedicant and postoperative antiemetic-antianuselectant, and it does not induce cycloplegia, confusion, psychomimetic reactions or other disturbing behavior.