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Original Contribution

Betamethasone in prevention of postoperative nausea and vomiting following breast surgery

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Abstract

Study Objective: To investigate whether betamethasone decreases the incidence of postoperative nausea/vomiting (PONV) and reduces postoperative pain following partial mastectomy.

Design: Prospective randomized, double-blinded study.

Setting: Operating room and Postanesthesia Care Unit of a university hospital.

Patients: 80 ASA physical status 1 and 2 women scheduled for elective breast cancer surgery.

Interventions: Patients were randomly allocated to two groups in double-blinded fashion: Group B (betamethasone; 37 pts) and Group C (control; 38 pts). Group B received 8 mg of betamethasone intravenously before the start of surgery.

Measurements: The rate of PONV and pain were recorded using a numeric rating scale (NRS; 0–10), as well as rescue doses of antiemetics (ondansetron) and analgesics (ketobemidone).

Main Results: There was a significant lower incidence of postoperative nausea (PON) scoring NRS ≥ 1 in Group B in the 4 to 12-hour period compared with Group C ($P = 0.02$). The cumulative incidence of PON was 57% in Group B versus 68% in Group C ($P = 0.27$). The overall incidence of postoperative vomiting (POV) was 18% and 20% in Groups B and C, respectively. Postoperative pain was reduced by 40% in Group B in the 4 to 12-hour period, but the mean dose of postoperative rescue analgesic did not differ between the groups.

Conclusions: Preoperative betamethasone reduces the severity of PONV and pain in patients undergoing elective breast surgery.

1. Introduction

Breast surgery is often associated with a high incidence of postoperative nausea and vomiting (PONV) and pain. About 47% to 68% of patients undergoing minor breast surgery, mastectomy, and breast reconstruction suffer from PONV [1,2]. Troublesome pain and PONV may prolong recovery and hospitalization, and are some of the most common causes of hospital admission following ambulatory surgery [3]. Since postoperative nausea, vomiting, and pain have a multifactorial pathophysiology, a multimodal approach of treatment usually is used today.

Glucocorticoids such as dexamethasone are useful agents in a multimodal strategy, decreasing both PONV and pain

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[4]. Ondansetron 4 mg and dexamethasone 4 mg are equally effective in the prevention of PONV following breast surgery [5]. The incidence of PONV was similar between the groups and was reduced to around 35%. This result agrees with early findings of a standardized general anesthetic with a volatile agent combined with a low dose of fentanyl intravenously (IV) [6].

Betamethasone, a potent, long-acting glucocorticoid steroid with anti-inflammatory and immunosuppressive properties but little or no mineral corticoid activity, has only been investigated in a few previous studies for potential postoperative antiemetic or analgesic properties [7,8]. Betamethasone has a plasma half-life of 5 hours and biological activity in tissues of more than 48 hours. Betamethasone is commercially available, inexpensive, and commonly used in daily practice, including conditions such as allergic reactions, asthma, cerebral edema, and spinal injury, and as an adjuvant to other PONV treatment.

Dexamethasone, with an equipotent anti-inflammatory and glucocorticoid effect as betamethasone [9], causes a reduction in the incidence of PONV, with a plateau effect at 8 mg [10], although other studies have demonstrated significant effects with lower doses [11].

The purpose of this study was to investigate whether betamethasone decreases the incidence of PONV and reduces postoperative pain following breast surgery.

2. Materials and methods

Approval from the Ethics Committee of Lund University Hospital and the Medical Products Agency (MPA) in Sweden was obtained for the study protocol. Eighty ASA physical status 1 and 2 women, aged 18 to 65 years, scheduled for elective partial mastectomy with or without axillary gland removal, gave written, informed consent to participate in the study. Exclusion criteria were previous PONV events or severe travel sickness, medication with corticosteroids or neuroleptics, known allergy to any of the study drugs, neurological disease, or pregnancy.

Patients were not treated with cytostatic drugs preoperatively. Patients were randomly allocated by sealed envelope assignment to two groups in double-blinded fashion, which resulted in 37 patients assigned to Group B (betamethasone) and 38 patients to Group C (control). Group B received 8 mg of IV betamethasone before the start of surgery, whereas Group C received no PONV prophylaxis before surgery.

All patients were premedicated with one gram of paracetamol orally 30 minutes before induction. Intravenous fluid with buffered 2.5% glucose solution was initiated in the operating room, starting with a bolus of 0.5 mL/kg body weight times the number of fasting hours, followed by a continuous infusion rate of 150 mL/hr. Monitoring included electrocardiogram, pulse oximetry, and noninvasive blood pressure. General anesthesia was induced with IV glycopyrrolate 0.2 mg, fentanyl 0.5 μg/kg, and propofol 2 to 2.5 mg/kg before insertion of a Laryngeal Mask Airway. Anesthesia was maintained with sevoflurane at an end-tidal concentration of 0.7 minimum alveolar concentration in 40% O_2 + 60% nitrous oxide using a fresh gas flow of one L/min. All patients maintained spontaneous breathing in a circle system with a CO_2 absorber. A second dose of fentanyl 0.5 μg/kg was given prior to skin incision. Additional doses of fentanyl (0.5 μg/kg) were given if systolic blood pressure increased above the baseline levels assessed at rest during the preoperative evaluation.

The nursing staff in the recovery room, blinded to group allocation details, used a numeric rating scale (NRS; 0–10) for evaluating the degree of nausea and pain (from 0 = no nausea or pain to 10 = worst nausea or pain imaginable) starting at patient arrival at the recovery room (time = 0), and then every hour for the first 6 hours, followed by the time points 12, 18, and 24 hours postoperatively. If pain intensity was ≥ 5, patients received IV ketobemidone in doses of 1 to 2 mg until effect (pain intensity ≤ 4). All patients received one gram of paracetamol orally every sixth hour. Nausea was treated with IV ondansetron 4 mg if NRS intensity was ≥ 5. The total dose of ketobemidone and ondansetron administered was recorded. Patients who were discharged before the end of the study period were contacted by telephone and asked about experiences of nausea, vomiting, and pain using the same NRS.

2.1. Statistics

A power analysis with NRS scoring of nausea and pain as the primary variable showed that a study population of 72 patients (36 per group) was needed to detect a statistically significant difference at the 5% level. A clinically relevant difference of 1.0 on NRS and an average standard deviation of 2.0, with this sample size, reached a power of 0.85 [12]. Data are presented as incidence, ie, percentages of patients, experiencing nausea or pain in the different time intervals. The Chi-Square and Fisher's Exact test were used for statistical analysis of these parameters. The other data were analyzed using Student's *t*-test or the Mann–Whitney

Table 1 Patient demographics

	Group B (betamethasone)	Group C (control)
Number	37	38
Age (yrs)	53 [35–65]	55 [31–66]
BMI (kg/m^2)	26.0 [18–40]	25.3 [16–38]
Smokers (%)	23	24
Duration of anesthesia (min)	95 [39–162]	97 [36–207]

Data are means, ranges, or relative frequencies. Values in brackets are ranges.
BMI=body mass index.