British Journal of Anaesthesia **83 (5)**: 772–5 (1999)

Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy

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We have evaluated the antiemetic effect of i.v. dexamethasone compared with saline in the prevention of nausea and vomiting after laparoscopic cholecystectomy. We studied 90 patients requiring general anaesthesia for laparoscopic cholecystectomy, in a randomized, double-blind, placebo-controlled study. The dexamethasone group ($n=45$) received dexamethasone 8 mg i.v. and the saline group received saline 2 ml i.v. at induction of anaesthesia. Anaesthesia was maintained with isoflurane in oxygen. We found that 10% of patients in the dexamethasone group compared with 34% in the saline group reported vomiting ($P<0.05$). Of note, the total incidence of nausea and vomiting was 23% in the dexamethasone group and 63% in the saline group ($P<0.001$). We conclude that dexamethasone 8 mg significantly decreased the incidence of nausea and vomiting after laparoscopic cholecystectomy.

Br J Anaesth 1999; **83**: 772–5

Keywords: surgery, laparoscopy; vomiting, nausea; vomiting, incidence; vomiting, antiemetics; pharmacology, dexamethasone

Accepted for publication: April 28, 1999

Since 1981, dexamethasone has been reported to be effective in reducing the incidence of emesis in patients undergoing chemotherapy.[1–5] The antiemetic effect of dexamethasone was reported to be equal to or better than the 5-HT_3 receptor antagonists, such as ondansetron and granisetron.[4 5] Recently, dexamethasone has also been reported to be effective in reducing the incidence of postoperative nausea and vomiting (PONV) in paediatric patients undergoing strabismus repair, tonsillectomy and adenoidectomy,[6–10] and in women undergoing major gynaecological surgery.[11–14]

In patients undergoing laparoscopic cholecystectomy for cholelithiasis, high incidences of PONV have been reported (53–72%).[15–19] As dexamethasone has an antiemetic effect in various situations,[6–14] we thought that it may also be effective in the prevention of emesis after laparoscopic cholecystectomy. Therefore, we have evaluated the antiemetic effect of i.v. dexamethasone in the prevention of nausea and vomiting after laparoscopic cholecystectomy in patients suffering from cholelithiasis.

Patients and methods

After obtaining approval from the Institutional Review Board and informed consent, we studied 90 patients, ASA I or II, aged 30–55 yr, undergoing general anaesthesia for elective laparoscopic cholecystectomy, in a randomized, double-blind, placebo-controlled study. Patients with a history of motion sickness or who had received antiemetics within 48 h before surgery were excluded. All operations were performed between 08:00 and 14:00.

In the preoperative holding area, patients were allocated randomly to one of two groups ($n=45$ each) using a computer-generated random number table. Study medications were prepared by a single nurse anaesthetist in identical 2-ml syringes to ensure blinding of the anaesthetists. One minute before induction of anaesthesia, patients in the dexamethasone group received dexamethasone 8 mg i.v. and those in the saline group received saline i.v. Patients and investigators who collected the postoperative data were blind to the randomization.

The anaesthetic was standardized. Anaesthesia was induced with propofol 2–2.5 mg kg^{-1} i.v., glycopyrrolate 0.2 mg i.v. and fentanyl 2 μg kg^{-1} i.v. Tracheal intubation was facilitated with vecuronium 0.15 mg kg^{-1} i.v. Anaesthesia was maintained with 1.0–2.5% (inspired concentration) isoflurane in oxygen. Ventilation was controlled mechanically and adjusted to maintain an end-tidal carbon dioxide partial pressure of 4.6–5.2 kPa, with an anaesthetic–respiratory gas analyser (Capnomac Ultima; Datex, Helsinki, Finland). Neuromuscular block was maintained with vecuronium i.v. After tracheal intubation, a nasogastric tube was placed to promote baseline emptying of the

stomach of air and gastric contents. During surgery, patients were positioned in the reverse Trendelenburg position with the right side of the bed elevated. The abdomen was insufflated with carbon dioxide, with an intra-abdominal pressure of 10–16 mm Hg. Laparoscopic cholecystectomy was performed under video guidance with four punctures of the abdomen. At the end of surgery, glycopyrrolate 0.6 mg i.v. and neostigmine 3 mg i.v. were administered for antagonism of neuromuscular block, and the trachea was extubated.

After surgery, patients were observed for 24 h. When patients complained of pain and requested analgesia, morphine 2 mg i.v. was given and a patient-controlled analgesia (PCA) machine (Lifecare 4200 PCA system, Abbott Laboratories, North Chicago, IL, USA) was connected to the patient's i.v. catheter. The device was programmed for on-demand delivery of morphine 1 ml (1 mg), with a minimal lockout interval of 10 min and a maximum dose of 6 mg h^{-1}. All patients were instructed on the use of the PCA device before surgery.

Throughout the 24-h study, vital signs such as arterial pressure, heart rate and ventilatory frequency were monitored every 4 h except during sleep. Arterial oxygen saturation (Sp_{O_2}) was monitored continuously using a pulse oximeter (HP78352C, Hewlett Packard, Boeblingen, Germany).

The incidence of nausea or vomiting was recorded every 4 h for 24 h, except during sleep. We made no distinction between vomiting and retching (i.e. a retching event was considered as a vomiting event). Nausea and vomiting were evaluated on a three-point ordinal scale (0=none, 1=nausea and 2=vomiting). Vomiting was treated with metoclopramide 10 mg i.v., repeated if necessary. Pain intensity was assessed using a 10-cm visual analogue scale (VAS; 0=no pain, 10=most severe pain). As postoperative pain after laparoscopic cholecystectomy has been reported to be more intense during the first 4 h,[17 19] we measured VAS pain scores and demand–delivery of PCA morphine at 1-h intervals over the first 4 h after operation. VAS pain scores at 24 h were also recorded.

Sample size was predetermined. We expected a 30% difference in the incidence of nausea and vomiting between groups, given an SD of 40%. The α error was set at 0.05 (two-sided) and β error at 0.10. The projected sample size was 37 patients in each group. Parametric data were analysed by an unpaired *t* test; the incidence of nausea and vomiting was analysed using Fisher's exact test. VAS pain scores and demand–delivery of PCA morphine were analysed using the Mann–Whitney *U* test. $P<0.05$ was considered significant.

Results

Of the 90 patients enrolled, 78 completed the study. Twelve patients who required open cholecystectomy were excluded. Patient characteristics were similar between groups (Table 1).

Table 1 Patient characteristics (mean (SD or range) or number). No significant differences between groups

	Dexamethasone group	Saline group
n	40	38
Age (yr)	41.3 (34–54)	43.2 (30–55)
Weight (kg)	74.1 (7.6)	71.3 (8.4)
Sex (M/F)	16/24	12/26
Duration of anaesthesia (min)	96.2 (25.8)	94.1 (24.5)
Duration of surgery (min)	68.1 (20.2)	63.8 (16.4)
Duration of CO_2 insufflation (min)	60.3 (19.4)	58.4 (15.8)

In the 4 h after operation, patients in both groups made a comparable number of demands and consumed similar amounts of morphine via the PCA (Table 2). Pain scores were also similar (Table 2). At 24 h after surgery, both groups reported similar median pain scores (1.6 in the dexamethasone group and 1.8 in the saline group).

Only 10% of patients in the dexamethasone group, compared with 34% in the saline group, reported vomiting ($P<0.05$) (Table 3). The total incidence of nausea and vomiting was 23% in the dexamethasone group compared with 63% in the saline group ($P<0.001$) (Table 3). During the 24-h study, arterial pressure, heart rate and ventilatory frequency were stable and there were no significant differences between groups. No patient had an Sp_{O_2} less than 90%.

Discussion

Laparoscopic surgery has decreased the morbidity associated with cholecystectomy and has become an accepted procedure for symptomatic cholelithiasis. [20–22] However, high incidences of PONV (53–72%) have been reported.[15–19] In our study, we found that the total incidence of PONV was 63% in the saline control group. After administration of dexamethasone, the incidence of PONV decreased significantly to 23%.

Dexamethasone was first reported to be an effective antiemetic agent in patients receiving cancer chemotherapy in 1981.[1] Since then, several studies have shown that dexamethasone is equal to or better than other antiemetic agents, such as metoclopramide, prochlorperazine, droperidol, ondansetron and granisetron, in preventing nausea and vomiting associated with chemotherapy.[2–5] Recently, dexamethasone has also been reported to be effective in the prevention of nausea and vomiting after paediatric and gynaecological surgery.[6–14] We found that dexamethasone was also effective in the prevention of nausea and vomiting after laparoscopic cholecystectomy.

The aetiology of nausea and vomiting after laparoscopic cholecystectomy is not fully understood. Risk factors such as a long period of carbon dioxide insufflation,[19] gall bladder surgery,[15–18] intraoperative use of isoflurane, fentanyl and glycopyrrolate,[23 24] female sex[17 23] and postoperative use of PCA morphine may contribute to these episodes. As these risk factors may interfere with the interpretation of the study data, we controlled these within the study design. All

Table 2 Postoperative hourly VAS pain scores, patient-controlled analgesia (PCA) demands, and dose of morphine received by the dexamethasone (Dex.) and saline groups. Values are median (range). No significant differences between groups

	VAS score		PCA demands		PCA morphine (mg)	
Time (h)	**Dex.**	**Saline**	**Dex.**	**Saline**	**Dex.**	**Saline**
1	3.5 (2.3–5.9)	3.8 (2.2–6.8)	11 (4–18)	14 (4–21)	3 (1–6)	4 (2–6)
2	2.8 (1.8–4.8)	3.1 (1.9–5.3)	6 (2–12)	8 (3–18)	2 (0–4)	3 (0–6)
3	2.2 (1.6–4.6)	2.4 (1.5–4.7)	4 (0–9)	5 (2–8)	2 (0–3)	2 (0–4)
4	2.1 (1.2–3.9)	2.3 (1.5–4.5)	3 (0–7)	4 (0–6)	1 (0–2)	2 (0–3)

Table 3 Incidence of nausea, vomiting, or both, after laparoscopic cholecystectomy in the dexamethasone and saline groups. Data are numbers of patients (%) with symptoms in a 24-h period (*P* values, Fisher's exact test)

	Dexamethasone group	Saline group	*P*
n	40	38	
Nausea	5 (13%)	11 (29%)	ns
Vomiting	4 (10%)	13 (34%)	<0.05
Total	9 (23%)	24 (63%)	<0.001

patients received laparoscopic cholecystectomy for cholelithiasis by the same team of anaesthetists and surgeons. Duration of anaesthesia, surgery and carbon dioxide insufflation, and anaesthetic drugs were similar in both groups. In addition, after random allocation, sex distribution in both groups was similar. Patients in both groups also consumed similar amounts of PCA morphine. Therefore, we believe that the differences in the incidence of PONV were attributed to the study drugs.

The exact mechanism of the antiemetic action of dexamethasone is not known. However, there have been some suggestions, such as central or peripheral inhibition of the production or secretion of serotonin,[25] central inhibition of the synthesis of prostaglandins[26] or changes in the permeability of the blood–brain barrier to serum proteins.[27]

We found that dexamethasone did not affect the severity of pain or the demand–delivery of PCA morphine. As dexamethasone has a potent anti-inflammatory effect,[28] theoretically it may be beneficial for postoperative pain. However, in our study, a potent opioid (fentanyl 2 $\mu g\ kg^{-1}$) was administered with dexamethasone before surgery. Therefore, the influence of dexamethasone on postoperative pain may have been masked.

A wide dose range of dexamethasone (8–32 mg) has been used in the prophylaxis of emesis related to chemotherapy and after paediatric and gynaecological surgery.[2–14] Dexamethasone 8 mg was used most frequently and was the reason behind our chose of 8 mg.

Adverse effects related to a single dose of dexamethasone are extremely rare. After an extensive literature search, we were unable to find a report of side effects associated with the use of a single dose of dexamethasone. Less than 24 h of dexamethasone therapy is considered safe and almost without adverse effects.[6–14]

In summary, prophylactic dexamethasone 8 mg significantly reduced the incidence of nausea and vomiting after laparoscopic cholecystectomy and it may be a valuable treatment in this situation.

Acknowledgements

This work was supported by Grant DOII 88-11R-402 from the National Health Research Institutes, Taiwan.

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