

Dexamethasone is a cost-effective alternative to ondansetron in preventing PONV after paediatric strabismus repair

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This study evaluated the antiemetic efficacy, cost-effectiveness and clinical utility of prophylactic ondansetron and dexamethasone compared with placebo in the prevention of postoperative nausea and vomiting (PONV) in 135 children (2–15 yr, ASA I–II) undergoing strabismus repair. After induction with halothane and nitrous oxide in oxygen or i.v. thiopental, the children received i.v. dexamethasone 1 mg kg⁻¹ to a maximum of 25 mg, ondansetron 100 µg kg⁻¹ to a maximum of 4 mg or placebo (*n*=45). Episodes of PONV were recorded for the first 24 h after the operation. True outcome measures (parental satisfaction score, duration of stay in the postanesthesia care unit and fast tracking time), therapeutic outcome measures (number needed to prevent (NNTP) PONV) and the cost to benefit a child with each drug were analysed. The incidence and severity of PONV in the first 24 h were significantly less in the dexamethasone and ondansetron groups than in the placebo group (*P*<0.05). The incidence (*P*=0.04) and severity (*P*=0.03) of PONV at the 6–24 h epoch were significantly less in the dexamethasone group than in the ondansetron group. Recovery time (*P*=0.07), fast tracking time (*P*=0.6), parental satisfaction scores (*P*=0.08) and NNTP PONV were comparable (NNTP=2) in both the ondansetron and the dexamethasone group. The cost to benefit a child with dexamethasone was approximately 22 times less than that of ondansetron.

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Postoperative nausea and vomiting (PONV) remains a distressing and common problem after strabismus repair despite the use of currently available antiemetics. Ondansetron is commonly used because of its efficacy and safety compared with other antiemetics, but its use has been criticized because of cost. A meta-analysis that reviewed the efficacy and safety data for ondansetron for preventing PONV has challenged the practice of routine prophylactic ondansetron based on benefit and risk.¹ Moreover, a number of studies and meta-analyses which evaluated the effects of ondansetron on PONV have reported surrogate outcome measures, such as the incidence of PONV and the number of emetic episodes per patient, rather than more meaningful outcome measures, such as patient satisfaction, hospital stay and the incidence of unanticipated hospital admission.² The higher cost of ondansetron has been a significant factor limiting its routine prophylactic use. Dexamethasone

1 mg kg⁻¹ (maximum 25 mg) has been shown to be an effective prophylactic antiemetic for PONV in children undergoing ambulatory adenotonsillectomy.³ In our study, we aimed to compare the efficacy, safety, cost-effectiveness and clinical utility of prophylactic dexamethasone, ondansetron and placebo with clinically more useful non-surrogate, therapeutic and pharmacoeconomic outcome measures.

Materials and methods

After obtaining institutional review board approval and informed parental consent, in this prospective, randomized, placebo-controlled, double-blinded study we enrolled 135 ASA physical status I or II children between the ages of 2 and 15 yr who were undergoing strabismus repair under general anaesthesia. We excluded children who had

received drugs with antiemetic effects (e.g. phenothiazines, benzamides, scopolamine, corticosteroids and tricyclic antidepressants) in the 24 h before surgery. Children did not consume milk or solid food for at least 6 h before operation; clear fluids were allowed until 3 h before induction. We did not control the volume of fluid children ingested within 3 h before surgery.

Children were not premedicated. Anaesthesia was induced with halothane and nitrous oxide in oxygen via a facemask or with i.v. thiopental. After induction of anaesthesia and establishment of venous access, tracheal intubation was facilitated with 100 $\mu\text{g kg}^{-1}$ i.v. vecuronium, and anaesthesia was maintained with halothane and nitrous oxide along with 0.5 mg kg^{-1} of i.v. meperidine. A random number generator was used to assign each child prospectively to receive dexamethasone 1 mg kg^{-1} (maximum 25 mg), ondansetron 100 $\mu\text{g kg}^{-1}$ (maximum 4 mg) or saline placebo. The study drugs were prepared by an anaesthetist not otherwise involved in patient care, to a fixed volume of 5 ml, to maintain the double-blind nature of the study. Intraoperative i.v. fluid management consisted of administration of lactated Ringer's solution sufficient to correct half of the preoperative fluid deficit in the first hour, followed by maintenance fluids according to body weight. At the end of the procedure, residual neuromuscular blockade was antagonized with 50 $\mu\text{g kg}^{-1}$ of neostigmine and 10 $\mu\text{g kg}^{-1}$ of glycopyrrolate and the trachea was extubated when the child was awake. The gastric contents were aspirated by suction via a tube passed before extubation. No nasogastric tube was left *in situ* during the procedure.

After operation, all children were transported to the postanesthesia care unit (PACU). The anaesthetist who provided intraoperative care assessed postanesthetic recovery using the modified Aldrete scoring system.⁴ Time to achieve complete recovery (score 10) was recorded for all children. After operation, analgesia was provided when older children complained or younger children cried in pain.⁵ Oral ibuprofen 10 mg kg^{-1} was given as the analgesic of first choice, and for pain in children who had PONV in the immediate postoperative period in the PACU, ketorolac 0.5 mg kg^{-1} i.v. was administered as the analgesic of second choice by the anaesthetist who provided intraoperative care. Intravenous fluid comprised lactated Ringer's solution replacing the remaining fluid deficit plus maintenance fluids in the recovery room.

All episodes of nausea and vomiting in the first 24 postoperative hours in the hospital during the intervals of 0–6 h and 6–24 h were evaluated using a numeric scoring system for PONV (0=no nausea or vomiting, 1=nausea but no vomiting, 2=vomiting once in 30 min or more, 3=persistent nausea (>30 min) or two or more vomits in 30 min) by the PACU and ward nursing staff, who were aware of the nature of the study but blinded to the study drug. We did not assess nausea in very young children (less than 6 yr of age). In older children, nausea was assessed by an observer and by self-reporting. Any child having a

PONV score of 3 was considered to have severe PONV and was treated with metoclopramide 150 $\mu\text{g kg}^{-1}$ i.v. as a rescue antiemetic. The time to achieve eligibility for fast tracking (fast tracking time, FTT) was calculated as the time from the discontinuation of anaesthesia to the time at which the child had a patent airway without support, no PONV, no pain and a recovery score of 10.

The criteria for discharge from PACU to ward included stable vital signs, adequate pain control and no nausea and vomiting in the first 2 h after surgery. Children who had PONV and pain in the first 2 h of stay were observed in PACU till they had remained free of PONV and pain for an hour.

Finally, at the end of 24 h after surgery, the primary caretaker was asked to give a global assessment of their satisfaction over the entire postoperative experience of the child (parental satisfaction score) using an 11-point verbal numeric scoring system (0=not at all satisfied, 10=fully satisfied).

Statistical analysis

Power analysis before the study showed that 41 children would be required in each group to have a 95% chance ($\beta=0.05$) of detecting a 50% relative reduction in PONV, from our Institute's basal incidence of 80%⁶ with a type-1 error of 5% ($\alpha=0.05$) and 95% confidence interval limits (Version 6.04b, Epi Info, Centre for Disease Control, Atlanta, GA, USA, and World Health Organization, Geneva, Switzerland, 1997). Two-sample *t*-tests and Mann–Whitney *U*-tests were used to compare the age, weight, duration of surgery, anaesthesia, recovery, fast tracking and PACU stay, perioperative fluid and analgesic requirements, and the parental assessment scores of the child's perioperative experience. The incidence and severity (requirement of rescue antiemetic) of PONV were compared by χ^2 and Fisher's exact tests with Yates' continuity correction wherever appropriate. The positive 'number needed to prevent' (NNTP) PONV (which indicates how many children had to be exposed to dexamethasone or ondansetron to prevent PONV) was calculated as the reciprocal of the absolute risk reduction of the incidences of PONV from the basal (placebo) incidence for children who received dexamethasone or ondansetron. The cost to benefit a child was calculated as the drug acquisition cost per patient times the NNTP for dexamethasone or ondansetron. *P*-values less than 0.05 were considered statistically significant, and data are presented as mean (SD) unless otherwise specified.

Results

Patient and clinical data, such as age, gender, weight, physical status, duration of surgery and anaesthesia, numbers of muscles operated, perioperative fluid, analgesic requirements and recovery time, were similar in all groups (Table 1).

Table 1 Demographic and clinical data. Sex, ASA status, previous PONV and oculocardiac reflex (OCR) are expressed as the number of children. Other values are expressed as mean (SD). All groups were statistically comparable

	Dexamethasone group (n=45)	Ondansetron group (n=45)	Placebo group (n=45)
Age (yr)	7.6 (3.8)	6.9 (3.5)	7.11 (2.91)
Sex (M/F)	21/24	18/27	23/22
Weight (kg)	20.6 (9.8)	21.9 (10.2)	20 (8.36)
ASA physical status (I/II)	44/1	43/2	41/4
Induction (halothane/thiopental)	33/12	28/17	31/14
Duration of surgery (min)	45.9 (21.7)	47.2 (10.9)	49.11 (16.83)
Recovery time (min)	15.4 (11.7)	15.9 (7.6)	20.4 (17.8)
Intraoperative			
fluids (ml kg ⁻¹)	16.7 (5.2)	16.2 (5.5)	18.1 (5.61)
analgesics (mg)	10.8 (4.9)	11.1 (5.1)	10 (5)
Previous PONV	2/45	4/45	4/45
OCR requiring atropine	4/45	5/45	6/45

Table 2 Incidence and severity of PONV. Values are expressed as the number (percentage) of children. ** $P<0.05$ (dexamethasone versus ondansetron, dexamethasone versus placebo). Dexamethasone versus placebo: incidence and severity of PONV at 0–6 h ($P=0.0001$ and $P=0.0114$ respectively), 6–24 h ($P=0.0031$ and $P=0.0006$) and 0–24 h ($P<0.0001$ and $P=0.0000$). Ondansetron versus placebo: incidence and severity of PONV at 0–6 h ($P=0.0000$ and $P=0.0053$ respectively), 0–24 h ($P=0.0001$ and $P=0.0007$) and comparable incidence and severity at 6–24 h ($P=0.4802$ and $P=0.2277$) respectively

PONV outcome	Dexamethasone group (n=45)	Ondansetron group (n=45)	Placebo group (n=45)
PONV: incidence			
0–6 h	11 (24.4)	8 (17.8)	30 (66.7)
6–24 h	3 (6.7)	11 (24.4)	14 (31.1)
0–24 h	11 (24.4)	15 (33.3)	34 (75.6)
Nausea: 24 h incidence	1 (2.2)	6 (13.3)	19 (42.2)
PONV: score (0–24 h)			
0	34 (75.6)	30 (66.6)	11 (24.4)
1	0 (0)	1 (2.2)	0 (0)
2	3 (6.6)	1 (2.2)	5 (11.1)
3 (rescue antiemetic)	8 (17.8)	13 (28.9)	29 (64.4)
Rescue requirements (score 3)			
early (0–6 h)	8 (17.8)	7 (15.6)	19 (42.2)
late (6–24 h)	0 (0)**	6 (13.3)	10 (30.3)

The incidence of PONV was significantly greater in the placebo group than in the ondansetron ($P=0.0001$) and dexamethasone groups ($P<0.0001$) (Table 2). The incidences in the dexamethasone (24.4%) and ondansetron (33.3%) groups were comparable ($P=0.49$). The incidence of early PONV (0–6 h) was significantly lower in the ondansetron ($P<0.0001$) and dexamethasone groups ($P=0.0001$) than in the placebo group. The early incidence was comparable in the ondansetron (17.8%) and dexamethasone (24.4%) groups ($P=0.61$). The incidence of PONV in the late postoperative period (6–24 h) was significantly lower in the dexamethasone group (6.67%) than in the ondansetron (24.4%) ($P=0.04$) and placebo groups (31.1%) ($P=0.003$). The incidence of late PONV was comparable in the ondansetron and placebo groups ($P=0.48$). The incidences of PONV in children who were induced with halothane or thiopental in each group were comparable (Table 1).

The severity of early PONV was significantly lower in the ondansetron ($P=0.005$) and dexamethasone ($P=0.01$) groups compared with placebo. The severity of early PONV (requirement for rescue antiemetics) (0–6 h epoch) was

comparable in the ondansetron (15.6%) and dexamethasone (17.8%) groups ($P>0.99$). The severity of late PONV (6–24 h epoch) was significantly less in the dexamethasone group (0%) than in the ondansetron (13.33%) ($P=0.03$) and placebo (30.3%) ($P=0.0006$) groups. The severity of late PONV in the ondansetron group was similar to that in the placebo group ($P=0.23$).

Recovery time was comparable in all groups. The FTT was similar in the ondansetron (28.4 (31.7) min) and dexamethasone (36.6 (44.5) min) groups ($P=0.67$). The FTT in the placebo group (67.5 (60.00) min) was significantly greater than that in the ondansetron ($P=0.0003$) and dexamethasone ($P=0.007$) groups. Duration of stay in the PACU was significantly longer in the placebo group (153.66 (41.41) min) than in the ondansetron ($P=0.0002$) and dexamethasone ($P=0.007$) groups, but comparable between the ondansetron and dexamethasone groups ($P=0.16$). The positive NNTP was comparable in the ondansetron (NNTP=2.36) and dexamethasone (NNTP=1.95) groups. The number of postoperative analgesic supplements in dexamethasone group (1.04 (0.7)) was significantly lower than in the ondansetron (1.7 (0.5)) and placebo (1.7 (0.7))

Table 3 True, therapeutic outcome measures and side-effects. NNTP PONV and side-effects are expressed as the number of children. Other values are expressed as mean (SD). Ondansetron and dexamethasone were statistically comparable for true, therapeutic outcome measures and side-effects. Ondansetron and dexamethasone groups had significantly higher parental satisfaction scores than the placebo group ($P<0.0001$). Both FTT and PACU stay were significantly longer in the placebo group than in the ondansetron ($P=0.0003$ and $P=0.0002$ respectively) and dexamethasone groups ($P=0.0068$ and $P=0.0074$)

PONV outcome	Dexamethasone group (<i>n</i> =45)	Ondansetron group (<i>n</i> =45)	Placebo group (<i>n</i> =45)
FTT (min)	36.6 (44.5)	28.44 (31.7)	67.46 (59.96)
PACU stay (min)	134.0 (24.7)	127.7 (17.2)	153.66 (41.14)
NNTP PONV	1.95	2.36	–
Side-effects			
Headache	3	4	2
Facial flushing	5	0	0
Wound problems	0	0	0
Parental satisfaction score	8.8 (1.6)	8.2 (1.6)	6.26 (2.24)

groups ($P=0.0000$) but comparable in the ondansetron and placebo groups ($P>0.99$). In the dexamethasone group, 11.1 and 7.1% of the children had facial flushing and headache respectively, and 8.8% of children in the ondansetron group had headache (Table 3). The parental assessment scores for the children's perioperative experiences were comparable in the dexamethasone and ondansetron groups ($P=0.08$). Children in the ondansetron and dexamethasone groups had significantly higher parental satisfaction scores than those in placebo group ($P<0.0001$).

The drug acquisition cost per patient was US\$0.47 (0.50 euros) in the dexamethasone group and US\$8.72 (9.26 euros) in the ondansetron group. The cost to benefit per patient (NNTP times the institutional drug acquisition cost) was 22.4 times higher in the ondansetron group than in the dexamethasone group.

Discussion

In children, strabismus repair is associated with a high incidence of PONV,⁷ which ranges from 41 to 88% in those who have not received antiemetic prophylaxis.^{8–9} Ondansetron had been shown to be effective in the prevention of PONV following strabismus repair.^{10–12} However, a meta-analysis¹ has challenged the clinical utility of prophylactic ondansetron in preventing PONV on the basis of its efficacy and safety. Recently, prophylactic use of ondansetron at $75 \mu\text{g kg}^{-1}$ has been shown to reduce the incidence of PONV from 80% to 30% and to improve the true outcome after strabismus repair in children.⁶ However, the higher cost of ondansetron remains a major concern.

Dexamethasone has been shown to be an effective antiemetic in children undergoing ambulatory adenotonsillectomy.^{3–13} Though the mechanisms of its antiemetic effects are still unclear, it may act through prostaglandin antagonism,¹⁴ serotonin inhibition in the gut¹⁵ and by releasing endorphins.¹⁶

In our study, the incidence of PONV was 33.3% in the ondansetron group, 24.4% in the dexamethasone group and

75.6% in the placebo group. Dexamethasone was as effective as ondansetron in decreasing the incidence and severity of PONV in the first 24 h after operation. The antiemetic efficacy of dexamethasone was most pronounced in the late postoperative period. The incidence and severity of PONV in the late postoperative period were significantly lower in the dexamethasone group than in the ondansetron and placebo groups. This prolonged antiemetic efficacy of dexamethasone may be explained by its prolonged biological half-life (36–72 h). Similar findings have been reported in patients undergoing ambulatory surgery.^{13–17–18} Dexamethasone has been shown to provide greater protection from delayed chemotherapy-induced nausea and vomiting compared with ondansetron¹⁹ and granisetron.²⁰

In this trial, the groups were comparable with respect to patient characteristics, surgical procedure, anaesthetics administered and i.v. fluids used in the perioperative period. Therefore, the difference in the incidence and severity of PONV and true and therapeutic outcome measures among the groups in this trial can be attributed to the study antiemetics that were administered.

Betamethasone prophylaxis has been shown to decrease postoperative pain and late PONV in ambulatory surgical patients.²¹ In our study, the requirement for postoperative analgesic supplements was significantly lower in the dexamethasone group. The antiemetic and analgesic effects of dexamethasone were more pronounced in the late postoperative period. This probably added to the comfort of the patients when they were discharged home.

In our trial, we used parental assessment scores of the child's perioperative experience, duration of PACU stay and fast tracking time as true outcome measures. Dexamethasone was as effective as ondansetron in improving true outcome measures in this group of patients.

We included a placebo group to allow us to calculate the absolute reduction in the risk of PONV, and thereby the NNTP. The NNTP indicates how many children need to be exposed to the treatment in order to prevent PONV in one of them. Meta-analyses have reported that the best NNTP with

the well-documented regimens were between 4 and 6 for ondansetron¹ and 4 for dexamethasone.²² In our trial, NNTP with dexamethasone (1 mg kg⁻¹) and ondansetron (100 µg kg⁻¹) was approximately 2. In the meta-analyses,^{1, 22} NNTP was reported to be greater possibly because of the heterogeneous patient population and defects in the meta-analyses of PONV.^{6, 23}

The timing of prophylactic antiemetic administration is important. We administered the drugs at the beginning of the procedure. It has been confirmed recently that dexamethasone is more effective when administered at induction than when given at the end of anesthesia.²⁴ Though it has been suggested that ondansetron given at the end of surgery will reduce antiemetic requirements more effectively in the postoperative period,²⁵ in short surgical procedures like strabismus surgery administering ondansetron at the beginning or end of surgery did not affect the outcome.²⁶

In this pharmacoeconomic era, the cost to benefit a patient for prophylactic antiemetic is a significant factor. In the ondansetron group, the acquisition cost of drug per patient was 18.6 times higher than in the dexamethasone group. The cost to benefit a patient (i.e. NNTP times the cost of drug per patient) was 22 times higher in the ondansetron group than in the dexamethasone group. This reasserts the value of prophylactic dexamethasone as a cost-effective alternative to ondansetron.

Facial flushing was seen in five children (11%) after administration of dexamethasone. There were no associated haemodynamic changes in any of these patients. We requested the surgeons to inform us if any child was admitted with wound infection or delayed wound healing. There were no wound-related problems in any group. Headache was seen in three, four and two children in the dexamethasone, ondansetron and placebo groups respectively. Our sample size was inadequate to identify an adverse effect with an incidence of less than 2.2% (100/45). Meta-analysis may be effective in identifying adverse effects with low incidence. The recent meta-analysis on dexamethasone and PONV did not reveal any significant side-effects.²² As yet, there is no evidence in the literature for dexamethasone's potential side-effects, such as hyperglycaemia, delayed wound healing and hypothalamic-pituitary adrenal axis suppression after a single dose.

References

- 1 Tramer MR, Reynolds DJ, Moore RA, McQuay HJ. Efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting: a quantitative systematic review of randomised placebo-controlled trials. *Anesthesiology* 1997; **87**: 1277-89
- 2 Fisher DM. The 'big little problem' of postoperative nausea and vomiting: do we know the answer yet? *Anesthesiology* 1997; **87**: 1271-3
- 3 Pappas AL, Sukhani R, Hotaling AJ, et al. The effect of preoperative dexamethasone on the immediate and delayed postoperative morbidity in children undergoing adenotonsillectomy. *Anesth Analg* 1998; **87**: 57-61
- 4 Aldrete JA. The post-anaesthesia recovery score revisited. *J Clin Anesth* 1995; **7**: 89-91
- 5 Pawar DK. Pain management. In: Brown TCK, Fisk GC, eds. *Anaesthesia for Children*, 2nd Edn. Melbourne: Blackwell Scientific Publications, 1992; 127-37
- 6 Sadhasivam S, Shende D, Madan R. Prophylactic ondansetron in prevention of postoperative nausea and vomiting following pediatric strabismus surgery: a dose response study. *Anesthesiology* 2000; **92**: 1035-42
- 7 Abramowitz MD, Oh TH, Epstein BS, et al. The antiemetic effect of droperidol following outpatient strabismus surgery in children. *Anesthesiology* 1983; **59**: 579-83
- 8 Hardy JF, Charest J, Girouard G, Lepage Y. Nausea and vomiting after strabismus surgery in pre-school children. *Can Anaesth Soc J* 1986; **33**: 57-62
- 9 Lin DM, Furst SR, Rodarte A. A double-blinded comparison of metoclopramide and droperidol for prevention of emesis following strabismus surgery. *Anesthesiology* 1992; **76**: 357-61
- 10 Watcha MF, Bras PJ, Cieslak GD, Pennant JH. The dose-response relationship of ondansetron in preventing postoperative emesis in pediatric patients undergoing ambulatory surgery. *Anesthesiology* 1995; **82**: 47-52
- 11 Shende D, Mandal NG. Efficacy of ondansetron and metoclopramide for preventing postoperative emesis following strabismus surgery in children. *Anaesthesia* 1997; **52**: 496-500
- 12 Rose JB, Martin TM, Corddry DH, et al. Ondansetron reduces the incidence and severity of poststrabismus repair vomiting in children. *Anesth Analg* 1994; **79**: 486-9
- 13 Splinter WM, Roberts DJ. Dexamethasone decreases vomiting by children after tonsillectomy. *Anesth Analg* 1996; **83**: 913-6
- 14 Rich WM, Abdulhayoglu G, DiSaia PJ. Methylprednisolone as an antiemetic during cancer chemotherapy—a pilot study. *Gynecol Oncol* 1980; **9**: 193-8
- 15 Fredrikson M, Hursti T, Furst CJ, et al. Nausea in cancer chemotherapy is inversely related to urinary cortisol excretion. *Br J Cancer* 1992; **65**: 779-80
- 16 Harris AL. Cytotoxic-therapy-induced vomiting is mediated via enkephalin pathways. *Lancet* 1982; **1**: 714-6
- 17 Rothenberg DM, McCarthy RJ, Peng CC, Normoyle DA. Nausea and vomiting after dexamethasone versus droperidol following outpatient laparoscopy with a propofol based general anaesthetic. *Acta Anaesthesiol Scand* 1998; **42**: 637-42
- 18 Wang JJ, Ho ST, Liu HS, Ho CM. Prophylactic antiemetic effect of dexamethasone in women undergoing ambulatory laparoscopic surgery. *Br J Anaesth* 2000; **84**: 459-62
- 19 Jones A, Hill AS, Soukop M, et al. Comparison of dexamethasone and ondansetron in the prophylaxis of emesis induced by moderately emetogenic chemotherapy. *Lancet* 1991; **338**: 483-7
- 20 The Italian Group for Antiemetic Research. Dexamethasone, granisetron or both for the prevention of nausea and vomiting during chemotherapy for cancer. *N Engl J Med* 1995; **332**: 1-5
- 21 Aasboe V, Raeder JC, Groegaard B. Betamethasone reduces postoperative pain and nausea after ambulatory surgery. *Anesth Analg* 1998; **87**: 319-23
- 22 Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. *Anesth Analg* 2000; **90**: 186-94
- 23 Smeeth L, Haines A, Ebrahim S. Numbers needed to treat derived from meta-analyses—sometimes informative, usually misleading. *Br Med J* 1999; **318**: 1548-51
- 24 Wang JJ, Ho ST, Tzeng JI, Tang CS. The effect of timing of dexamethasone administration on its efficacy as a prophylactic

- antiemetic for postoperative nausea and vomiting. *Anesth Analg* 2000; **91**: 136–9
- 25** Sun R, Klein KW, White PF. The effect of timing of ondansetron administration in outpatients undergoing otolaryngologic surgery. *Anesth Analg* 1997; **84**: 331–6
- 26** Madan R, Perumal T, Kathirvel S, et al. The effect of timing of prophylactic ondansetron administration on postoperative emesis following paediatric strabismus surgery. *Anaesth Intensive Care* 2000; **28**: 27–30