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# Prevention of postoperative nausea and vomiting in children following adenotonsillectomy, using tropisetron with or without low-dose dexamethasone

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**Abstract**

*Purpose.* Postoperative nausea and vomiting (PONV) after adenotonsillectomy in children is, in spite of the prophylactic administration of tropisetron, still a frequent event. The aim of this study was to evaluate the benefit of the additional systemic administration of low-dose dexamethasone ($0.15\,mg{\cdot}kg^{-1}$) for the prevention of PONV.

*Methods.* With hospital ethics committee approval, we investigated children undergoing adenotonsillectomy receiving tropisetron ($0.1\,mg{\cdot}kg^{-1}$; maximum dose, 2 mg) or tropisetron ($0.1\,mg{\cdot}kg^{-1}$; maximum dose, 2 mg) plus dexamethasone ($0.15\,mg{\cdot}kg^{-1}$; maximum dose, 6 mg) intraoperatively. The incidence of vomiting episodes and the need for postoperative analgesics were recorded. Patient data were analyzed using the *t*-test and the $\chi^2$ test (significance level of $P = 0.05$). Data values are means ± SD.

*Results.* Ninety children (39 girls and 51 boys), aged 5.6 ± 2.8 years and weighing 21.9 ± 8.8 kg, were enrolled in the study. The overall incidence of vomiting was 38.9% within the first 24 h (67 vomiting events) and 44.4% within 48 h postoperatively (87 vomiting events). The incidence of vomiting in the tropisetron-only group was 53.3% (24/45) at 24 h and 60% (27/45) at 48 h (24 h: $P < 0.001$ and 48 h: $P = 0.04$) and 24.4% (11/45) at 24 h and 28.9% (13/45) at 48 h in the tropisetron-dexamethasone group. The need for postoperative nalbuphine was double in patients treated with tropisetron-dexamethasone ($0.61\,mg \pm 0.36\,mg{\cdot}kg^{-1}{\cdot}48\,h^{-1}$) compared to that in patients receiving only tropisetron ($0.31\,mg \pm 0.28\,mg{\cdot}kg^{-1}{\cdot}48\,h^{-1}$; $P < 0.0001$).

*Conclusion.* A low-dose bolus of dexamethasone ($0.15\,mg{\cdot}kg^{-1}$) in combination with tropisetron, compared to tropisetron alone, considerably reduced the incidence of vomiting in children following pediatric adenotonsillectomy.

**Key words** PONV · Children · Adenotonsillectomy · Tropisetron · Dexamethasone

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## Introduction

The incidence of postoperative vomiting and nausea (PONV) in children undergoing adenoidectomy and/or tonsillectomy has been reported to be up to 89% [1]. PONV following tonsillectomy is a very unpleasant experience for the patients, parents, and the nursing personnel, and can lead to a prolonged stay in the Post Anesthesia Care Unit (PACU) delayed discharge from hospital, or even unplanned hospitalization [2]. Prophylactic medication to avoid or to reduce PONV in this group of children is therefore highly needed.

Tropisetron, a long-acting $5HT_3$ receptor antagonist, has been shown to be effective in reducing PONV in children undergoing adenoidectomy and/or tonsillectomy [1,3,4]. In our department, from 1998 to 2003, a single dose of tropisetron was routinely administered in children undergoing adenoidectomy and/or tonsillectomy. Recently, we reported on a still high incidence of PONV in children undergoing adenoidectomy and tonsillectomy in spite of the prophylactic medication with intravenous tropisetron, most likely due to opiate adminsitration [5]. In 2004 we started to combine tropisetron with a small dose of intravenous dexamethasone ($0.15\,mg{\cdot}kg^{-1}$) for further reduction of PONV in this group of children.

The aim of this study was to evaluate the benefit of the additional systemic administration of a small dose of dexamethasone ($0.15\,mg{\cdot}kg^{-1}$) in combination with tropisetron for the prevention of PONV in children following adenotonsillectomy.

## Methods

With hospital ethics committee approval, two groups of children (American Society of Anesthiologists [ASA] classes I and II) undergoing adenotonsillectomy were retrospectively analyzed: group I (2003) received

tropisetron alone, and group II (2004) received tropisetron and dexamethasone. Data were obtained from the electronic anesthesia and recovery room records, as well as from surgical ward protocols. Patients receiving preoperative antiemetics, steroids, antihistames, or psychoactive drugs before surgery, propofol for the induction of anesthesia, or analgesics other than those given by the standardized anesthesia protocol were excluded.

Premedication consisted of 0.5 mg midazolam, administered orally or rectally (maximum dose, 15 mg). Inhalational induction using sevoflurane in oxygen/nitrous oxide (1:1) was performed in all children studied. After induction, an intravenous cannula was inserted and muscle paralysis, using atracurium, was established to facilitate tracheal intubation. For intraoperative analgesia, intravenous morphine (0.1 mg·kg$^{-1}$) was given prior to intubation, and 20–25 mg acetaminophen with codeine was given rectally after tracheal intubation. Children with known obstructive sleep apnea (OSA) did not receive premedication, and intraoperative morphine was restricted to 0.05 mg·kg$^{-1}$. Anesthesia was maintained with sevoflurane in oxygen/nitrous oxide (2:1). Glycopyrrolate and prostigmine were given to reverse neuro-muscular blockade if required. Asleep extubation was performed with the child in the lateral recovery and head-down position.

Patients in group I received tropisetron 0.1 mg·kg$^{-1}$ (maximum dose, 2 mg) intravenously at the end of surgery. In group II patients, dexamethasone 0.15 mg·kg$^{-1}$ (maximum dose, 6 mg) was intravenously administered immediately after the induction of anesthesia, and tropisetron was given intravenously before the end of surgery, at a dose of 0.1 mg·kg$^{-1}$ (maximum dose, 2 mg). Postoperative rescue medication to treat vomiting consisted of intravenous tropisetron 0.1 mg·kg$^{-1}$ (maximum dose, 2 mg), given twice a day as the first rescue drug, and intravenous droperidol 10 µg·kg$^{-1}$ (maximum dose, 30 µg·kg$^{-1}$·day$^{-1}$) as a second rescue drug if tropisetron was not successful. Postoperative analgesia consisted of acetaminophen (maximum dose, 100 mg·kg$^{-1}$) with codeine administered orally or rectally, and intravenous nalbuphine at single bolus doses of 0.2 mg·kg$^{-1}$ as required. Postoperatively, children were allowed to drink as soon as they requested it. The incidence of vomiting and retching episodes and the need for postoperative analgesics within the first 24 and 48 h postoperatively were recorded. Patient data were analyzed using the *t*-test and $\chi^2$ analysis (significance level, $\alpha = 0.05$). Data values are means ± SD.

## Results

Ninety children (39 girls and 51 boys) aged 5.6 ± 2.8 years and weighing 21.9 ± 8.8 kg were enrolled in the study. Demographic patient data and duration of surgery and anesthesia were not significantly different between the two groups (Table 1).

The overall incidence of vomiting was 38.9% ($n = 35$ patients) within the first 24 h postoperatively (67 vomiting events) and 44.4% ($n = 40$ patients) within 48 h postoperatively (87 vomiting events).

As shown in Table 2, the incidence of vomiting was 53.3% (24/45) in the first 24 h and 60% (27/45) within 48 h for the tropisetron-only group (24 h: $P < 0.001$ and 48 h: $P = 0.04$); and 24.4% (11/45) at 24 h and 28.9% (13/45) at 48 h in the tropisetron + dexamethasone group. The need for postoperative nalbuphine in the recovery room and in the surgical ward was double in patients pretreated with tropisetron-dexamethasone (group II, 0.61 mg ± 0.36 mg·kg$^{-1}$·48 h$^{-1}$) compared to that in patients receiving tropisetron only (group I, 0.31 mg ± 0.28 mg·kg$^{-1}$/48 h$^{-1}$; $P < 0.0001$), while the acetaminophen requirement was only 8.3% less in group II compared to group I ($P = 0.03$).

## Discussion

In this study, we evaluated the benefit of the additional systemic administration of low-dose dexamethasone in

**Table 1.** Demographic patient data and durations of surgery and anesthesia

| | Group I (tropisetron) | Group II (tropisetron and dexamethasone) | *P* |
|---|---|---|---|
| *n* (female/male) | 45 (16/29) | 45 (23/22) | NS |
| Age (years) | 5.5 ± 2.8 | 5.6 ± 2.6 | NS |
| Body weight (kg) | 21.5 ± 8.9 | 22.2 ± 8.7 | NS |
| Height (cm) | 13.8 ± 19.0 | 116.4 ± 17.9 | NS |
| Patients with OSA (*n*) | 8 | 12 | NS |
| Patients with previous PONV (*n*) | 1 | 0 | NS |
| Duration of surgery (min) | 34.4 ± 12.3 | 30.0 ± 9.0 | NS |
| Duration of anesthesia (min) | 81.2 ± 16.1 | 81.1 ± 16.0 | NS |

OSA, obstructive sleep apnea; PONV, postoperative nausea and vomiting

**Table 2.** Postoperative data

| | Group I (tropisetron; $n = 45$) | Group II (tropisetron and dexamethasone; $n = 45$) | $P$ |
|---|---|---|---|
| Emergence delirium | 12 | 9 | NS |
| Vomitus 0–24 h, *n* patients (%) | 24 (53.3%) | 11 (24.4%) | 0.047 |
| Vomitus 0–24 h, *n* episodes | 49 | 18 | <0.001 |
| Vomitus 0–48 h, *n* patients (%) | 27 (60%) | 13 (28.9%) | 0.036 |
| Vomitus 0–48 h, *n* episodes | 64 | 23 | <0.0001 |
| Nalbuphine administered 0–48 h ($mg \cdot kg^{-1}$) | 0.31 ± 0.28 | 0.61 ± 0.36 | <0.0001 |
| Acetaminophen administered 0–48 h ($mg \cdot kg^{-1}$) | 87.3 ± 13.5 | 79.8 ± 18.3 | 0.03 |

combination with tropisetron to prevent postoperative vomiting in children following adenotonsillectomy. The main finding was that a low dose of dexamethasone ($0.15\,mg \cdot kg^{-1}$) in combination with tropisetron reduced the incidence of PONV by about 50% compared to tropisetron alone.

5-$HT_3$ antagonists have been reported to be effective for the reduction of PONV in children following adenotonsillectomy and to have minimal adverse effects. Nevertheless, in spite of prophylaxis with intravenous tropisetron, the incidence of postoperative vomiting is unacceptably high, ranging from 29% to 55% with a trend to higher values when opioids are used perioperatively (Table 3) [1,3–5]. Similar results have been reported for other 5-$HT_3$ antagonists [6–10].

Dexamethasone is a corticosteroid with potent anti-inflammatory effects and a prolonged antiemetic effect lasting up to 48 h. Dexamethasone is used as an antiemetic drug, with limited side effects, in patients undergoing chemotherapy, and seems to be superior to 5-$HT_3$ antagonists [11,12]. Potential side effects such as delayed wound healing and an increased incidence of wound infection do not seem to be relevant with the application of a single dose of dexamethasone.

There are several studies on the efficacy of dexamethasone alone for the prevention of PONV in children undergoing adenotonsillectomy [13–17]. Three of them reported an incidence of postoperative vomiting of only 20%–24%, although opioids were given during and after surgery (Table 3) [15–17]. In a recent meta-analysis, Steward and colleagues [18] found that children scheduled for adenotonsillectomy and receiving prophylactic dexamethasone at doses ranging from 0.15 mg to $1.0\,mg \cdot kg^{-1}$ (maximum dose, 8–25 mg) were two times less likely to vomit within the first 24 h than children being given placebo. In addition, children being given dexamethasone were more likely to progress to a soft-solid diet on the day after tonsillectomy day [18,19]. However, insufficient data are available to determine whether children pre-treated with dexamethasone experience less pain and require fewer analgesics after adenotonsillectomy. It is concluded that the routine use of a single intravenous dose of dexamethasone during pediatric tonsillectomy is justified, because of the frequency of tonsillectomy and the relative safety and low cost of the drug, and because of the reduction in PONV [18,20].

Our data demonstrate that the combination of low-dose dexamethasone and tropisetron resulted in a significant reduction in the number of patients suffering from postoperative vomiting, from 53.3% to 24.4% within the first 24 h, when compared to tropisetron alone. Our results are consistent with the findings of Holt and colleagues [21]. However, they used dexamethasone at a dose of $0.5\,mg \cdot kg^{-1}$, three times higher than that given in our study ($0.15\,mg \cdot kg^{-1}$). Celiker and colleagues [22] studied the efficacy of even lower doses of dexamethasone to prevent vomiting, in combination with ondansetron. They investigated the minimum effective dose of dexamethasone, with 0.05 vs 0.100 vs $0.15\,mg \cdot kg^{-1}$ (maximum dose, 8 mg) in combination with ondansetron ($0.05\,mg \cdot kg^{-1}$) being given just before the end of surgery [22]. No statistically significant difference was found between the three study groups; however, the number of patients in their study was small.

A comparison of studies that used combinations of dexamethasone and 5-$HT_3$ antagonists [21–23, current study] (Table 4) with studies using dexamethasone alone [15–17] (Table 3) for the prevention of PONV in children following tonsillectomy shows the incidence of vomiting to be virtually the same (Tables 3 and 4). This raises the question of whether the costs and risk associated with the routine application of a 5-$HT_3$ antagonist are justified in these patients or whether this group of drugs should be reserved as postoperative antiemetic rescue medication.

The finding that children in our study population receiving dexamethasone plus tropisetron required twice the amount of nalbuphine than those in the tropisetron-only group was surprising and unexpected. One would expect that the dose of analgesics would be reduced by the anti-inflammatory effect reducing edema, fibrin deposition, capillary dilatation, and leucocyte migration in the surgical field [24]. Pain

**Table 3.** Literature on tropisetron and dexamethasone for prevention of PONV in children following tonsillectomy

| Author | Premedication | Induction | Maintenance analgesia | Dexamethasone $mg \cdot kg^{-1}$ (max) | 3-HT Antagonist $mg \cdot kg^{-1}$ (max) | *n* | Age (years) | Postoperative analgesic/Antiemetic | Vomitus at 24 h | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Ang [3] 1998 | Paracetamol, EMLA cream | Thiopentone, atracurium | Halothane or isoflurane, nitrous oxide, pethidine, neostigmine/ atropine | | Saline<br>Tropisetron 0.1 (not stated) | 23<br>24 | 2–12 | Pethidine, paracetamol, metoclopramide | 65%<br>29% | 0.019 |
| Dillier [4] 2000 | Flunitrazepam | Sevoflurane, nitrous oxide | Sevoflurane, nitrous oxide, paracetamol | | Saline<br>Tropisetron 0.1 (2) | 49<br>49 | 2–12 | Paracetamol, nalbuphine, metoclopramide, droperidol | 66%<br>34% | <0.01 |
| Jensen [1] 2000 | — | Halothane, nitrous oxide, atracurium/ vecuronium | Halothane, nitrous oxide | | Saline<br>Tropisetron 0.2 (5) | 36<br>35 | 2–14 | Paracetamol, metoclopramide | 89%<br>42% | <0.001 |
| Gross [5] 2006 | Midazolam | Sevorane in nitrous oxide, atracurium | Sevoflurane, nitrous oxide, morphine acetaminophen, codeine | | Tropisetron 0.1 (2) early<br>Tropisetron 0.1 (2) late | 60<br>60 | 1–12 | Acetaminophen + codeine, nalbuphine | 55%<br>45% | *NS* |
| Splinter [13] 1996 | Midazolam | Halothane, nitrous oxide, propofol, muscle relaxants, midazolam | Halothane, nitrous oxide, codeine, midazolam | 0<br>0.15 (8) | | 70<br>63 | 2–12 | Dimenhydrinate, ondansetron, morphine, acetaminophen, codeine | 72%<br>40% | <0.001 |
| Pappas [14] 1998 | Midazolam | Halothane, nitrous oxide, mivacurium | Isoflurane, nitrous oxide, fentanyl | 0<br>1.0 (25) | | 65<br>63 | 2–12 | Acetaminophen + codeine, fentanyl, metoclopramide, ondansetron | 62%<br>24% | <0.05 |
| Vosdaganis [15] 1999 | — | Sevoflurane/ Halothane, propofol, rocuronium | Isoflurane/ Halothane, nitrous oxide, paracetamol, pethidine | 0<br>0.4 (8) | | 19<br>22 | 2–12 | Paracetamol, codeine, ondansetron | 63%<br>45% | 0.02 |
| Aouad [16] 2001 | Midazolam, atropine | Sevorane, nitrous oxide, rocuronium | Sevorane, nitrous oxide, fentanyl, propacetamol | 0<br>0.5 (8) | | 53<br>53 | 2–12 | Paracetamol | 51%<br>23% | 0.004 |
| Elhakim [17] 2003 | Midazolam | Sevoflurane, nitrous oxide, suxamethonium | Sevoflurane, nitrous oxide fentanyl | 0<br>0.5 (8) | | 55<br>55 | 4–11 | Acetaminophen, pethidine, metoclopramide | 56%<br>20% | <0.001 |

**Table 4.** Literature on combined regimens using dexamethasone and 5-HT3 antagonists for the prevention of PONV in children following adenotonsillectomy

| Author | Premedication | Induction | Maintenance analgesia | Dexamethasone mg·kg$^{-1}$ (max) | 3-HT-Antagonist mg·kg$^{-1}$ (max) | *n* | Age (years) | Postoperative analgesic/ antiemetic | Vomitus at 24 h | *P* |
|---|---|---|---|---|---|---|---|---|---|---|
| Holt [21] 2000 | — | Thiopethone or halothane, nitrous oxide | Halothane, nitrous oxide, morphine, paracetamol | 0 | Tropisetron 0.1 (2) | 59 | 2–14 | Paracetamol | 53% | 0.002 |
| | | | | 0.5 (8) | Tropisetron 0.1 (2) | 66 | | | 26% | |
| Sukhani [23] 2002 | Midazolam | Sevoflurane Mivacurium | Sevoflurane, nitrous oxide, acetaminophen, fentanyl | 1 (25) | Ondasetron 0.15 (4) | 50 | 2–12 | Acetaminophen, codeine, fentanyl, ondasetron, droperidol | 18% | <0.05 |
| | | | | 1 (25) | Dolasetron 0.5 (25) | 49 | | | 29% | |
| | | | | 1 (25) | Saline | 50 | | | 54% | |
| Celiker [22] 2004 | Midazolam | Sevorane, nitrous oxide, mivacurium, atropine | Sevoflurane, nitrous oxide, metamizol | 0 | 0 | 25 | 2–12 | Metamizol, dimenhydrinate | 28% | NS |
| | | | | 0.05 (8) | Ondasetron 0.05 (8) | 24 | | | 29% | |
| | | | | 0.1 (8) | Ondasetron 0.05 (8) | 27 | | | 37% | |
| | | | | 0.15 (8) | Ondasetron 0.05 (8) | 26 | | | 27% | |

reduction in pediatric adenotonsillectomy was reported by Tom and colleagues [25], using dexamethasone 1 mg·kg$^{-1}$ (maximum dose, 10 mg), and by Elhakim et al. [17], using dexamethasone 0.5 mg·kg$^{-1}$ (maximum dose, 8 mg). However, other authors, administering similar doses of dexamethasone, failed to show a difference related to dexamethasone in the incidence of postoperative sore throat or in analgesic requirements [14,21,22]. After excluding changing surgical factors or factors in the pain protocol over the study period, we cannot explain this finding of an increased postoperative analgesic requirement. We can only hypothesize that, in our study population, the application of low-dose dexamethasone (0.15 mg·kg$^{-1}$) probably resulted in more alert patients but not in increased analgesia, and therefore increased the need for nalbuphine for sedation and analgesia. Further studies will have to investigate this finding and to determine whether it is dose-dependent or not!

In conclusion, a low-dose bolus of dexamethasone (0.15 mg·kg$^{-1}$) in combination with tropisetron considerably reduced the incidence of vomiting in children following adenotonsillectomy compared to tropisetron alone. Future studies are required to compare the efficacy and cost-benefit balance of using dexamethasone at different doses with or without 5-HT$_3$ antagonists for the prevention of PONV in children undergoing adenotonsillectomy.

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