

Preoperative gabapentin decreases the incidence of postoperative vomiting and analgesic requirements after pediatric adenotonsillectomy

Mahmoud H. Mohamed^a, Hesham Al-Sersy^b

^aDepartments of Anesthesia and ^bENT, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence to Mahmoud H. Mohamed, MD, Department of Anesthesia, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Tel: +20 100 988 2538; fax: ???;
e-mail: m_hsn33@hotmail.com

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Objective

The aim of the study was to evaluate the effect of preoperative gabapentin on the incidence of postoperative vomiting (POV) and on analgesic requirements after adenotonsillectomy in pediatrics.

Patients and methods

A total of 144 pediatric patients (4–8 years) scheduled for elective adenotonsillectomy were randomly assigned to either the gabapentin (G) group (20 mg/kg, 2 h before surgery) or the placebo (P) group. A standard technique was used for anesthesia. Ondansetron (0.1 mg/kg) was used as a rescue antiemetic and ketorolac (1 mg/kg) was used as a rescue analgesic postoperatively. The prevalence of POV and number of patients who required ketorolac as a rescue analgesic were assessed in the first 6 h after surgery.

Results

Of the 72 patients, 15 patients (20.8%) in the G group and 21 patients (43%) in the P group developed POV; the difference was statistically significant ($P=0.007$). The number of patients who required analgesics in the G group was 14 (19.4%) and in the P group was 35 (48.6%), and the difference was statistically significant ($P=0.0004$).

Conclusion

Our data show that preoperative gabapentin reduces the incidence of POV and the analgesic requirements after pediatric adenotonsillectomy.

Keywords:

gabapentin, pediatric adenotonsillectomy, postoperative vomiting

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Introduction

Postoperative vomiting (POV) is a frequent (62 and 73% when no prophylactic antiemetic is given) and important cause of morbidity in children [1]. POV occurs twice as frequently in children as in adults, and the two most common emetogenic surgical procedures studied in children are strabismus repair and adenotonsillectomy [2]. Vomiting may be so severe leading to bleeding from the operative site, dehydration, wound dehiscence, and aspiration pneumonia up to death [3]. Even mild POV may result in delayed discharge with subsequently increased costs, as well as unpleasant experience for both patient and parents [4]. Etiology of POV is multifactorial including anesthetic factors such as premedication, anesthetic methods, and drugs or other factors such as irritability and timing of oral intake [5].

Gabapentin is a structural analogue to γ -aminobutyric acid. It was originally approved by the Food and Drug Administration in 1994 for use as an adjunctive medication to antiseizure drugs. In 2002, an indication was added for treating postherpetic neuralgia and other painful neuropathies [6]. The exact mechanism

of action is unknown, but the therapeutic effect on neuropathic pain is thought to involve voltage-gated N-type calcium ion channels. It is thought to bind to the $\alpha 2\delta$ -subunit (1 and 2) of the voltage-dependent calcium channel in the central nervous system [7]. Gabapentin has been shown to reduce postoperative pain and opioid analgesic requirements in a variety of acute postoperative pain models – for example, after total abdominal hysterectomy [8] and spinal surgery [9]. Gabapentin has been studied as a prophylactic antiemetic drug for laparoscopic cholecystectomy [10] and as an adjuvant antiemetic with chemotherapy for patients with breast cancer [11].

We discussed the use of preoperative oral gabapentin as an antiemetic and analgesic medication and its effect on the quality of the early postoperative period after pediatric adenotonsillectomy.

Patients and methods

The study was conducted in the ENT Surgical Department at Ain Shams University Hospital. It was designed as a prospective double-blinded placebo-

controlled study. After approval of the institutional ethics committee and written informed parental consent, 144 pediatric patients (4–8 years) ASA physical status I–II scheduled for adenotonsillectomy were studied. Exclusion criteria included patients with central nervous system disorders, history of POV, intake of antiemetic medication within 24 h before surgery, and history of motion sickness.

All patients were visited for preanesthetic assessment and to explain the study protocol to the parents the day before surgery. Parents were ordered to stop oral intake of their children by midnight before surgery. Clear fluids were permitted up to 3 h before surgery.

Patients were randomly selected by a computer-generated program and then classified into two groups: the gabapentin (G) group or the placebo (P) group. Two hours before surgery, an independent nurse blinded to both the patient and the drug gave each patient a similar amount of liquid in a plastic cup for patients in the G group (20 mg/kg gabapentin oral syrup) and patients in the P group received placebo solution.

Upon arrival in the operating room, vital data monitoring initiated. ECG, heart rate, and oxygen saturation were monitored continuously, and noninvasive arterial blood pressure was recorded at 5-min intervals throughout the procedure.

Patients were allowed to inhale sevoflurane in oxygen mixture until satisfactory depth of anesthesia was obtained, then an intravenous access was secured and 1 µg/kg fentanyl was administered intravenously. Atracurium (0.5 mg/kg) was administered intravenously to facilitate endotracheal intubation and no further doses were administered. Controlled mechanical ventilation was conducted to sustain the end-tidal CO₂ between 35 and 40 mmHg. After intubation, anesthesia was maintained with 1–1.5 vol% isoflurane in oxygen to maintain blood pressure within ±20% of baseline. Tonsillectomy was performed using an electrodissection technique and adenoidectomy was performed using palliative curettage, and all techniques were performed by the same surgeon who was blinded to the study groups. All patients received 10 ml/kg lactated Ringer's solution during the operation. At the end of surgery, the neuromuscular blockade was reversed with neostigmine (0.05 mg/kg) and atropine (0.02 mg/kg), and suctioning of gastric contents was performed by an orogastric tube before extubation. Patients were extubated when extubation criteria were met, which included positive head lift and eye-opening following command, then they were transferred to the postanesthesia care unit (PACU).

In the PACU and during the first 6 h after discharge from the PACU to the ward, all episodes of emetic symptoms (retching, vomiting) were recorded. Nausea was not assessed in this study considering that the patients were pediatrics. Retching was defined as the labored, spasmodic, rhythmic contraction of the respiratory tract muscles, including the diaphragm, chest wall, and abdominal wall muscles without expulsion of gastric contents; vomiting was defined as the forceful expulsion of gastric contents from the mouth. Retching and vomiting both were defined as POV. Data were collected at the PACU, and thereafter in the ward at 2, 4, and 6 h. When attacks of vomiting or retching occurred more than once, it was treated with 0.06 mg/kg ondansetron intravenously. In children who complained of considerable postoperative pain, 1 mg/kg ketorolac was injected slowly intravenously.

The number of patients who suffered from any attack of vomiting and the number of patients who required intravenous analgesic during the early postoperative period were recorded by a physician who was blinded to the study.

Statistical analysis

Comparison between the two groups was made using analysis of variance and Fisher's exact tests by standard SPSS software package version 20 (Chicago, IL) version 20 program. Measurements were expressed as mean ± SD or percentile values. A *P* value less than 0.05 was considered statistically significant.

Results

There were no demographic differences (sex distribution, age, BMI), mean arterial pressure, pulse rate, intraoperative intravenous fluid, and duration of surgery between the two study groups (Table 1).

In the first 6 h postoperatively, 15 patients (20.8%) in the G group and 21 patients (43%) in the P group

Table 1 The demographic characteristics of the patients

| Variable | Gabapentin (G group) (n = 72) | Placebo (P group) (n = 72) | <i>P</i> value |
|--|-------------------------------|----------------------------|----------------|
| Females | 30 (41.66) | 32 (44.44) | 0.866 |
| Males | 42 (58.33) | 40 (55.55) | 0.866 |
| Age (years) | 5.4 ± 2.3 | 5.1 ± 2.8 | 0.484 |
| BMI | 23.5 ± 3.05 | 23.6 ± 2.82 | 0.838 |
| MAP (mmHg) | 75.8 ± 7.83 | 73.2 ± 6.27 | 0.89 |
| Mean pulse rate | 108 ± 15 | 113 ± 17 | 0.063 |
| Intraoperative intravenous fluid (ml/kg) | 10.3 ± 0.7 | 10.5 ± 1.5 | 0.307 |
| Duration of surgery | 30.8 ± 14.7 | 31.1 ± 13.0 | 0.897 |

Values are expressed as mean ± SD or number and percentage; MAP, mean arterial pressure.

Table 2 Number of patients who experienced vomiting and number of patients who required analgesic

| Variable | Gabapentin (G group) (n = 72) | Placebo (P group) (n = 72) | P value |
|-------------------------------|-------------------------------|----------------------------|----------|
| Patients experienced vomiting | 15 | 31 | 0.007** |
| Patients required analgesics | 14 | 35 | 0.0004** |

**Statistically significant results.

developed POV ($P = 0.007$) (Table 2). During the same time period, 14 patients (19.4%) in the G group and 35 patients (48.6%) in the P group complained of highly significant postoperative pain and required analgesic medication ($P = 0.0004$).

Discussion

Our study showed that gabapentin significantly reduced the incidence of POV after pediatric adenotonsillectomy. It also reduced the need for postoperative analgesic medication (ketorolac), thus indicating that gabapentin possesses antiemetic and analgesic properties.

Postoperative nausea and vomiting (PONV) is well considered to be a main cause of morbidity in children, and if not properly prevented and managed it may lead to mortality. Because of a child's limited ability to express distress effectively after experiencing nausea, POV is more commonly studied in children than postoperative nausea [3].

Numerous antiemetic medications have been studied for the management of POV after pediatric adenotonsillectomy, such as traditional antiemetics (e.g. metoclopramide, droperidol, and antihistamines such as dimenhydrinate) used for POV. Other nontraditional antiemetics such as propofol, dexamethasone, and midazolam were also studied. Serotonin receptor antagonists (e.g. ondansetron, granisetron) are more effective than traditional antiemetics. Nonpharmacological techniques include acustimulation, acupressure, and acupuncture point [2].

Preoperative gabapentin reduces postoperative pain and opioid analgesic requirements in a variety of acute postoperative pain models [8,9,12–14] and behaves as an adjuvant hypotensive agent in functional endoscopic sinus surgery [15]. Its use as an antiemetic medication has been studied in adult population. Gabapentin reduced the incidence of PONV and analgesic requirements after open cholecystectomy [16]. It also reduced the incidence of PONV and the use of postoperative fentanyl for pain control after laparoscopic cholecystectomy. However, it did not have

any significant effect on the severity of PONV [17]. In another study, it was shown that preoperative gabapentin significantly reduced the severity of PONV and the analgesic needs after laparoscopic surgery for assisted reproductive technologies, but it did not reduce the incidence of PONV [18]. However, preoperative gabapentin has not been studied as a prophylactic medication for POV in pediatric population.

Gabapentin has been known as an effective medication for treatment of vomiting induced by cytotoxic drugs [11]. The exact mechanism of action of gabapentin in the prevention of nausea and vomiting induced by cytotoxic drugs is not well understood, but mitigation of tachykinin neurotransmitter activity has been postulated to be useful [19]. Tachykinins activity has been proved to be a part of the pathogenesis of chemotherapy-induced emesis in ferrets; thus, a selective tachykinins-receptor antagonist should improve both acute and delayed nausea and vomiting induced by chemotherapy [20]. Although there is a difference of etiology of PONV and emesis induced by cytotoxic drugs, we assume that the mechanism of prevention by gabapentin is the same.

Conclusion

Our data show that preoperative gabapentin reduces the incidence of POV and the analgesic requirements after pediatric adenotonsillectomy.

Acknowledgements

Conflicts of interest

None declared.

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