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Low-dose propofol for the treatment of postoperative emesis in children

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The objective of this study was to determine the efficacy of intravenous (iv), low-dose propofol for the treatment of postoperative emesis in children. We performed a randomized, prospective, double-blind, placebo-controlled investigation in the ambulatory surgical unit on 90 healthy children, aged 1–16 yr following elective, outpatient surgery. After an episode of postoperative vomiting, patients were randomized to receive iv propofol, 0.25 mg kg^{-1}, or an equivalent volume of 10% lipid emulsion (Intralipid®). A second dose of study drug was administered if emesis recurred. All episodes of emesis and postinjection sedation scores following study drug administration were recorded. The study was terminated after analysing the results of 45 children in each group. There were no complications in either study group. We concluded that propofol 0.25 mg kg^{-1} was not an effective treatment for postoperative emesis in healthy children undergoing elective outpatient surgery. It is possible that increasing the dose and/or the duration of administration may improve propofol's ability to treat postoperative emesis in children.

Key words: Anaesthesia: paediatric; complications, postoperative: vomiting; antiemetic: propofol

Introduction

With an incidence of 20–33%, emesis is the most common postoperative complication in paediatric ambulatory patients[1,2]. Not only is it bothersome because of its unpleasant and oftentimes painful nature, but it may contribute to parental and patient anxiety, dehydration, post-tonsillectomy rebleeding, and is the main cause of unanticipated overnight admission for the ambulatory surgical unit[2,3].

A variety of agents may be used to treat postoperative emesis in children. These include trimethobenzamide, prochlorperazine, metoclopramide, droperidol and serotonin antagonists such as ondansetron. These agents have varying degrees of effectiveness and some are associated with unacceptable side effects, such as excess sedation and extrapyramidal movements. A more effective strategy might be to prevent postoperative emesis by administering antiemetics before certain high risk surgical procedures such as tonsillectomy[4] or strabismus repair[5]. However, routine prophylaxis will invariably expose some children to potential risks and additional expense and will not be effective in all cases anyway. Recent studies in the paediatric population have demonstrated that propofol, when used for induction or maintenance of general anaesthesia, decreased the incidence of postoperative emesis by as much as 50%[6,7]. In adults, propofol was superior to placebo in treating postoperative nausea and vomiting[8] and is postulated to possess direct antiemetic activity[8,9].

The objective of this prospective, randomized, double-blind, placebo-controlled study was to determine the efficacy of intravenous (iv), low-dose propofol for the management of postoperative emesis in children undergoing elective, outpatient surgery.

Methods

Healthy (ASA I and II) children, aged 1–16 yr who had indwelling intravenous catheters inserted while undergoing elective, outpatient surgery were eligible to participate. Exclusions included children with a known allergy to propofol or its constituents (egg products), having any pre-existing systemic disease, taking medication affecting the upper gastrointestinal tract, or greater than 150% ideal body weight. Written and verbal informed consent was obtained from parents and children (where appropriate). Prior approval was obtained by the Research Subjects' Review Board of Strong Memorial Hospital.

Preoperative fasting, premedication, intraoperative fluids and anaesthetic management were not dictated by the study. After an episode of vomiting or retching in the postanaesthesia care unit (PACU) or ambulatory

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surgical unit (ASU), children were randomized to receive either iv propofol 0.25 mg kg^{-1}, or placebo (10% lipid emulsion – Intralipid®). Intralipid by itself does not possess antiemetic properties[10]. Lidocaine 1% was added to each study syringe in an equal volume as the study medication (equivalent to 0.25 mg kg^{-1} lidocaine) to prevent pain on injection of propofol[11]. The study medications were computer-randomized and provided to us by the clinical pharmacy in coded syringes. One of the authors (AAB) was a blinded observer and recorded a sedation score (adapted from Borgeat et al.[8]) before and 60 s after injection (1 = fully awake; 2 = somnolent – responds to verbal stimulation; 3 = somnolent – responds only to tactile stimulation; 4 = asleep – responds only to noxious stimulation). The times of all subsequent episodes of emesis were recorded. If a second episode of vomiting occurred, a second dose from the same syringe was administered and sedation scores were recorded as before. Additional emesis was treated using other antiemetics as prescribed by the surgical or anaesthetic care team. Patients were discharged according to routine age-appropriate discharge criteria and were not required to drink before going home. All parents were telephoned the following day to determine the incidence and times of emesis following discharge. The following patient characteristics and anaesthetic or surgical factors were determined: age, sex, weight, type of surgery and whether opioids or reversal agents were administered.

To determine differences between the propofol and placebo groups, statistical analysis was performed using the Mann–Whitney U test for nonparametric interval data and χ^2 and Fisher exact analysis for nominal data. A P value <0.05 was taken to indicate statistical significance. All statistical calculations were performed by SigmaStat statistical software for Windows (Jandel, San Rafael, CA).

Results

Ninety patients were enrolled after being identified as having either vomited or retched while in the ASU. Table 1 lists the patient characteristics and Table 2 compares the types of surgery performed in the two groups. Nearly all children received oral midazolam premedication and most had induction of anaesthesia using inhalation anaesthesia with halothane and nitrous oxide. Eight children in the control group and five children in the propofol group received propofol as part of their anaesthetic management (P = 0.4). Initial success (defined as lack of recurrent emesis within 30 min) after the first dose of study drug was achieved in 38 patients (84%) who received propofol and 35 patients (78%) who received placebo (P = 0.4). Twenty-one patients (47%) who received propofol and 16 patients (36%) who received placebo were completely emesis-free after the first dose (P = 0.3). The median time to relapse was 22 min after receiving propofol and 24 min after placebo (P = 0.6). Initial success after the second dose of study drug was achieved in 20 of 24 patients (83%) who received propofol and 23 of 29 patients (80%) who received placebo (P = 0.7). Following the second dose of study drug, 12 of 24 patients (50%) who received propofol and 9 of 29 patients (31%) who received placebo were completely emesis free (P = 0.2). The median times to relapse after the second dose were 25 min in the propofol group and 40 min in the placebo group (P = 0.2). When the results from the two doses were combined, 20 children (44%) who received placebo had subsequent emesis as opposed to only 12 children (27%) who received propofol. This difference approached statistical significance (P = 0.07). When only those children who received intraoperative opioids and only those who received reversal agents (neostigmine in all cases) were analysed separately, the similarities in responses remained between the propofol and placebo groups. Of 68 total injections of propofol, 9 children (13%) had an increase in their sedation score as compared with 7 of 67 (10%) injections of placebo (P = 0.6). There were no apparent complications in either study group.

Table 1. Patient characteristics

	Propofol	*Control*
n	45	45
Age (yr)*	5.7 ± 3	6.7 ± 3.4
Weight (kg)*	23.5 ± 12.3	25.8 ± 11.2
Sex (M : F)	29 : 16	28 : 17
Opioids (Y : N)	35 : 10	36 : 9
Muscle relaxants (Y : N)	36 : 9	33 : 12
Reversal agents (Y : N)	17 : 28	19 : 26

* Mean ± SD.
There were no statistically significant differences between the groups.

Table 2. Types of surgery

	Propofol	*Control*
ENT	30	27
Ophtho	0	3
Dental	3	2
General/GU	8	8
Peripheral	4	5

$P>0.5$ for 2 × 5 table (χ^2).

Discussion

Our study in children was initiated following a report by Borgeat et al. who demonstrated that propofol successfully alleviated postoperative nausea in adults[8]. However, they too demonstrated that emesis relapse rates within 30 min were similar for both propofol and placebo groups. While Borgeat et al. lumped together nausea and vomiting to arrive at a 60 s postinjection improvement score, we did not attempt to identify or treat nausea. If propofol is more effective in alleviating nausea than vomiting in children, we would not have identified this.

It is possible that 0.25 mg kg^{-1} of propofol was too low a dose to demonstrate an antiemetic effect in our paediatric patients. Propofol requirements for induction

and maintenance of general anaesthesia are increased in the paediatric population[12,13]. A larger dose may result in a stronger antiemetic effect. Although not statistically significant, more patients assigned to receive propofol had ultimate relief from subsequent emetic episodes, indicating that propofol may be more successful if used in larger doses or administered over a longer time period. A dose-response study would be useful to delineate this phenomenon and to measure the dose at which side effects (e.g. sedation) occur.

Lidocaine, 0.25 mg kg^{-1}, was added to both the propofol and placebo syringes to mask the pain associated with the injection of propofol. Lidocaine decreases the incidence of postoperative emesis in children undergoing strabismus repair but in larger doses than those given to our patients[14]. Since lidocaine was added to both treatment groups it is unlikely that its administration appreciably affected the results.

Caution should be used when interpreting a negative study such as this. It is entirely possible that a type II statistical error occurred, in that 90 patients may have been too small a sample to detect significant differences between the groups. However, since analysis of the results on 90 patients showed no clinically significant decrease in emesis with propofol, we decided not to enroll more patients (even though doing so may have resulted in a statistically significant difference) so that more effective antiemetics could be used in our paediatric patients. Based on a method proposed by Detsky and Sackett with which to assess negative trials, 90 patients was sufficient to exclude a true risk reduction of 25%[15].

In summary, we found that the administration of propofol 0.25 mg kg^{-1}, to treat postoperative emesis in children, was not associated with a decrease in subsequent emetic episodes. On the basis of our results, we recommend that future investigations assess higher dose regimens of propofol and/or longer durations of administration.

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