

A study to compare dexamethasone and ondansetron for preventing postoperative nausea and vomiting in children undergoing tonsillectomy

Tonsillektomi yapılan çocuklarda postoperative bulantı ve kusmayı önlemek için deksametazon ve ondansetronun karşılaştırmalı bir çalışması

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SUMMARY

Objective: Various drugs have been used as antiemetics for treatment of postoperative nausea and vomiting. The present study was undertaken to assess the efficacy of ondansetron and dexamethasone for preventing postoperative nausea and vomiting in children undergoing tonsillectomies.

Method: Sixty children having ASA physical status Grade I or II in the age group 4-12 years undergoing tonsillectomy under general anaesthesia were included in the study. These were allocated to three groups of twenty patient each. After induction patients were given test solution A (2 mL) comprising of normal saline or dexamethasone 500 µg/kg or 150 µg/kg in Group I, II and III respectively. At the end of surgery before switching off anaesthetics, test solution B (2 mL) was given comprising of ondansetron 0.15 mg/kg (maximum upto 4 mg) or normal saline or ondansetron 0.1 mg/kg (maximum upto 2 mg). Postoperatively incidence of nausea, number of vomiting episodes, frequency of administration of rescue antiemetic and analgesic were recorded.

Results: In Group II 80% of patients had nausea as compared to 70% in Group I and 50% in group III and the difference between Group II and III was statistically significant (p<0.05). 30% of the patients had vomiting in Group I and II and only 15% of the patients in Group III. The frequency of rescue analgesic among the three groups was comparable except at 0.5 hours. 50% of patients showed complete response in Group III, as compared to 30% and 20% in Group I and Group II respectively.

Conclusion: The combined regimen of ondansetron with dexamethasone was more efficacious as an antiemetic in controlling postoperative nausea and vomiting in children undergoing tonsillectomy.

Keywords: Postoperative nausea and vomiting, dexamethasone, ondansetron, tonsillectomy

ÖZET

Amaç: Postoperatif bulantı ve kusmanın tedavisi için antiemetic olarak çeşitli ilaçlar kullanılmaktadır. Bu çalışmada tonsillektomi yapılan çocuklarda postoperative bulantı ve kusmayı önlemek için ondansetron ve deksametazonun etkinliği değerlendirilmektedir.

Yöntem: Genel anestezi altında tonsillektomi yapılan 4-12 yaşları arasında Grade I ve Grade II ASA fiziksel durumuna sahip 60 çocuk çalışmaya dahil edildi. Bunlar her biri 20'şer kişiden oluşan üç gruba ayrıldı. İndüksiyondan sonra sırasıyla Grup I, Grup II ve Grup III'deki hastalara normal salin ya da deksametazon 500 µg/kg ya da 150 µg/kg'dan oluşan test solüsyonu A (2 mL) verildi. Cerrahinin sonunda, anestezikleri "switch" yapmadan önce test solüsyonu B (2 mL) At the end of surgery before switching off anaesthetics, ondansetron 0.15 mg/kg (maksimum 4 mg) ya da

normal salin ya da ondansetron 0.1 mg/kg (maksimum 2 mg)'dan oluşan test solüsyonu B (2 mL) verildi. Postoperatif bulantı ve kusma sayısı, antiemetik ve analjezik uygulama sıklığı kaydedildi.

Bulgular: Grup II'de hastaların %80'inde, Grup I'deki %70 ve Grup III'deki %50 ile karşılaştırıldığında bulantıya sahipti. Grup II ve III arasındaki fark istatistiksel olarak anlamlı idi ($p < 0.05$). Grup I ve II'de hastaların %30'unda, Grup III'deki hastaların %15'inde kusma vardı. Her üç grupta analjezikten kurtarma sıklığı ilk yarım saatte aynı idi. Grup III'de hastaların %50'si, Grup I ve II'de ise sırasıyla %30 ve %20'si tam yanıt gösterdi.

Sonuç: Deksametazonla ondansetronun combine rejimi tonsillektomi yapılan çocuklarda posoperatif bulantı ve kusmanın kontrolünde bir antiemetik olarak daha etkilidir.

Anahtar sözcükler: Postoperatif bulantı ve kusma, deksametazon, ondansetron, tonsillektomi

INTRODUCTION

Postoperative nausea and vomiting (PONV) poses problems for patients undergoing all types of procedures requiring anaesthesia or sedation. The incidence of PONV ranges from 1%-43%. It has led to one third of unexpected hospital admissions among paediatric patients after ambulatory surgery, delayed discharge and increased cost of care¹⁻³.

There are methods both pharmacological as well as non pharmacological to deal with the problem of PONV. Various classes of drugs are used as antiemetics for the prevention and treatment of PONV. The 5-hydroxytryptamine (5 HT3) antagonist which include drugs such as granisetron, tropisetron and ondansetron have been found to be more effective than the other groups of antiemetics like butyrophenones (droperidol), anticholinergics (hyoscine), antidopaminergic like metoclopramide^{1, 4}. Ondansetron is not associated with side effects like sedation, drowsiness, drug interaction and extrapyramidal symptoms as occurring with other antiemetics.

Dexamethasone is effective in decreasing the incidence of PONV in patients undergoing tonsillectomy, abdominal hysterectomy, thyroidectomy and cholecystectomy. Dexamethasone may potentiate the main effect of other antiemetics by sensitizing the pharmacological receptors^{5, 6}.

The present study was conducted to compare the effect of ondansetron, dexamethasone or combination of the two on postoperative nausea and vomiting in children being operated for tonsillectomies.

MATERIAL AND METHODS

This study was conducted in the Department of Anaesthesiology and Critical Care,

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A total of 60 children having ASA physical status Grade I or II in the age group 4-12 years undergoing tonsillectomy under general anaesthesia were included in the study. Written informed consent from the parents/ guardians was taken.

Patients with history of preoperative nausea and vomiting in the 24 hours prior to surgery, hypersensitivity to study drugs, diseases prolonging gastric emptying e.g. pyloric stenosis, sleep apnea and congenital anomalies were excluded. In addition patients on antiemetics were also excluded. Children were kept fasting for 6 hours for solids and 2 hours for clear fluids.

On arrival of patient in the operating room, preoperative vital parameters including pulse rate, blood pressure and respiratory rate were recorded. Anaesthesia was induced with oxygen, nitrous oxide and halothane via face mask and intravenous line was secured or in some cases anaesthesia was induced by first securing intravenous line and using thiopentone sodium 4-5 mg/kg. Intubation of trachea was facilitated using vecuronium bromide (0.1 mg/kg). Anaesthesia was maintained with halothane and 67% nitrous oxide in oxygen. Intraoperatively analgesia was provided with pethidine 1 mg/kg intravenously after induction. All the children were allocated to three groups of twenty each, using coded slips. After induction patients were given test solution A (2 mL) comprising of normal saline or dexamethasone 500 µg/kg or 150 µg/kg in Group I, II and III respectively. Throughout the procedure, vital parameters and oxygen saturation were recorded. At the end of surgical procedure before switching off anaesthetics, test solu-

tion B (2 mL) was given comprising of ondansetron 0.15 mg/kg (maximum upto 4 mg) or normal saline or ondansetron 0.1 mg/kg (maximum upto 2 mg). Anaesthesia was reversed with neostigmine 0.05mg/kg and atropine 0.02 mg/kg. On ensuring satisfactory recovery from anaesthesia patients were shifted to recovery room where they were observed for 2 hours. Nausea, vomiting and pain were recorded every 30 minutes. Then the patients were shifted to ward where these parameters were recorded every 3 hours for 12 hours (i.e. at 3, 6, 9 and 12 hours postoperatively) and then at 18 and 24 hours. Mild to moderate pain was treated with tablet nimuselide (dispersible) 50 mg postoperatively and severe pain was treated with pethidine 1 mg/kg alongwith promethazine 0.5 mg/kg intramuscularly. Evaluation of the incidence of PONV was carried out by a numeric scoring system. Emetic episode was considered as a single vomit or retching or a combination of the vomit in one minute.

0-No nausea/ vomiting

1-Nausea only, no emetic episode

2-Emetic episode once

3-Emetic episode twice or more or requiring rescue antiemetic

Ondansetron 0.15 mg/kg intravenous was given as rescue antiemetic both in the recovery room and in the ward after first emetic episode or persistent nausea. The frequency and total dose of rescue antiemetic given was also recorded.

Pain was measured by 11 point 10 cm visual analogue numerical scale where 0-no pain, 1-3-mild pain, 4-6-moderate pain and 7-10- severe pain. Response to the study

drug was defined as complete response- no nausea and no vomiting episode, moderate response- nausea or one emetic episode, failure of response- persistent nausea or two or greater than two emetic episodes or use of rescue antiemetics

Statistical analysis

The data obtained was analysed using statistical package for social science (SPSS version 16 Inc., USA) evaluation version. Data were expressed as means, standard deviation and percentages. The categorical variables were analysed using “Chi square test”, while the intergroup comparison of the parametric data (age, weight, duration of fasting for solids and liquids and duration of anaesthesia) was done using students unpaired “t” test. Comparison of incidence of nausea at different time intervals in postoperative period, number of postoperative vomiting episodes at different time intervals, frequency of administration of rescue analgesic, rescue antiemetic and efficacy data of different study groups were done using “Chi-square test” and Fisher’s exact test. The p value was determined to finally evaluate the levels of significance $p < 0.05$ was considered to be significant.

RESULTS

Age difference between Group I and Group II was significant with $p=0.017$. Mean weight and sex ratio among the three groups were comparable. Mean duration of fasting hours for solids and liquids and mean duration of anaesthesia were comparable in all the three groups as shown in Table 1.

Table 1: Demographic variables, duration of fasting and anaesthesia.

| Variables | Group I (n=20) | Group II (n=20) | Group III (n=20) |
|-----------------------------------------|------------------|-------------------|-------------------|
| | Mean \pm S D | Mean \pm S D | Mean \pm S D |
| Age (years) | 7.33 \pm 2.39 | 9.23 \pm 2.44* | 8.05 \pm 2.63 |
| Weight (kg) | 21.35 \pm 5.12 | 23.20 \pm 5.74 | 20.45 \pm 5.04 |
| Sex | Male | 16 | 16 |
| | Female | 4 | 4 |
| Duration of fasting for solids (hours) | 9.78 \pm 1.30 | 9.99 \pm 1.66 | 9.95 \pm 1.74 |
| Duration of fasting for liquids (hours) | 8.77 \pm 1.51 | 8.40 \pm 1.53 | 8.12 \pm 1.39 |
| Duration of anaesthesia (minutes) | 48.7 \pm 9.44 | 44.55 \pm 15.53 | 46.40 \pm 15.87 |

For age and weight - Students unpaired “t” test; for sex- Chi-square test; * $p < 0.05$ (significant); for duration of fasting and anaesthesia-Students unpaired ‘t’ test

Table 2: Incidence of nausea and number of postoperative vomiting episodes.

| Time interval (Hours) | Incidence of nausea at different time intervals in postoperative period | | | Number of postoperative vomiting episodes at different time intervals | | |
|-----------------------|-------------------------------------------------------------------------|-------------|---------------------------------|-----------------------------------------------------------------------|------------|------------|
| | Group I | Group II | Group III | Group I | Group II | Group III |
| 0 | 5 | 11 | 7 | 4 | 3 | 3 |
| 0.5 | 4 | 8 | 4 | 2 | 3 | 1 |
| 1.0 | 2 | 7 | 2 | 0 | 1 | 1 |
| 1.5 | 3 | 3 | 0 | 1 | 0 | 0 |
| 2.0 | 2 | 4 | 2 | 0 | 0 | 0 |
| 3.0 | 1 | 2 | 0 | 0 | 0 | 0 |
| 6.0 | 3 | 2 | 1 | 1 | 1 | 0 |
| 9.0 | 4 | 1 | 0 | 1 | 0 | 0 |
| 12.0 | 2 | 0 | 0 | 0 | 0 | 0 |
| 18.0 | 2 | 0 | 0 | 0 | 0 | 0 |
| 24.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Number of patients# | 14/20 (70%) | 16/20 (80%) | 10/20 (50%); PIIvsIII=0.0467 | 6/20 (30%) | 6/20 (30%) | 3/20 (15%) |

Chi square test; observed $p > 0.05$; #Fisher's exact test; observed $p < 0.05$ significant. Chi square test; observed $p > 0.05$; #Fisher's exact test; observed $p > 0.05$

Table 3: Efficacy data of different study groups.

| Response | Grade PONV | Group I | Group II | Group III | #p value |
|----------|------------|--------------|----------|-------------------------------|-----------------------------------------|
| Complete | 0 | 6 (30%) | 4 (20%) | 10 (50%) | #pIIvsIII=0.04; *pIIvsIII=0.04 NS |
| Moderate | 1 2 | 7 3 (50%) | 9 1 | 10 (50%) 6 9 3 (45%) | |
| Failure | 3 | 4 (20%) | 6 (30%) | 1 (5%) | #pIIvsIII=0.03 |

Chi square test; * $p < 0.05$ (significant); # Fisher's exact test; # $p < 0.05$ (significant)

In Group II 80% of patients had nausea as compared to 70% in Group I and 50% in Group III and the difference between Group II and III was statistically significant ($p < 0.05$). In Group II more patients received rescue antiemetics in the early postoperative period so the incidence of nausea was less in late postoperative period as compared to Group I where there were more patients who had nausea in late postoperative period (Table 2). It was observed that 30% of the patients had vomiting in Group I and II and only 15% of the patients in Group III but the difference was not statistically significant. In Group III none of the patients vomited after initial 1 hour period postoperatively (Table 2).

The frequency of administration of rescue antiemetic among the three groups was comparable. It was observed that more patients in Group I required rescue antiemetics in late postoperative period as compared to group II in which rescue antiemetic was required in early postoperative period. Overall more patients in Group II required rescue antiemetic (30%) as com-

pared to Group I (20%) and Group III (10%).

The frequency of rescue analgesic among the three groups was comparable except at 0.5 hours in Group I where 5 patients required rescue analgesic as compared to none in Group III. It was observed that 50% of the patients in Group I required rescue analgesics as compared to 40% in group II and 30% in Group III.

It was observed that there was more incidence of abdominal discomfort in Group I (20%), while there was more incidence of headache in Group III (15%) respectively. In Group II one patient had abdominal discomfort. Distribution of these complaints were comparable in the three groups.

There were more number of patients who showed complete response i.e. no nausea and vomiting, in Group III (50%), as compared to group I and Group II i.e. 30% and 20% respectively and the difference between Group II and III was statistically significant. It was also observed that the

overall response between Group II and III was statistically significantly different (Group II vs III $p=0.04$). More number of patients in Group II (30%) showed failure response. In Group I it was 20% and in Group III 5% of patients and the difference between Group II and III was significant ($p<0.05$) Table 3.

DISCUSSION

PONV has a complex and multifactorial etiology and there are certain recognized contributory factors like patient factors, type of surgical procedure and anaesthetic technique. Within the paediatric population, postoperative emesis increases with age to reach a peak incidence in the preadolescent (11-14 years) age group. The incidence of PONV in children undergoing tonsillectomy ranges from 35%-75%^{7,8}.

PONV poses problems for patients undergoing all types of procedures requiring anaesthesia or sedation. The surgeries associated with increased incidence of nausea and vomiting in children include adenotonsillectomy, strabismus surgery, hernia repair and orchidopexy. Anderson and Krohg have suggested postoperative pain as an important cause of PONV and that relief of pain was associated with relief of PONV⁹. In another study Stanko et al.¹⁰ reported nausea in 33% of patients on day 3, dropping to 11.6% by day 7 in patients undergoing adenotonsillectomy. A similar trend was observed for postoperative vomiting. A wide variety of pharmacological as well as non pharmacological approaches have been reported but none of them have been able to completely control PONV and are not without the adverse effects.

Ondansetron is a carbazole compound which produces antiemetic and antinauseating effects via selective antagonism of serotonin 3 (5HT₃) receptors. Dexamethasone is an effective antiemetic agent. It acts through blockage of corticoreceptors in the nucleus tractus solitarius of CNS and some of the peripheral mechanism.

Sukhani et al.¹¹ in a study of 149 children pretreated with dexamethasone (1 mg/kg) who underwent tonsillectomy and received either ondansetron (0.15 mg/kg) or dolasetron (0.5 mg/kg) found the incidence of vomiting before home discharge to be sig-

nificantly less (10%) vs placebo (30%). Similar results were obtained at 24-48 hours after discharge (6% in ondansetron group and 18% in placebo group). They concluded that compared to placebo ondansetron showed complete response (no vomiting) in 76% vs 44% in placebo. We used ondansetron 0.1 mg/kg and dexamethasone 0.15 mg/kg. In our study incidence was only 15% which is similar to the study conducted by these authors.

In our study more number of patients in Group I required rescue antiemetics in the late postoperative period as compared to Group II. This was associated with more incidence of pain in the late postoperative period⁹.

The incidence of PONV was significantly less in group III where combination of dexamethasone and ondansetron was used than the patients with one of these drugs. The results of our study are in agreement with other studies conducted by various authors¹²⁻¹⁷.

In our study more patients in Group I required rescue antiemetics in late postoperative period as compared to Group II in which rescue antiemetic was required in early postoperative period. This indicates that dexamethasone is not particularly effective in preventing vomiting occurring early in the postoperative period. Iris et al.⁶ in his quantitative systematic review of efficacy of dexamethasone concluded that the dexamethasone was more efficacious in preventing nausea in the late postoperative period similar to its effect on late vomiting. Reasons for better late efficacy were unclear. Dexamethasone has a biological half life of 36-72 hours. Thus late efficacy may be a result of favourable pharmacokinetics. Late failure of prophylaxis in the ondansetron group was attributed to the shorter duration of action of ondansetron compared to that of dexamethasone.

The timing of prophylactic antiemetic administration is important. Wang et al.¹⁸ concluded that dexamethasone is more effective when administered at induction than when given at the end of anaesthesia⁵. Also ondansetron given at the end of surgery reduces antiemetic requirements more effectively in the postoperative period. So we used dexamethasone at the induction of

anaesthesia and ondansetron at the end of surgery.

Figg et al.¹⁹ reported that ondansetron is devoid of any extra pyramidal symptoms and that the most common side effects are headache and sedation. Markham has also reported headache as the most common adverse event associated with ondansetron⁴. In the present study, in the ondansetron alone group only two patients had headache. Goldman et al.²⁰ reported that dexamethasone in a single perioperative dose is not associated with any adverse outcomes. Bellis et al.²¹ in a systematic review and meta-analysis did not demonstrate a statistically significant increase in the risk of post tonsillectomy haemorrhage with dexamethasone with/without NSAID use in children. However, in another study Mahant et al.²² reported that dexamethasone use was associated with a small absolute risk of revisits for bleeding yet suggested and supported the recommendations for the routine use of dexamethasone.

In dexamethasone treated patients i.e. Group II, the requirement of rescue analgesic in the late postoperative period (6-24 hours) was least. With its strong anti-inflammatory action, dexamethasone has been shown to decrease postoperative pain²³.

Limitations of our study was that satisfaction of patients with regards to overall management were not assessed. In addition using antiemetics in this way, does raise cost effectiveness issues.

To conclude, the combined regimen of ondansetron with dexamethasone was more efficacious as an antiemetic in controlling postoperative nausea and vomiting in children undergoing tonsillectomy as compared to either of the drugs used alone.

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