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The prophylactic effect of rectal diclofenac versus intravenous pethidine on postoperative pain after tonsillectomy in children

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Abstract

Background: Postoperative pain in children is common after tonsillectomy. Rectal diclofenac has been used effectively for postoperative pain management in small children.

Aim: To evaluate the prophylactic effect of rectal diclofenac versus intravenous pethidine on postoperative pain management in children undergoing tonsillectomy.

Methods: This was a prospective, double-blinded randomized study. A total of 100 children, aged 3–10 years, American Society of Anesthesiologists status I or II, and scheduled for elective tonsillectomy or adenotonsillectomy, were recruited for the study. Patients were randomized to receive either rectal diclofenac 2 mg/kg (group A) or intravenous pethidine 0.5 mg/kg (group B) after induction of general anesthesia. The postoperative pain was assessed using Face, Legs, Activity, Cry, and Consolability scale for the first 6 h. The need for rescue analgesic, rectal paracetamol 40–60 mg/kg, was recorded also after surgery. Moreover, estimation of sedation using Ramsay sedation scale was assessed. Postoperative complications considering mainly vomiting and respiratory depression were recorded. Data were statistically described in terms of mean ± SD, median and range, or frequencies (number of cases) and percentages when appropriate.

Results: Pain scores were significantly lower in diclofenac group at different times and needed less rescue analgesic. Postoperative sedation and vomiting were significantly higher in pethidine group. Respiratory depression occurred only in pethidine group.

Conclusion: Prophylactic rectal diclofenac is effective in reducing pain after adenotonsillectomy and postoperative analgesic requirement. Moreover, it is generally safe.

Keywords: Analgesia, Diclofenac, Pethidine, Tonsillectomy pain

Background

Adenotonsillectomy is the most frequent ENT operation performed in children. Pain is an unpleasant subjective sensation which can only be experienced, so it is extremely difficult to be expressed in children who depend on their parents or care providers for their well-being (Owezarzak and Haddad 2006). Post-tonsillectomy pain needs special extra care and control as it may affect child's ability to tolerate oral pain medication and fluid intake, resulting in nausea, vomiting, and or more serious dehydration (Pickering et al. 2002). Many studies were concerned with the post-tonsillectomy pain management. These studies studied different routes, drugs, and mechanisms for pain management—for example, intravenous, intramuscular, rectal, and local infiltration (Moss et al. 2014; Rhendra et al. 2010; Heidari et al. 2012). In contrast, post-tonsillectomy analgesia requires a unique choice to be a nonsedating, nonrespiratory-depressing analgesic that can be used in an outpatient setting to allow early mobilization and return to regular function. Opioids do not fit easily with these requirements;

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they are limited by adverse effects and have monomodal action. Non-steroidal anti-inflammatory drugs (NSAIDs) are nonsedating and nonrespiratory-depressing, can be used in outpatients, and are free from the nauseating effects of the opioid group. These drugs act by inhibiting tissue prostaglandin production at either the site of injury or centrally (Power and Barratt 1999). We preferred the rectal route, because it is a safe route, with very limited adverse effect, and widely used for postoperative analgesia in our hospital.

In this randomized blind study, we assessed the prophylactic effect of rectal diclofenac versus intravenous pethidine on postoperative pain management in children undergoing tonsillectomy.

Patients and methods

The study was conducted in the ENT operating theaters of Abu El-Rish Hospital and Cairo University Hospitals through the period from March 2015 to September 2015 on 100 pediatric patients after being approved by the Departmental Research and Ethical Committee and after obtaining informed consents from the parents. A total of 100 patients, with American Society of Anesthesiologists (ASA) physical status I and II, aged 3–10 years old, and body weight less than 35 kg, were included in the study. Patients with ASA physical status of at least III, age below 3 years or above 10 years old with body weight more than 35 kg, and with any contraindications to the drugs used (asthma, renal or liver diseases, coagulopathy, neurological or cardiac diseases, or hypersensitivity) were excluded from the study.

All patients were visited preoperatively on the day before surgery. The whole procedure was explained to the parents or care providers, and informed consent was taken. Full history was taken, including diseases, bleeding tendency, drug intake, history of allergy or sensitivity to any drugs, and previous anesthetic experience. Full general examination was done including airway assessment and chest and cardiac auscultation. All patients fasted for a suitable period of time (6 h for food and 4 h for water). Laboratory evaluation included complete blood count, prothrombin time and concentration, international normalized ratio, liver function tests, and kidney function tests.

On arrival to the operating theater, intravenous access was established by insertion of 22-G cannula after applying EMLA cream 1 h at the site of insertion then intravenous fluids according to body weight "Hartmann's solution": first 10 kg 4 ml/kg, second 10 kg 2 ml/kg, and for each kg above 20 kg 1 ml/kg fluids.

Monitoring was done by five-lead ECG, pulse oximeter, and noninvasive arterial blood pressure. Injection of premedications was done with atropine sulfate 0.01 mg/kg intravenously and dexamethasone 0.2 mg/kg intravenously. Induction of anesthesia was done by thiopental sodium 5 mg/kg and atracurium 0.5 mg/kg, and then oral endotracheal tube with appropriate size was inserted. Maintenance of anesthesia was achieved by isoflurane inhalation. Randomization was done by closed envelope method.

Patients were allocated into two equal groups as follows: group A ($n = 50$) included patients who received rectal diclofenac 2 mg/kg and group B ($n = 50$) included patients who received intravenous pethidine 0.5 mg/kg after induction of anesthesia.

After completion of tonsillectomy operation, neuromuscular blockade was reversed with neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg). Anesthesia was discontinued, and tracheal tube was removed in lateral position. After extubation, patients were transferred to postanesthesia care unit (PACU).

In PACU, an independent observer, not involved in the study, assessed the following: postoperative vomiting occurrence and postoperative pain using FLACC (Face, Legs, Activity, Cry, and Consolability) score (Merkel et al, 1997). This scale (Table 1) was scored on a range of 0–10, with 0 representing no pain. The scale has five criteria, with each assigned a score of 0, 1, and 2. Pain was recorded at 15, 30, 45, 60, 90, 120, 180, 240, 300, and 360 min postoperatively.

Postoperative rectal paracetamol (40–60 mg/kg) was used as rescue analgesia if pain was scored greater than 5. Postoperative sedation using Ramsay sedation score (Ramsay et al, 1974) (Table 2) and postoperative adverse effects

Table 1 FLACC pain score

Criteria	Score 0	Score 1	Score 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, uninterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid, or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Table 2 Ramsay sedation score

Score	Observations
1	Anxious, agitated, or restless
2	Cooperative, oriented, and tranquil
3	Responsive to commands
4	Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
5	Asleep, sluggish response to glabellar tap or auditory stimulus
6	Asleep, no response

such respiratory depression, edema, rash, or itching were also recorded.

Statistical analysis

Data were statistically described as mean ± SD, median and range, or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Student's *t* test for independent samples in comparing two groups when normally distributed and Mann–Whitney *U* test for independent samples when not normally distributed. For comparing categorical data, chi-square test was performed. Exact test was used instead when the expected frequency is less than 5. *P* values less than 0.05 were considered statistically significant. After obtaining preliminary data of this study, mean ± SD was 4.6 ± 0.74 after diclofenac and 5.5 ± 0.73 after pethidine administration. Sample size was calculated by G.power program and with the use of unpaired *t* test. At α error of 0.05 and power of 95%, the total number of patients calculated was 38, with 19 per each group. The number was increased to 23 per group for possible dropouts.

All statistical calculations were done using computer program statistical package for the social science (SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

Results

One hundred patients were recruited for this study and randomly allocated into two groups: group A (diclofenac) and group B (pethidine).

ASA status was the same in all patients of both groups, with ASA status 1.

There was no statistically significant difference in age, weight, and sex between the two groups (Table 3).

FLACC pain score was measured after recovery from anesthesia (postoperatively). There was a statistically significant difference concerning pain score between groups A and B, as pain score in group A (ranging from 3.18 ± 0.87 to 4.68 ± 0.74) was lower compared with group B (ranging from 3.90 ± 0.76 to 5.54 ± 0.73) 6 h postoperatively, with *P* value less than 0.05, except scores at 90 and 120 min, which were observed to be statistically non-significant (Fig. 1).

Table 3 Demographic data

Demographic data	Groups		
	A	B	*P* value
Age	5.18 ± 1.17	5.04 ± 1.26	0.57
Weight	17.06 ± 4.2	16.28 ± 4.63	0.57
Sex (male/female)	39/11	36/14	0.49

Data presented as mean ± SD and count

The number of patients who needed rescue analgesia [rectal paracetamol (40–60 mg/kg)] was recorded. None of the patients required analgesia in the first 2 h (as pain score was < 5) postoperatively in both groups. There was a significant difference concerning the analgesic need between the two groups, being lower in group A compared with group B, which was statistically significant in 2–4 h after surgery (group A, 8% of cases, whereas group B, 32% of cases ($P < 0.05$)) and statistically non-significant in 4–6 h after surgery, but with lower number of cases in group A compared to group B (12 and 18% of cases, respectively), producing *P* value more than 0.05 (Fig. 2).

Ramsay sedation score was significantly higher in group B when compared with group A at 0 and 30 min after recovery. However, both groups have the same score (which is 2) from 30 min to 6 h postoperatively (Fig. 3).

Incidence of vomiting was monitored after surgery and was statistically significant between both groups, being higher in group B compared with group A which required intervention (Fig. 4).

Although 6% of cases (three of 50 cases) in group B developed respiratory depression, which was statistically insignificant as *P* value less than 0.05, it is clinically significant and vitally important and required immediate intervention (Table 4).

Regarding bleeding, there was no incidence of primary (bleeding requiring intervention within 24 h) or secondary (bleeding requiring readmission) hemorrhage. Two of the children required a second operation to achieve adequate hemostasis (one in each group). There was no serious postoperative complication detected in either group.

Discussion

Pain is a main postoperative complication worldwide, which in turn impairs normal body performance and increases postoperative morbidities. It also increases hospital stay and susceptibility to infections and may progress to chronic pain (Owezarzak and Haddad 2006; Pickering

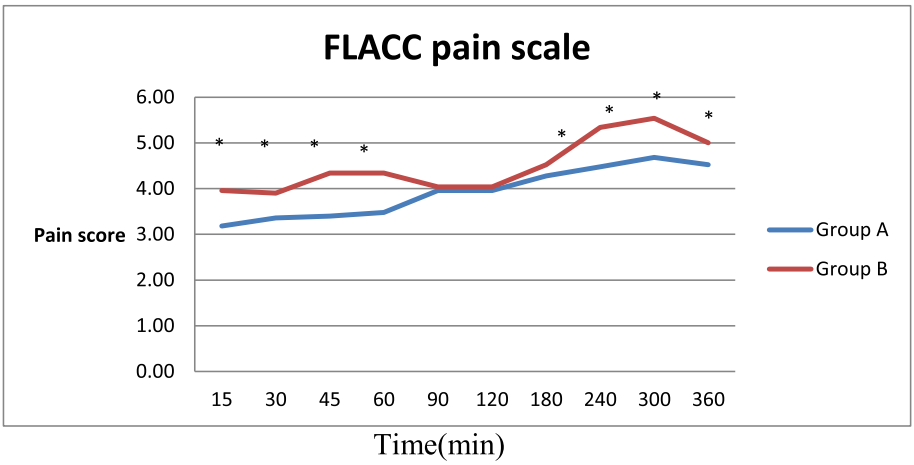

Fig. 1 FLACC (Face, Legs, Activity, Cry, and Consolability) pain scale 6 h postoperatively in both groups. Data were expressed as mean ± SD. *$P < 0.05$

et al. 2002). Adequate postoperative pain management is a chief goal in all operations. Although many studies were concerned with the post-tonsillectomy pain management and these studies have studied different routes, drugs, and mechanisms for pain management, for example, intravenous, intramuscular, rectal, and local infiltration (Moss et al. 2014; Rhendra et al. 2010; Heidari et al. 2012), it still represents a clinical dilemma and challenge for the anesthetist to get pain-free child after tonsillectomy operation. As tonsillectomy surgery is considered one of the shared airway operations, so post-tonsillectomy analgesia requires a nonsedating, nonrespiratory depressing analgesic that can be used in an outpatient setting to allow early mobilization and return to regular function. Opioids do not fit easily with these requirements, as they are limited by adverse effects and have monomodal action. NSAIDs are nonsedating and nonrespiratory depressing, can be used in outpatients, and are free from the nauseating effects of the opioid group. These drugs act by inhibiting tissue prostaglandin production either at the site of injury or centrally, and their extensive use has confirmed that NSAIDs are effective postoperative analgesics (Power and Barratt 1999).

With this randomized clinical study, we investigated whether treatment was safe and effective with diclofenac (Voltaren) compared with meperidine (pethidine) regarding postoperative tonsillectomy pain in children.

In this study, we found that patients had less pain in group A, with FLACC pain score ranging from 3.18 ± 0.87 to 4.68 ± 0.741, compared with group B, with FLACC pain score ranging from 3.90 ± 0.763 to 5.54 ± 0.734, 6 h postoperatively, and rescue analgesia was needed in less number of patients at 2–4 and 4–6h in group A (20%) compared with group B (50%), which was statistically

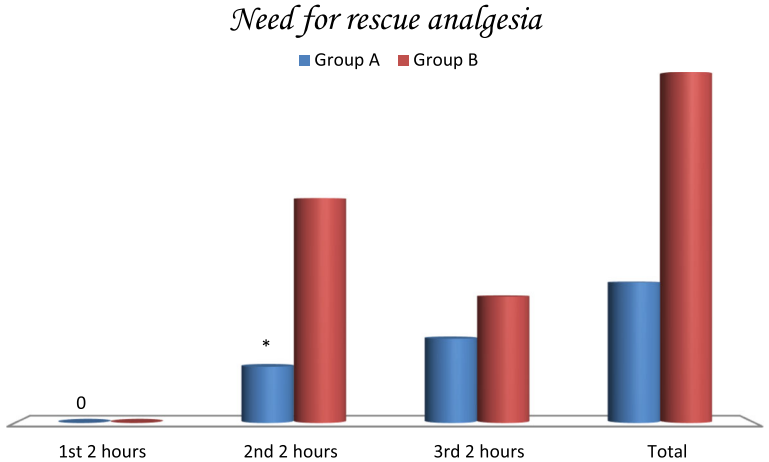

Fig. 2 Need for rescue analgesia in both groups. Data were expressed as count. *$P < 0.05$

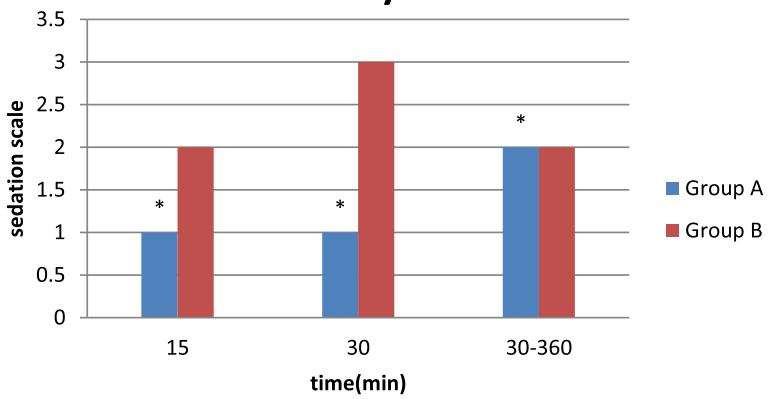

Fig. 3 Sedation score in both groups. Data were expressed as median. *$P < 0.05$

significant. So rectal diclofenac (group A) reduces pain intensity and postoperative analgesic requirements compared with meperidine (pethidine) (group B) after adenotonsillectomy in children, and it persists for a longer period of time.

The study by Tarkkila and Saarnivaara (Tarkkila and Saarnivaara 1999) compared the consumption of oxycodone postoperatively following tonsillectomy in adults versus using different NSAIDs (diclofenac, ketoprofen, and ketorolac) compared with placebo. The best result was noticed with diclofenac (75 mg/kg) which reduced the opioid consumption by 42%, then ketorolac 32%, and least was ketoprofen 25%.

Moreover, Bone and Fell (Bone and Fell 1988) indicated that intraoperative use of diclofenac (2 mg/kg) offered satisfactory postoperative analgesia compared with papaveretum (0.2 mg/kg) after tonsillectomy in children at 3 and 6 h after recovery; in addition, no respiratory depression was detected with the use of diclofenac.

Another study done by Dashti et al. (Dashti et al. 2009) studied the prophylactic effect of rectal acetaminophen on postoperative pain and opioid requirements after adenotonsillectomy in children. A total of 104 children, 7–15 years, ASA I or II, and scheduled for elective adenotonsillectomy, were recruited for the study. Patients were randomized to receive either rectal acetaminophen 40 mg/kg or nothing after induction of standard anesthesia. The postoperative pain was assessed using visual analog scale every 2 h for the first 6 h. The need for rescue analgesic was recorded at 24 h after surgery. They concluded that prophylactic rectal acetaminophen is effective in reducing pain after adenotonsillectomy and postoperative analgesic requirement.

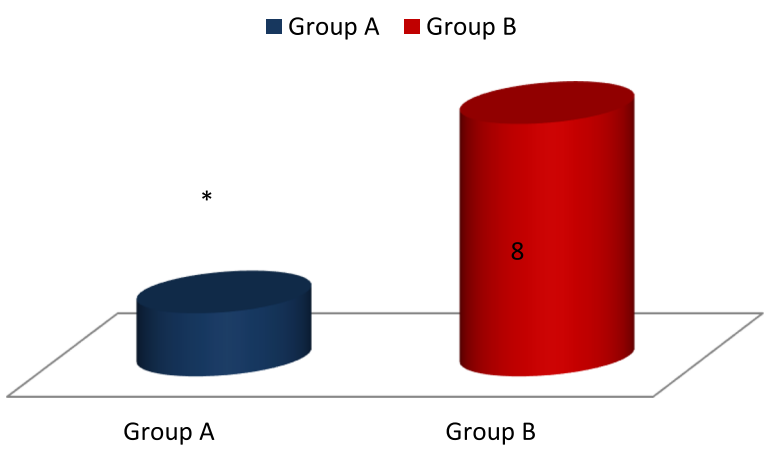

Fig. 4 Vomiting in both groups. Data were expressed as count. *$P < 0.05$

Table 4 Respiratory depression in both groups

	Group A	Group B	*P* value
Respiratory depression			
Count	0/50	3/50	0.08
Within group (%)	0	6	

Data presented as count and percentage

In contrast to our study, Schmidt et al. (Schmidt et al. 2001) found preoperative rectal diclofenac given to patients undergoing tonsillectomy was associated with no better analgesia compared with rectal paracetamol. This is may be related to a lower dose of 1 mg/kg used than ours.

In this study, we found that patients in group B were significantly more sedated compared with patients in group A using Ramsay sedation score at 15 and 30 min after recovery. Sedation score was 2.08 ± 0.9 at 15min and 2.56 ± 0.541 at 30 min in group B and was 1 ± 0 at 15 and 30 min in group A, which was statistically significant. Sedation score was the same in the remaining observational hours after recovery in both groups and was statistically insignificant. So, meperidine (pethidine) produces more sedation and less agitation during early postoperative period, which is not preferred in ENT operations in general and in pediatric surgeries in specific.

In consistence with the study, Watters et al. (Watters et al. 1988) studied the effects of intraoperative intramuscular diclofenac versus intramuscular meperidine on post-tonsillectomy pain in children. In total, 42% of the diclofenac group could react with visual analog scale for 30 min compared to the 12% only of the mepridine group reflecting the sedative effect of diclofenac. They concluded that intramuscular meperidine provided adequate analgesia, less sedation, and earlier readiness for recovery room discharge among pediatric patients undergoing tonsillectomy and was associated also with earlier readiness for discharge from PACU. Although there were some differences, these may be owing to different routes of administration and different concentration of the used drugs. The diclofenac was superior to pethidine overall.

In this study, we found that incidence of postoperative vomiting was significantly higher in group B (16%) compared with that in group A (4%). This is explained as opioids alter lower esophageal sphincter activity, resulting in sphincter relaxation. Gastric emptying is delayed by opioids via supraspinal (vagus nerve-mediated), spinal, and peripheral mechanisms. Meperidine reduces antroduodenal motility and is associated with an increase in gastric pH (Schurizek et al. 1989).

Moreover, the study revealed that incidence of postoperative respiratory depression occurred in group B (6%) compared with that in group A, in which no patient developed respiratory depression (0%), which was statistically insignificant but clinically vital, as it required immediate intervention. Explanation of that is meperidine has significant depressant effect on the respiratory center. Many physicians believe it is safe in terms of respiration, but this was proved to be wrong (Tarkkila et al. 1998). Therefore, meperidine (pethidine) use and also opioid use are generally not preferred in postoperative pain management in pediatric patients.

In agreement with this study, Hamza et al. (Hamza et al. 2012) compared the efficacy of ketorolac and pethidine for postoperative pain relief in the first 24 h after tonsillectomy. A total of 100 patients aged 5–12 years undergoing tonsillectomy were divided into groups A and B randomly, who received either injectable ketorolac 0.5 mg/kg or injectable pethidine 1 mg/kg intramuscularly, respectively, postoperatively on 6 h basis. Patients were assessed in recovery room and ENT ward for pain according to Faces Pain Scale and for any adverse effects. Amount of rescue analgesia required by both groups was also recorded. They concluded that ketorolac provides similar analgesic effects as pethidine in the aforementioned doses, with much less incidence of nausea, vomiting, and drowsiness in the first 24 h after tonsillectomy.

Limitation to the study was that patients were not followed up for more than 6 h, as adequate acute pain management should be controlled and followed up in the first 3 months as regards the definition of acute pain of International Association for the Study of Pain for better healthcare service and reducing a lot of morbidities, which is an important issue for future studies. This was because of the fact that tonsillectomy was performed on an ambulatory basis, and most of the patients came from rural areas, where it would have been very difficult to track them after they had left the hospital. Another potential criticism of the study is the use of rectal diclofenac as opposed to intravenous meperidine. This was done because rectal diclofenac is available, is administered through safe route, has very limited adverse effect, and is widely used for postoperative analgesia in our hospital.

Conclusion

Rectal diclofenac is effective in reducing pain intensity and postoperative analgesic requirements after adenotonsillectomy in children. Moreover, it is generally safe, owing to the absence of respiratory depression and a very low incidence of postoperative complications, especially vomiting, which is an important target. So it is recommended to administer prophylactic rectal diclofenac to decrease the child's postoperative discomfort and pain after adenotonsillectomy. It is recommended that the use of multimodal analgesia is the best way for acute postoperative pain management after adenotonsillectomy surgery.

Abbreviations
ASA: American Society of Anesthesiologists; FLACC: Face, Leg, Activity, Cry, and Consolability; NSAIDs: Non-steroidal anti-inflammatory drugs; PACU: Postanesthesia care unit

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Availability of data and materials
Not applicable

Declarations
Informed written consent has been obtained from all participants.

Authors' contributions
PFH conceived of the study and participated in the design of study. AHS participated in the design of study and drafted the manuscript. PFH performed the statistical analysis and data interpretation and helped draft the manuscript. Both authors read and approved the final manuscript.

Ethics approval and consent to participate
Ethical approval was obtained by local ethical committee of the anesthesia department, Cairo University. Informed consent was taken from the parents of the participants.

Consent for publication
Not available

Competing interests
The authors declare that they have no competing interests.

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References

Bone ME, Fell D (1988) A comparison of rectal diclofenac with intramuscular papaveretum placebo for pain relief following tonsillectomy. Anaesthesia 43:277–280
Dashti GA, Amini S, Zanguee E (2009) The prophylactic effect of rectal acetaminophen on postoperative pain and opioid requirements after adenotonsillectomy in children. Middle East J Anesthesiol 20:245–249
Hamza A, Hayat U, Khan Q, Khan M (2012) To compare the efficacy of ketorolac and pethidine for postoperative pain relief in first 24h after tonsillectomy. Pak J Med Health Sci 6:326–328
Heidari SM, Mirlohi SZ, Hashemi SJ (2012) Comparison of the preventive analgesic effect of rectal ketamine and rectal acetaminophen after pediatric tonsillectomy. Int J Prev Med 3:150–155
Merkel S, Voepel-Lewis T, Shayevitz JR, Malviya S (1997) The FLACC: a behavioral scale for scoring postoperative pain in young children. Pediatr Nurs 23:293–297
Moss JR, Watcha MF, Bendel LP, DL MC, Witham SL, Glover CD (2014) A multicenter, randomized, double-blind placebo-controlled, single dose trial of the safety and efficacy of intravenous ibuprofen for treatment of pain in pediatric patients undergoing tonsillectomy. Paediatr Anaesth 24:483–489
Owezarzak V, Haddad J (2006) Comparison of oral versus rectal administration of acetaminophen with codeine in postoperative pediatric adenotonsillectomy patients. Laryngoscope 116:1485–1488
Pickering AE, Dridge HS, Nolan J, Stoddart PA (2002) Double-blind placebo-controlled analgesic study of ibuprofen or rofecoxib in combination with paracetamol for tonsillectomy in children. Br J Anaesth 88:72–77
Power I, Barratt S (1999) Analgesic agents for the postoperative period. Surg Clin North Am 79:275–290
Ramsay MA, Savege TM, Simpson BR, Goodwin R (1974) Controlled sedation with alpaxalone-alphadolone. Br Med J 2:656–659
Rhendra HMZ, Zayuah MS, Baharudin A, Wan AWA, Shamsul KH, Hashimah I et al (2010) The effects of topical viscous lignocaine 2% versus per-rectal diclofenac in early post-tonsillectomy pain in children. Int J Pediatr Otorhinolaryngol 74:374–377
Schmidt A, Bjokman S, Akeson J (2001) Preoperative rectal diclofenac versus paracetamol for tonsillectomy. Acta Anaesthesiol Scand 45:48–52
Schurizek BA, Willacy LH, Kraglund K (1989) Antroduodenal motility, pH and gastric emptying during balanced anaesthesia: comparison of pethidine and fentanyl. Br J Anaesth 62:674–682
Tarkkila P, Saarnivaara L (1999) Ketoprofen, diclofenac or ketorolac for pain after tonsillectomy in adults. Br J Anaesth 82:56–60
Tarkkila P, Tuominen M, Lindgren L (1998) Comparison of respiratory effects of tramadol and pethidine. Eur J Anaesthesiol 15:64–68
Watters CH, Patresson CC, Mathews HM, Campbell W (1988) Diclofenac sodium postoperative pain in children. Anaesthesia 43:641–643