Iranian Journal of Otorhinolaryngology
No.2, Vol.23, Serial No.63, Spring-2011

Original Article

Comparison of Acetaminophen with or without Codeine to Ibuprofen on the Postoperative Pain of Pediatric Tonsillectomy

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Abstract

Introduction:
Management of pain in children is often inadequate and numerous clinical practice guidelines and policy statements have been published on the subject of pediatric pain. Tonsillectomy is among the most frequent otorhinolaryngologic surgeries, especially in the pediatric age group and after tonsillectomy the patients usually suffer from mild to severe pain for three postoperative days which may limit activity level and intake, leading to dehydration and a prolonged hospital stay. In this study acetaminophen, acetaminophen codeine and ibuprofen have been compared in a single study.

Materials and Methods:
A randomized, prospective, double-blind study was conducted at the Tabriz pediatric hospital. Patients were selected randomly from the hospitalized patients undergoing tonsillectomy suffering from recurrent tonsillitis or adenotonsillar hypertrophy and assigned to one of three groups (acetaminophen (ACT)-acetaminophen codeine (ACT/C)-ibuprofen (IBU) according to a predetermined randomization code. All the operations were taken place under same conditions by the same surgeon. Objective pain score used for pain assessment and adverse drug reactions were collected on checklists and analyzed using SPSS software.

Results:
Chi square test results revealed a significant difference between ACT ACT/C IBU groups. Neither acetaminophen nor Ibuprofen at the doses given was able to provide sufficient analgesia. The rate of bleeding in all groups did not show any significant difference according to Pearson-chi-square test (P=0.22). The incidence of anorexia in ACT, ACT/C and IBU groups was 15.7, 7.8 and 25.8 percent, respectively, which showed a significant difference by chi-square test (P=0.045).

Conclusion:
According to our study it can be concluded that acetaminophen codeine posses more analgesic effect than acetaminophen and ibuprofen in post tonsillectomy pain management in pediatric patients.

Keywords:
Acetaminophen, Acetaminophen codeine, Ibuprofen, Pain, Tonsillectomy

Received date: 27 Nov 2010
Accepted date: 1 Feb 2011

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Introduction

Awareness and treatment of postoperative pain in children has improved over the past few years. Numerous clinical practice guidelines and policy statements have been published on the subject of pediatric pain (1). Management of pain in children is often inadequate and there is no evidence to support the idea that pain is less intense in neonates and young children due to their developing nervous system (2). According to Verghese and colleagues, children suffer from postoperative pain in the same way as adults do, but factors such as fear, anxiety, coping style and lack of social support can further exaggerate the physical pain in children (3).

Tonsillectomy is one of the most frequent otorhinolaryngologic surgeries, especially in the pediatric age group (4). After tonsillectomy the patients usually suffer from mild to severe pain for three postoperative days whereas the pain gradually decreases in the following days (5).

Respectfully, postoperative pain and nausea can limit the patient's activity level and intake of liquids, leading to dehydration and a prolonged hospital stay (6). As already known, pain assessment is a critical component in pain management; although the assessment of pain in young children can be challenging.

Self reporting is possible only in older children, but the measurement of pain in infants and young children who are unable to self-report is particularly challenging and merits increased attention (1). Therefore, objective assessments have great benefits in young children (7).

Non-steroidal anti-inflammatory drugs such as acetaminophen and salicylates, and opioid analgesics are commonly used to minimize postoperative pain in children (8, 9,10). Severe side effects such as nausea, vomiting and respiratory depression have been reported after the application of opioid analgesics therapeutic regimens. These could be potentially problematic, especially in the management of post operative pain in children, for example after tonsillectomy, and may worsen the morbidity related to this type of surgery (10,11).

Acetaminophen is the most commonly used mild analgesic for pediatric outpatients (7,12). Rosming et al investigated the analgesic effect of 90 mg/kg of acetaminophen and 2-3 mg/kg of diclofenac and concluded that neither diclofenac nor acetaminophen were able to provide sufficient analgesia after tonsillectomy (9). This is in accordance with previous reports in children following scheduled oral acetaminophen therapy, 60 mg/kg every 24 hours (13). In another study no difference was observed in the level of pain control when comparing acetaminophen versus acetaminophen/codeine, but the overall oral intake was significantly higher in children treated with acetaminophen alone (14). On the other hand, Charles et al compared ibuprofen and acetaminophen codeine after tonsillectomy. Their results indicated that ibuprofen was as effective as acetaminophen/codeine with significantly less nausea. In this investigation no bleeding was observed following the administration of ibuprofen (15). Also according to Harley et al, acetaminophen/codeine was a more efficacious agent in the treatment of early post tonsillectomy / adenotonsillectomy pain in children in comparison to ibuprofen. Furthermore, children treated with acetaminophen/codeine appeared to resume normal night time sleeping patterns and return to a regular diet sooner. In addition, the significant adverse effect on bleeding time and the increase in postoperative bleeding make ibuprofen a poor choice for post-tonsillectomy pain in children (16).

In view of the fact that there is no standardized protocol for post-tonsillectomy pain management and the lack of a broad investigation on the efficacy of the commonly used analgesics, the present study aimed to compare acetaminophen, acetaminophen/codeine and ibuprofen in the management of post-tonsillectomy pain.

Materials and Methods

A randomized, prospective, double-blind study was conducted at Tabriz pediatric hospital. Study cases were selected randomly from the hospitalized patients undergoing tonsillectomy, suffering from recurrent tonsillitis or adenotonsillar hypertrophy and assigned to one of the three groups: acetaminophen (ACT)-acetaminophen/codeine (ACT/C) and ibuprofen (IBU), based on a predetermined randomization code. Those with mental disorders or under chronic drug therapy were excluded from the study. In total 70 patients in the acetaminophen group, 77 patients in the acetaminophen-codeine group and 31 patients in the ibuprofen group were selected for the study.

All operations were performed by the same surgeon. General anesthesia protocol remained the same for every patient. Accordingly, anesthesia was initially achieved using thiopental 5-6 mg/kg and succinyl choline 1-2 mg/kg. Subsequently, oxygen and nitrogen oxide both (3-4 L/min) and Halothane (1%) were used during the surgery. All patients received fentanyl with 3µg/kg dosage, and none of the patients received any additional analgesic during surgery. After surgery and total recovery the patients received either acetaminophen 10 mg/kg, acetaminophen/codeine (with the dosage of 10 mg/kg and 0.5 mg/kg, respectively) or Ibuprofen with the dosage of 5mg/kg. The analgesics were used at 4-hour dosing interval.The objective pain score (OPS) was used for the assessment of pain (17).

Ten hours after surgery a check list containing information such as pain score, drug adverse effects and need for the administration of additional analgesics was filled in for each patient.

Results

Because of severe adverse gastro-intestinal reactions in the ibuprofen group, total number of patients in this group was reduced to 31. In acetaminophen and acetaminophen/codeine groups 70 and 77 patients were studied, respectively.

According to student t-test (P= 0.176) there was no significant age difference between the three groups (mean age was 8.94, 8.59 and 7.99 for ibuprofen, acetaminophen and acetaminophen-codeine groups, respectively). Table 1 summarizes the Chi-square test results which revealed no statistical difference in the sex of the examined patients (P= 0.168).

Table 1: Sex distribution of each group

Group	Female	Male	Total
Acetaminophen	40(46%)	30(33%)	70(39.3%)
-Acetaminophen codeine	32(36.8%)	45(49.5%)	77(43.3%)
Ibuprofen	15(17.2%)	16(17.6%)	31(17.4%)
Total	87	91	178

Objective pain score (OPS) for each group is recorded in Table 2; the comparison between the OPS of patients in different drug groups showed a significant difference between the three groups (P= 0.02). When the analgesic behaviour of the drugs were compared pair wise (Tables 3,4,5), the Pearson chi-square analysis showed that the acetaminophen-codeine group was significantly different from the acetaminophen and ibuprofen groups.

However, acetaminophen was not statistically different from ibuprofen. In other words, acetaminophen codeine was a more effective analgesic than the other two drugs, with a significantly higher percentage of patients showing an objective pain score of 0. Adverse effects such as bleeding, anorexia, vomiting, nausea and self-reported need for another analgesic dose and also the numbers of visits were recorded.

Table 2: Objective pain score for each group

OPS	Acetaminophen	Acetaminophen -codeine	Ibuprofen	Total	P value
0	27 (38.6%)	58 (75.3%)	12 (38.7%)	97 (54.5%)	0.000
1	10 (14.3%)	7 (9.7%)	4 (12.9%)	21 (11.8%)	0.276
2	19 (27.1%)	9 (11.7%)	12 (38.7%)	40 (22.5%)	0.139
3	9 (12.9%)	3 (3.9%)	3 (9.7%)	15 (8.4%)	0.091
4	1 (1.4%)	.	.	1 (0.6%)	
5	3 (4.3%)	.	.	3 (1.7%)	
6	1 (1.4%)	.	.	1 (0.6%)	
Total	70	77	31	178	

Table 3: Objective pain score comparison of acetaminophen and acetaminophen codeine groups

Objective pain score	Acetaminophen	Acetaminophen Codeine	P value
0	27	58	0/001
1	10	7	0/467
2	19	9	0/059
3	9	3.	0/083

Table 4: Objective pain score comparison of ibuprofen and acetaminophen codeine groups

Objective pain score	Ibuprofen	Acetaminophen Codeine	P value
0	12	58	0.000
1	4	7	0.366
2	12	9	0.513
3	3	3.	1.000

Table 5: Objective pain score comparison of ibuprofen and acetaminophen groups

Objective pain score	Ibuprofen	Acetaminophen	P
0	12	27	0.3
1	4	10	0.109
2	12	19	0.209
3	3	9	0.083

In some cases bleeding occurred immediately after surgery which was due to impaired haemostasis. Acetaminophen and acetaminophen-codeine groups each had one incidence of bleeding with the ibuprofen group showing two cases of bleeding. However, the difference between the groups in terms of bleeding incidence was not statistically significant (*P*=0.221). In the cases of post-operative bleeding the patients were immediately transferred to the operating room where the bleeding was controlled. It should be noted that there was no coagulation disorder in the studied cases.

Anorexia was experienced in 11 patients (15.7%) taking acetaminophen, 6 patients taking acetaminophen codeine (7.8%), and 8 patients taking ibuprofen (25.8%). A significant difference was observed between the drugs in terms of this side effect (*P*=0.045).

The prevalence of nausea and vomiting was significantly different between the mentioned drugs (*P*=0.000); it was higher in the patients taking ibuprofen and particularly high in the second day after the operation. This often resulted in epigastric pain and feeding difficulty. Therefore, the ibuprofen therapy had to be terminated due to severe side effects.

Four patients all in the acetaminophen group had to be seen by the physician because of severe pain. Furthermore, two patients in the acetaminophen group required more analgesic doses which did

not show any significance difference (*P*=0.21).

Discussion

The rate of analgesia in the acetaminophen codeine, acetaminophen and ibuprofen groups was 75.3, 38.6 and 38.7 percent, respectively; which is obviously higher in the first group. There was no meaningful difference between the other two groups (*P*=0.992). This indicates that in contrast to acetaminophen codeine, ibuprofen and acetaminophen were not able to relieve pain significantly. Similar results were obtained by Romsing et al, indicating no significant reduction in patient's pain after tonsillectomy by diclofenac sodium or paracetamol (12). Contrary to our results, Moir et al showed that both acetaminophen and acetaminophen codeine had a similar effect on pain relief on the basis of Wong-Baker FACES (14). In another study, Charles stated that ibuprofen had similar effect on pain relief to acetaminophen codeine (15).

Although the results of Charles et al are in contrast to our study, but Earl and colleagues reported that acetaminophen codeine could be a safer drug than ibuprofen in post tonsillectomy pain management (15,16). The rate of bleeding in all groups did not show any significant difference according to Pearson chi-square test (*P*=0.22).

It should be noted that post tonsillectomy bleeding in the ibuprofen group was not due to coagulation dysfunction. Romsing et al reported that none of the studies were able to clarify the relationship between bleeding and NSAIDs (13).

The results showed that the incidence of anorexia in acetaminophen, acetaminophen codeine and ibuprofen groups was 15.7, 7.8 and 25.8 percent, respectively, which showed a significant difference by Chi-square test between these three groups (*P*=0.045). Moir et al reported a high percentage of anorexia in the acetaminophen codeine group in comparison to the acetaminophen group (14).

Number of patients having suffered from nausea and vomiting after drug therapy is listed in Table 5. The table shows a significant difference between these groups using Pearson Chi-square test, (*P*=0.000)

According to Table 5, the incidence of nausea in the ibuprofen group was higher than the other groups. In some cases we decided to exclude the patient because of severe side effects such as dehydration. Because Charles et al did not report any similar side effects in their study, it is highly recommended to be further investigated by future studies. Nevertheless, It may be due to the fasting period (12 hours or more) or racial differences.

Conclusion

According to our study it can be concluded that acetaminophen codeine possesses a greater analgesic effect in comparison to acetaminophen and ibuprofen in post tonsillectomy pain management in paediatric patients. Patients in the ibuprofen group experienced more side effects such as nausea and vomiting than the other two groups. In our centre, acetaminophen is the main analgesic drug for management of post tonsillectomy pain with even lower doses than this study; so we think that the majority of our patients experience pain after tonsillectomy. We therefore suggest a revision on the post-tonsillectomy pain management protocol in our department on the basis of this study and also recommend further studies with larger populations regarding this issue.

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