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Original Paper

Comparison of Analgesic Effects of Intravenous or Rectal Acetaminophen for Controlling Post-Tonsillectomy Pain

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ABSTRACT

Background: Acetaminophen is a simple analgesic and antipyretic administered in varied formats and from different routes. The purpose of this study was to compare the efficacy of intravenous (IV) and rectal acetaminophen (RA) for controlling post-tonsillectomy pain. **Methods:** In a double-blinded randomized clinical trial, 70 children scheduled for adenotonsillectomy were randomly allocated into two groups, each containing 35 patients.In the first group, 40 mg/kg of rectal acetaminophen and in the second group, 15 mg/kg of IV acetaminophen was administered at the end of surgery before extubation. Systolic and diastolic blood pressure and heart rate were measured every 15 minutes after intubation. Face pain score was recorded for every 30 minutes between extubation and discharge from recovery room. The data from both groups were analyzed using SPSS program. **Results:** All demographic findings (age, gender and weight), the size of used endotracheal tubes, initial heart rate, systolic and diastolic blood pressure were comparable in both groups.The pain intensity was reduced in both groups. But this decrease was more prominent in the group who received IV acetaminophen (P=0.006). The changes in systolic blood pressure were not significant in both groups, as well as the changes in systolic blood pressure in recovery room and the ward. Diastolic blood pressure increased both in the recovery room and the ward. The changes were not significant in the ward; whereas, the changes in diastolic blood pressure in recovery room were statistically significant (P=0.008). Heart rate decreased significantly both in the recovery room (P=0.001) and in the ward (P=0.002). **Conclusion:** Intravenous acetaminophen is more effective than rectal acetaminophen for attenuating post adenotonsillectomy pain in children.

BACKGROUND

Pain is defined as an unpleasant sensation that can potentially be a consequence of a real tissue injury. Nowadays, it is widely accepted that the pain must be safely and effectively controlled both in adult and in children. Unfortunately, postoperative pain is not addressed in pediatric patients as it should be (1). Anatomic, physiologic, pharmacodynamics and pharmacokinetic factors are the barriers in effective pain management in children (2). Oral analgesics are recommended for treatment of mild pain management in children, because narcotics have multiple side effects as nausea, vomiting, hypotension, hypoventilation, allergic reactions and pruritus that can be dangerous in pediatric patients (3). Acetaminophen and centrally acting analgesic and antipyretic drug are used for temporary relief of mild to moderate pain associated with common cold, headache, toothache and myalgia. It is also used as an antipyretic in children and adult (4). Use of acetaminophen via rectal route has been recently recommended (4, 5). In several studies long acting local anesthetics were injected into the tonsillar bed for post tonsillectomy pain control. In another group of studies systemic & local corticosteroids were used. Also, the effects of oral analgesics e.g., acetaminophen, Ibuprofen and acetaminophen codeine were studied. (6.7)

In one study analgesic effect of intravenous and oral acetaminophen was associated with early discharge from recovery. (8) Capici et al. demonstrated that rectal acetaminophen was better than intravenous acetaminophen in controlling painful procedures in children. (9)

Jabbariy et al. Showed no significant differences in analgesic effects of rectal acetaminophen and rectal diclofenac

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(13). According to Oscier et al. the most efficient way of analgesic administration in children was intravenous followed by rectal route. (11)

Oral route produces unpredictable blood levels, and it is not tolerated by the most children, and is not acceptable post operatively due to nausea and vomiting.

Rectal route is used after induction of anesthesia but is not tolerable by awake children. More over it produces unpredictable blood levels. (5) Unfortunately, there are limited numbers of studies regarding two different routes of acetaminophen. Considering two routes of acetaminophen in controlling mild to moderate pain and its low expenses, it is widely used as rectal forms for controlling post adenotonsillectomy pain in children.

MATERIALS/PATIENTS AND METHODS

After ethical committee confirmation and written parental consent 70 children under the age of 14, ASA class I and II were randomly assigned to two groups according to entrance to operating room using the online randomization software. 35 patients were assigned to each of the two group's namely rectal acetaminophen (RA) and intravenous acetaminophen. (IA)

The patients with known allergy to acetaminophen, history of renal, hepatic, respiratory, cardiac and neuromuscular diseases, seizure, chronic pain and a history of analgesic usage were excluded from the study.

After being NPO for 8 hours, all the patients received intravenous midazolam 0.03 mg/kg and fentanyl 1 µg/kg 10 minutes before admission to operating room. Anesthesia was induced with lidocaine 1 mg/kg, propofol 3-4 mg/kg, atracurium 0.5 mg/kg and dexamethasone 0.5 mg/kg (Max 8 mg).

The patient was intubated with appropriate size of endotracheal tube. Maintenance of anesthesia was with isoflurane 1.5-2% in O_2/N_2O. First group (RA) received rectal acetaminophen 40 mg/kg at the end of the surgery and before extubation while in the second group (IA), intravenous acetaminophen 15 mg/kg was administered during 15-20 min before extubation. After reverse of neuromuscular blockade, lidocaine 1 mg/kg was administered and the patient was extubated after return of effective spontaneous respiration.

Systolic and diastolic blood pressure (SBP, DBP), heart rate (HR) arterial oxygen saturation (Sao2) were recorded every 15 minutes. This monitoring control continued in the recovery room. Pain intensity was monitored using Wong- Baker Faces Pain scale every 15 minutes.

Also, Aldrette score was recorded and the patients with a score of 8 or more were discharged from the recovery room. "Fourpoint agitation" system was used for scoring the level of agitation of patients: A patient with a score of 3-4 was considered "agitated"

1. Calm (No intervention)
2. Tranquil able (by the parents)
3. Rest less (cries and screams)
4. Aggressive (must be tied up to prevent self-injury)

This scoring system was applied in the ward every 4 hours.

If the face pain score was more than 5, the patients received fentanyl 1 µg/kg in the operating room or rectal acetaminophen in the recovery room or the ward, respectively. The time and dose of analgesic administration was recorded.

The patients were discharged from the ward 24 hour after the surgery. The physician who recorded pain score in the recovery room and the patients were blind for the route of the Acetaminophen.

All the data were analyzed using SPSS 16 software. Descriptive methods were used for the analysis. For comparing qualitative variables, chi square test (or Fischer test) and for quantitative variables independent T-test was used.

Quantitative variable changes in the groups were compared using repeated measure of ANOVA. P values less than 0.05 were considered significant in this study.

RESULTS

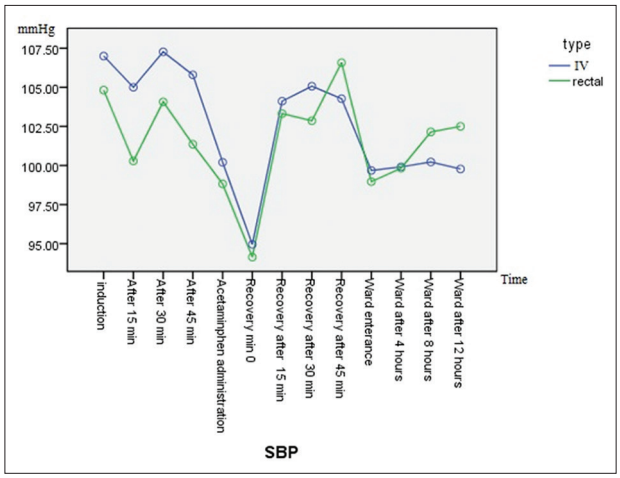
In this study 70 pediatric patients were assigned into two groups namely rectal acetaminophen group (RA) (N=35) and intravenous acetaminophen (IV) group (n=35). There were not significant differences in age, weight, and sex, and basic heart rate, systolic and diastolic blood pressures between two groups so the two groups were comparable.

Systolic blood pressure changes as well as changes trend were not significant in neither of groups P=0.193 and P=0.658 respectively. This means trend change is similar in both groups. The trend of systolic blood pressure changes in the recovery room and ward were not significant respectively (P=0.783, p=0.178). Over all systolic blood pressure of the patients was similar in both groups.

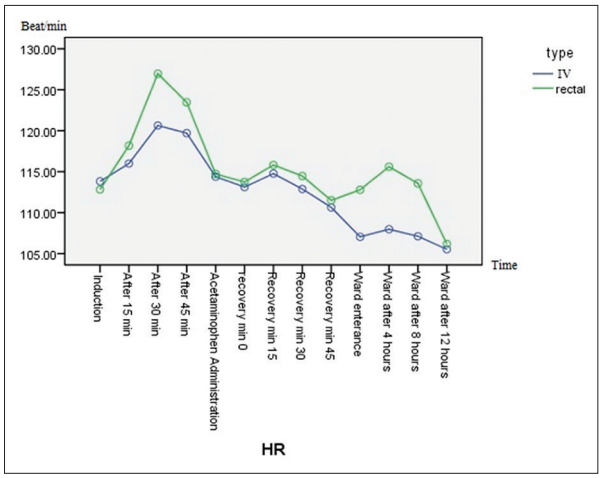
Diastolic blood pressure changes as well as changes trend were not significant in neither of groups. This means trend change is similar in both groups. The trend of diastolic blood pressure changes in the operating room (P=0.235), recovery room (0.797) and ward (p=0.325) were not significant. But the trend changes in the recovery room was significant (p=0.008). The heart rate decreased during operation in both groups significantly p=0.00, the comparison of the changes in the first, third, fourth 15 min demonstrate decreasing HR but in the second 15 min it increases. The comparison between two groups did not change significantly (p=0.611), in the recovery room and ward HR decreased significantly in both groups respectively (p=0.001, P=0.002). The pain intensity was reduced in both groups significantly (IV group P=0.001, RA P=0.000). But this decrease was more prominent in the group who received IV acetaminophen (P=0.006). Complications of two methods were also studied in the patients. These complications include nausea, vomiting, bleeding, laryngospasm, apnea, desideration and agitation. While there were only two cases of bleeding in intravenous acetaminophen group, the difference in the rate of complications in two groups was not significant (P=0.422).

DISCUSSION

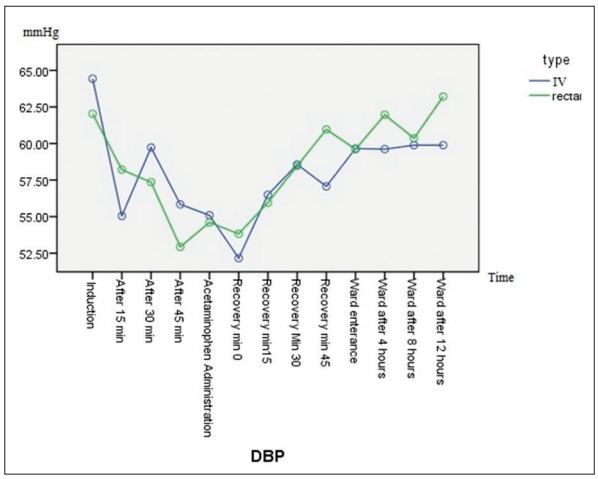
Pain is not just a tissue injury. Pain is a phenomenon which involves various somatic and psychotic aspects; therefore, control of the pain is very important particularly in children (16). In Boroumand et al. study, 104 pediatric patients were scheduled for tonsillectomy, advised acetaminophen plus



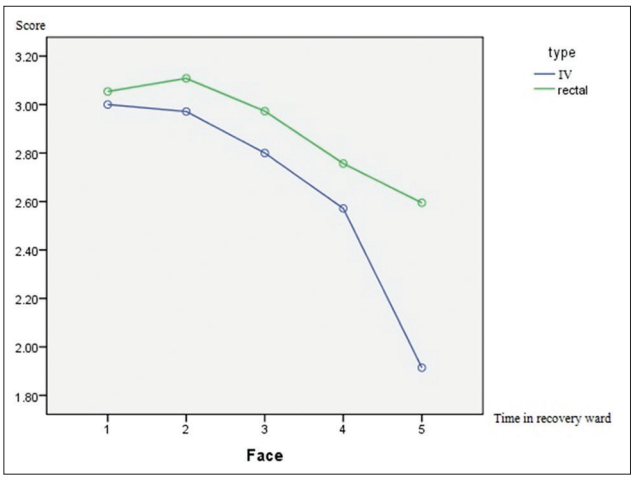
Systolic blood pressure changes in two groups



Heart rate changes in two groups



Diastolic blood pressure changes in two groups



Trend of pain score in the ward in two groups

honey or acetaminophen plus placebo. They reported that honey administration reduced post-operative pain.

We used 40 mg/kg for rectal and 15 mg/kg for intravenous acetaminophen. In a review article with the title of "Acute pain management in children" in which 102 articles were reviewed, above doses has obviously been confirmed as the standard doses. More over total dose of acetaminophen should not exceed 100 mg/kg/24hr because hepatotoxic complications have been observed at doses above this threshold.

We did not use doses more than the recommended doses so; complications such as bleeding and hepatic complications may not be attributed to the drug.

As mentioned previously there were only 2 cases of bleeding in intravenous acetaminophen group and there was no significant difference between two groups (P=0.422).

Although we concluded that intravenous acetaminophen was considerably more effective in reducing pain intensity (P=0.001) but both methods were successful in attenuating the pain which is in contrast to other studies which question the ability of the mentioned doses of acetaminophen in reducing the pain intensity (17).

The efficacy of acetaminophen in different forms of drugs (rectal or intravenous) has been established in several studies (9-13). The differences between the results of above studies could be explained by the pharmacokinetics and various routes of administration. As mentioned above, intravenous acetaminophen is more effective than oral acetaminophen (P=0.006) which is in accordance with the results of the study of Prins et al. (12) and Oscier et al. (15) and in contrast to the results of the study of Capici et al. Although we reviewed the above studies we couldn't find any obvious reason for the differences. It may be explained by earlier administration (15-20 minutes before the end of surgery), different pharmacokinetics and routes of administration of Acetaminophen. The difference in systolic blood pressure as well as the trend of changes of the SBP of the patients during the surgery, in the recovery room and in the ward were not significant in two groups (P=0.193, P=0.783, P = 0.078 respectively). Diastolic blood pressure as well as the trend of changes of DBP were significant in the ward (P=1.492).

This means that diastolic blood pressure changes were similar in two groups (P=0.235, P=0.797 & P=0.325 respectively).

Comparing patients heart rate during surgery, in the recovery room and in the ward, there were significant difference between two groups (P=0.000, P=0.001 and P=0.002 respectively) but the trend of the changes in heart rate was

not significantly different (P=0.061, P=0.937 and P=0.060 respectively). This means that heart rate changes was similar in two groups.

Overall. It has been concluded that use of acetaminophen (both intravenous and rectal) caused no change in systolic blood pressure, decreased heart rate in the ward and recovery room and increased in diastolic blood pressure in the recovery room which we didn't find any particular reason for this. In contrast to the theory that intravenous acetaminophen is not effective in reducing the pain intensity, we showed that it is particularly effective compared to rectal acetaminophen. The limitations of this study were the small size of two sample groups and the lack of similar studies for better comparison of the results. It seems that intravenous acetaminophen is more effective and has a more prolonged effect than rectal acetaminophen in attenuating post adenotosillectomy pain.

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