

**Original article:**

## **Assessment of antipyretic efficacy of rectal and oral acetaminophen in paediatric patients: A comparative study**

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### **Abstract**

**Background:** Acetaminophen is one of the most common antipyretic and analgesic agents used in paediatric patients. Pharmacokinetic studies of rectal administration of acetaminophen showed up to 9-fold variation of the peak drug levels, often not achieving therapeutic levels. Hence, we conducted the present study to assess the efficacy of acetaminophen in paediatric patients when given through oral and rectal route.

**Materials & methods:** The present study included comparative assessment of efficacy of rectal and oral acetaminophen in paediatric patients. We included a total of 40 febrile paediatric patients who were admitted to the paediatric department. All the patients were randomly divided into two study groups with 20 patients in each group - group A and group B. Group A included patients who were administered with 15 mg/kg of acetaminophen rectally, while group B included patients who were given same dose of acetaminophen orally. Measurement of temperature was done at 60 minutes and 180 minutes time after administration of the drug. All the results were analyzed by SPSS software.

**Results:** A total of 40 patients were included in the present study. Mean baseline temperature of patients of group A and group B was 39.1 and 39.8 degree centigrade. Mean temperature of the patients of the group A after 60 minutes and after 180 minutes was 38.72 and 37.85 degree centigrade respectively. Mean temperature of the patients of group B at 60 minutes and 180 minutes was 38.61 and 37.80 respectively. Non-Significant results were obtained while comparing the mean temperature change after 180 minutes.

**Conclusion:** Rectal route is equally acceptable as the oral route in paediatric patients, in terms of efficacy.

**Key words:** Acetaminophen, Antipyretic, Oral, Rectal

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### **Introduction**

Acetaminophen is one of the most common drugs administered to children, mostly as an antipyretic and analgesic agent, and is currently available for oral and rectal administration as different preparations. The rectal suppositories are often essential for treating febrile children with emesis or other circumstances in which oral treatment is contraindicated. Previous studies on the antipyretic efficacy of rectal acetaminophen have shown conflicting results.<sup>1-4</sup> Pharmacokinetic studies of rectal administration of acetaminophen showed up to 9-fold variation of the peak drug levels, often not achieving therapeutic levels. Moreover, the time to peak levels was substantially longer than with oral administration, and the appropriate drug interval was longer, 6 to 8 hours compared with 4 to 6 hours for oral administration. The variations in pharmacokinetic measures could be a result of variability of venous drainage from the rectum. Drugs administered distally bypass the liver, whereas drugs administered in the proximal part of the rectum are drained into the portal system and are subject to the

hepatic firstpass effect.<sup>5, 6</sup> Hence; we conducted the present study to assess the efficacy of acetaminophen in paediatric patients when given through oral and rectal route.

### **Materials & methods**

The present study was planned in the department of paediatric medicine of the medical institute and included comparative assessment of efficacy of rectal and oral acetaminophen in paediatric patients. Ethical approval was taken from institutional ethical committee and written consent was obtained from the parents/guardians of the patients after explaining in detail the entire research protocol. For the present study, we included a total of 40 febrile paediatric patients who were admitted to the paediatric department. Inclusion criteria for the present study included:

- Patients between the age group of 6 months to 8 years of age,
- Patients with negative history of any systemic illness,
- Patients with negative history of any known drug allergy,
- Patients with rectal temperature of  $\geq 39^{\circ}\text{C}$ ,
- Patients without diminished level of consciousness,
- Patients suffering from any of oral lesion or condition that preclude oral or rectal drug administration,
- Patients with history of antipyretics and antibiotics within 48 hours prior to the initiation of the study.

All the patients were randomly divided into two study groups with 20 patients in each group - group A and group B. Group A included patients who were administered with 15 mg/kg of acetaminophen rectally, while group B included patients who were given same dose of acetaminophen orally. Complete demographic details of all the patients were recorded along with clinical presentation. Rectal temperature was recorded in all the patients, prior to acetaminophen administration, using rectal temperature probe (RTP). Same thermometer probe was used in all the patients, with new probe end after each use. Same paediatrician was employed for measurement of rectal temperature after one hour and after three hours of drug administration. Lipophilic suppositories were used for rectal administration of the drug. In patients of group B, syrup containing 120 mg/5mL of acetaminophen was used. The physician who controlled the temperature and the statistician were blinded to the treatment allocation. A single 10cm long visual analogue scale (VAS) was used for assessment of paternal satisfaction.<sup>7</sup> All the results were analyzed by SPSS software. Chi-square test and one way ANOVA were used for assessment of level of significance. P-value of less than 0.05 was taken as significant.

### **Results**

A total of 40 patients were included in the present study. All the patients were randomly divided into two study groups; group A included patients who were given drug through rectal route while the other group included patients who were given drug through oral route. Mean age of patients of group A and group B was 2.8 years and 3 years respectively. Mean weight of patients of group A and group B was 13.2 and 14.2 Kg respectively. Mean baseline temperature of patients of group A and group B was 39.1 and 39.8 degree centigrade. Mean temperature of the patients of the group A after 60 minutes and after 180 minutes was 38.72 and 37.85 degree centigrade respectively. Mean temperature of the patients of group B at 60 minutes and 180 minutes was 38.61 and 37.80 respectively. Significant results were obtained while comparing the mean temperature change within group A and group B at various time intervals. Significant results were obtained while comparing the mean temperature change after 60 minutes.

Graph 1: Description of demographic and clinical details of the patients

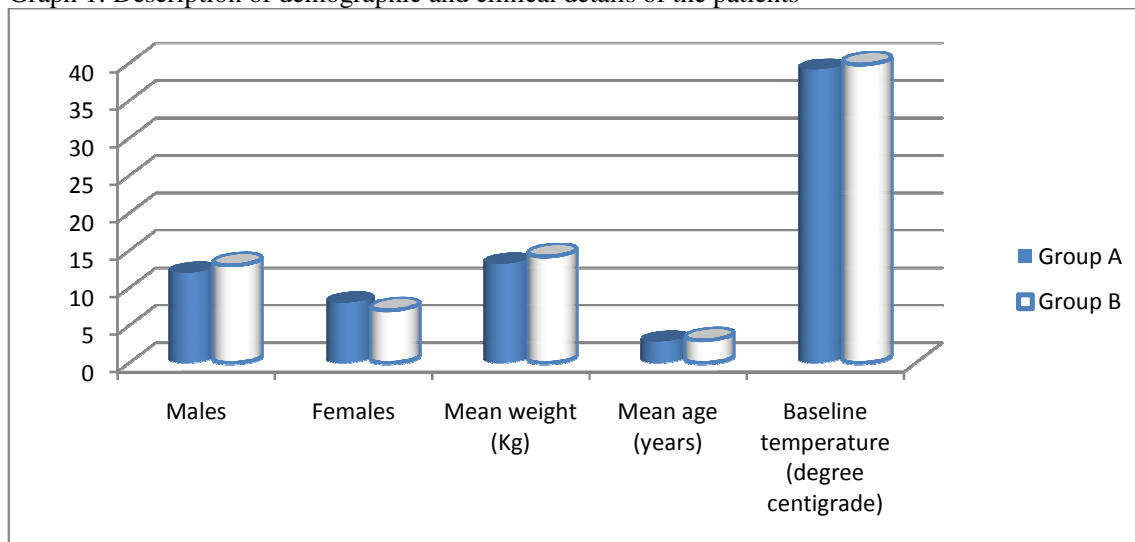


Table 1: Comparison of mean temperature of patients of both the study groups at different time intervals

Group	Mean baseline temperature	Temperature after 60 minutes	Temperature after 180 minutes	p- value
Group A	39.1	38.72	37.85	0.02*
Group B	39.8	38.61	37.80	0.01*

\*: Significant

Table 2: Comparison of mean change in the temperature of the patients at different time intervals

Group	Mean temperature change after 60 minutes (degree centigrade)	P- value	Mean temperature change after 180 minutes (degree centigrade)	p- value
Group A	0.38	0.028*	1.25	0.25
Group B	1.19		2	

\*: Significant

### Discussion

Acetaminophen has been widely used as antipyretic in children. Although both rectal and oral forms have been shown to be effective as fever-reducing agents, controversy regarding the comparative antipyretic effectiveness of equal doses of both preparations still exists.<sup>7-9</sup> In the present study, we observed non-significant results in terms of mean change in temperature in comparison to the baseline values in between patients of both the study groups after 180 minutes (P- value > 0.05). van der Marel CD compared the analgesic efficacy of rectal versus oral acetaminophen in children after major craniofacial surgery. Forty children, mean (standard deviation) age, 10.3 (2.3) months, received 20 mg/kg acetaminophen either orally (n = 20) or rectally (n = 20) every 6 hours after a rectal loading dose (40 mg/kg) during elective craniofacial correction. Blood samples were taken 1 hour before and 2 hours after administration of acetaminophen maintenance doses; pain scores were obtained every 3 hours. Acetaminophen plasma concentrations were higher in patients receiving rectal acetaminophen (mean area under the concentration-time curve [AUC], 171.2 mg x h/L) than in patients receiving oral acetaminophen

(mean AUC, 111.9 mg x h/L). Pain scores were higher in patients receiving oral acetaminophen. However, after exclusion of the patients who vomited from the group receiving oral acetaminophen, acetaminophen plasma concentrations and pain scores did not differ between the groups. There was no relation between acetaminophen plasma concentrations and pain scores. Although 9 of all 40 patients (22.5%) did not reach the expected analgesic acetaminophen plasma concentrations of 10- to 20 mg/L, <7.5% of the visual analog scale pain scores exceeded 4 cm, which was considered as a cutoff point. Their results showed that the analgesic acetaminophen plasma concentration after major surgery in this age group does not always reach the 10 to 20 mg/L level.<sup>10</sup> Karbasi SA et al compared a dose of oral and rectal acetaminophen and to evaluate acceptability of rectal acetaminophen, since oral and rectal acetaminophen is widely used as an antipyretic agent in febrile children and the comparative effectiveness of these two preparations is not well established. In this prospective parallel group designed study, 60 children who presented to the emergency department or outpatient pediatric clinic at a tertiary hospital and aged from 6 months to 6 years with rectal temperature over 39 degrees C were enrolled. Patients were randomly assigned to two equal-sized groups. Group 1 received 15 mg/kg acetaminophen rectally and group 2 received the same dose orally. Temperature was recorded at baseline and 1 and 3 hours after drug administration. In the first group, mean decrease in temperature, 1 and 3 hours after administration of acetaminophen was 1.07+/-0.16 (p < 0.001) and 1.74+/-0.25 degrees C (p < 0.001), respectively, and in the second group it was 1.98+/-0.19 (p < 0.001) and 1.70+/-0.14 degrees C (p < 0.001), respectively (p > 0.05). Rectal and oral acetaminophen preparations have equal antipyretic effectiveness in children. The rectal route proved to be as acceptable as the oral one among parents.<sup>11</sup>

Goldstein LH et al determined, on the basis of published studies, the efficacy of rectal vs oral acetaminophen as treatment of fever and pain. MEDLINE, PubMed, and the Cochrane database as well as major pharmacologic textbooks and the references of all included studies were searched for studies comparing oral and rectal administration of acetaminophen. Randomized and quasi-randomized controlled studies comparing rectal and oral administration of acetaminophen were included. Reviews, letters, and studies that compared combined treatments or additional drugs were excluded. For temperature reduction, 4 studies met the inclusion criteria. The decline in temperature 1 hour after administration of acetaminophen was no different between rectal and oral administration. There was no difference in the decline of temperature 3 hours after administration, the maximum decline in temperature, or the average time to temperature reduction of 1 degrees C. They did not perform a meta-analysis comparing rectal and oral acetaminophen for pain reduction because only 1 study fulfilled the inclusion criteria. Rectal and oral acetaminophen are comparable with respect to temperature reduction.<sup>12</sup>

### **Conclusion**

From the above results, the authors concluded that rectal route is equally acceptable as the oral route in paediatric patients, in terms of efficacy. However; future studies are recommended.

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