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Comparison of Efficacy of Oral and Rectal Acetaminophen in Rapid Reduction of Fever in Children between Ages of 6 Months to 17 Years Admitted To Ward

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ABSTRACT

Introduction:

The most common presenting symptom to the pediatric OPD is fever. The cause of fever can be infectious or post vaccination or other causes like autoimmune disorders etc.

If fever is not reduced quickly it can result in complications like febrile convulsions and brain damage. This study was done to compare the efficacy of rectal acetaminophen and oral acetaminophen to identify which has a quicker action.

Aims and objectives:

To compare the efficacy of oral versus rectal acetaminophen to identify which route of administration helps to rapidly reduce fever.

Materials and methods:

An observational single dose study was done in Kempegowda Institute of medical science, Bangalore, in Department of Pediatrics between October to December 2018, by selecting children of the age group 6months to 17 years who were admitted to ward with complaints of fever. Children were randomly assigned into 2 groups comprising of 200 children each. Group A was given Oral acetaminophen and group B was given rectal acetaminophen with dosage of 15mg/kg. Temperature was recorded at 30 minute intervals. 6 readings were taken. The results were compared.

Results:

Statistically significant differences were noted in the rate of fall in temperature which was in favor of the rectal acetaminophen group when compared to those receiving oral acetaminophen. Adverse effects were noticed in 16 patients receiving rectal acetaminophen.

Conclusion:

In conclusion rectal acetaminophen helps to reduce temperature quickly and effectively than oral acetaminophen thereby helping to avoid complications following high fever spikes.

Keywords: NIL

INTRODUCTION

Fever is quiet a common presentation in clinical practice amongst children. It is stated to be an oral temperature of >37.2 °C (>98.9 °F) during the daytime or >37.7 °C (>99.9 °F) during night time [1].

The aetiology of fever ranges from potentially dangerous illnesses to relatively benign diseases. The aetiology includes: Infectious causes, vaccination, drug induced, tissue injury, malignancy, autoimmune diseases, inherited disorders, gout etc. [2]

Fever if untreated can lead to **dehydration or febrile seizure** (also known as a febrile convulsion) – particularly in children between the ages of three months and five years. [3]

Parents of febrile children usually suffer from something called "fever phobia." thereby causing them to give an antipyretic overdose. [4,5,6]

Acetaminophen is extensively used to reduce temperature in febrile children. [7,8,9,10]

A dose of 10-15 mg/kg is considered safe and could be used rectally or orally.[7,8,10,11]

Acetaminophen was first used clinically in 1887 but it was during the mid- 1950s that it was widely marketed in the United States. [12]

It is one of the most widely used and safest antipyretic and analgesic drugs.[12,13,14] and it also has high therapeutic index (approximately 10) [12]

Pharmacologically paracetamol is a synthetic, non-opiate which acts on the central nervous system which is derived from p-aminophenol.

Acetaminophen's mechanism of action is understood to be associated with centrally acting cyclooxygenase (COX) inhibition with weak peripheral effects, which explains the antipyretic effect of acetaminophen. The weak peripheral effects could be responsible for the lack of side effects. [15]

Acetaminophen is available in different forms including oral and rectal forms.

The rectal suppositories are often essential for treating febrile children with emesis or other circumstances in which oral treatment is contraindicated. The dose in children is 10-15 mg/kg 4 hourly, to a maximum of 100mg/kg/day, and no patient should receive more than 4 g/day. [16]

It is yet to be proven whether rectal and oral acetaminophen have similar efficacy or if either one is better than the other modality, in reducing fever. Studies had done previously have shown varying results. Hence this study was done to assess the efficacy of rectal and oral paracetamol at a dose of 15mg/kg/dose. Also the incidence of adverse effects of rectal and oral paracetamol was assessed.

MATERIALS AND METHODS:

This study was an observational single dose study done in Kempegowda Institute of Medical sciences, Bangalore, which is a tertiary care hospital affiliated with the Rajiv Gandhi University, Karnataka, India. A written and informed consent was taken from the parents prior to the study.

The study was conducted between the months of October to December in 2018. A total of 456 children of the age group 6 months to 17 years were taken up for the study of which only those with febrile illness were included in the study. Children who had received medicines with antipyretic effects within 48 h prior to admission or required more than a single dose of acetaminophen were excluded from the study. As per the exclusion criteria 56 children were excluded from the study. The study subjects were consecutively divided into 2 groups of 200 each and were named Group A and Group B. Initial temperature was recorded and oral paracetamol was given to Group A and rectal paracetamol was given to group B with a dose of 15mg/kg/dose. The dose was not exceeded beyond 100mg/kg/day. Axillary temperature was then recorded at an interval of 30 minutes and a total of 6 readings were recorded. Children were monitored for any adverse effects.

Statistical analysis was performed using SPSS version 20. The clinical profile of patients was analyzed by Student t test (quantitative variables), chi-square test (qualitative variables). Five percent probability level was considered to be statistically significant i.e., $p < 0.05$.

RESULTS:

Amongst the 400 children included in the study 200 were taken in group A for whom oral acetaminophen was given and another group of 200 children were taken up as Group B for whom rectal acetaminophen was given.

Of the 400, 236 children were male and remaining 164 children were females. Mean age was 6.6 years and the mean weight was 24.8 kgs. The rectal acetaminophen group showed a more gradual fall in temperature than the oral group. 3.5 % children had rashes with itching, 3 % had dryness of mouth and 1.5% had constipation after giving rectal acetaminophen whereas no child suffered any adverse event following oral administration of acetaminophen.

Our study showed that oral acetaminophen brought a more rapid reduction of fever as compared to rectal acetaminophen. Statistically significant difference in the weighted sum of temperature differences (WSTD) in 180 min ($p < 0.004$) was noted which went in favor of the oral acetaminophen as against the group receiving rectal acetaminophen. The basal temperature was attained by 5 hours after administering the drug in both the groups which

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shows that though both routes reach basal temperature by 5 hours post drug administration.

A quicker descent in temperature was noticed amongst the oral group. This could be because of the fact that the rectal acetaminophen suppository has unpredictable pharmacokinetic and pharmacodynamics properties.

DISCUSSION:

Fever in children is caused by various reasons ranging from infectious to post vaccination to more uncommon causes like malignancy. Fever if left untreated can lead to dehydration or febrile convulsions. Fever per se does not worsen the course of illness or cause any life threatening complications. The main aim is to reduce the discomfort for the child and reduce the risk of the child developing dehydration or febrile convulsions thereby reducing the stress levels among parents.

Hence a quick and safe method to reduce temperature has to be sought out. This study was done to compare the efficacy of the oral method and the rectal method of administering acetaminophen to identify which helps to reduce fever quickly.

Pharmacokinetic studies of rectal modality of acetaminophen have revealed up to 9-fold variation of the peak drug levels. These studies also show that rectal acetaminophen often is not able to achieve the desired therapeutic levels. The time to peak action was significantly longer than with oral route of giving paracetamol. The appropriate drug interval was much longer i.e. 6 to 8 hours for rectal when compared with 4 to 6 hours for oral route. Also there is variability in the venous drainage of the rectum hence resulting in variations in pharmacokinetic measures. Drugs given distally in the rectum will bypass the liver during their first pass metabolism whereas when given proximally in the rectum the drug drains into the portal system and are exposed to hepatic first pass effect. The American Academy of Pediatrics (AAP) has discouraged using rectal suppositories of acetaminophen with regard to its toxic effects and unreliable pharmacokinetics and pharmacodynamics due to poor and undependable absorption. [17]

Our study reveals that oral acetaminophen helps reduce fever more rapidly than rectal acetaminophen and also has lower risk of side effects than rectal thus making the oral route a better accepted route of administering the drug.

There are other studies which prove the same. In a study conducted by Leary et al. they showed that oral acetaminophen was more effective than rectal preparation in reducing temperature in febrile children. [18]

Keinanen et al., demonstrated that oral acetaminophen was reported to be more effective and its effect was observed faster. [19] But the limitations were that this study was not randomized and they used low dose (10 mg/kg) acetaminophen, and also they used a polyethylene glycol base suppository, which, has been shown to be inferior to the lipophilic formulation.

In a study conducted by Karbasi SA et al the oral and rectal acetaminophen had similar efficacy and the rectal route was as acceptable as the oral route. [20]

According to a study conducted by Nabulsi et al, [21] oral and rectal acetaminophen was compared with two doses of 15 mg/kg and 30 to 40 mg/kg, oral and rectal acetaminophen seemed to have equal effectiveness and that there is no evidence to support the belief that rectal suppositories, whether prescribed in the standard dose of 15 mg/kg, or in the high dose of 30– 40 mg/kg, are superior to oral acetaminophen in terms of rapidity of action, or in the extent of temperature reduction.

In a study conducted by Scolnik et al [22] they showed that the effect of single-dose rectal and oral acetaminophen at 15 mg/kg was the same and also that doubling the dose of rectal acetaminophen did not produce any additional benefit. Also the rectal route was considered to be satisfactory to the parents. But their study had a limitation that it was randomized but not blinded or placebo controlled and also each group had only 23 to 24 patients.

Vernon et al. also reported no difference between rectal and oral acetaminophen in a dose of 15 to 20 mg/kg. [23]

Our study had certain limitations that it was not a randomised trial and also that axillary temperature was used but our study had the advantage of a larger sample size.

CONCLUSION:

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In conclusion oral acetaminophen proved to be more effective in reducing the temperature than rectal acetaminophen and oral route also showed no side effects in comparison to the rectal route thereby making the oral route a better accepted method than rectal acetaminophen.

Table 1: Gender distribution of all cases

Sno	Male n (%)	Females n (%)	P value
Rectal group	122 (61.0)	78 (39.0)	0.4
Oral group	114 (57.0)	86 (43.0)	

Table 2: Baseline characteristics of all cases

Statistics	Age (Years)	Weight (in Kg)	HR (per min)	RR (per min)
Mean	6.6	24.8	124.0	32.1
Standard deviation	4.8	15.2	16.3	10.5
Percentile 25	2	14	112	26
Median/ 50^{th} percentile	6	20	120	28
Percentile 75	10	30	130	32
Minimum	0.5	5	90	18
maximum	17	70	70	68

Table 3: Comparison of adverse effects between the groups

Adverse effects	Oral group n (%)	Rectal group n (%)	P value
Rash, itching	0	7 (3.5)	0.008
Constipation	0	3 (1.5)	0.1
Dry mouth	0	6 (3.0)	0.01

Table-4: Comparison of temperature between the two groups

Mean temperature	Rectal group Mean (SD)		Oral group Mean (Sd)		Mean difference	P value
0 hrs	103.4	0.6	103.2	0.6	0.2	0.001
30 minutes	103	0.7	102.1	0.8	0.9	<0.001
60 minutes	102.5	0.7	101.1	0.7	1.4	<0.001

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1.5 hrs	102.1	0.7	99.7	6.4	2.4	<0.001
2 hrs	101.6	0.7	99.2	0.7	2.4	<0.001
2.5 hrs	101.2	0.7	98.7	0.4	2.5	<0.001
3 hrs	100.8	0.7	98.6	0.2	2.2	<0.001
3.5 hrs	100.3	0.8	98.6	0.1	1.7	<0.001
4 hrs	99.8	0.8	98.6	0	1.2	<0.001
4.5 hrs	99.4	0.7	98.6	0	0.8	<0.001
5 hrs	98.9	0.6	98.6	0	0.3	<0.001
5.5 hrs	98.7	0.4	98.6	0	0.1	<0.001
6 hrs	98.6	0.2	98.6	0	0.03	0.004

Figure 1:

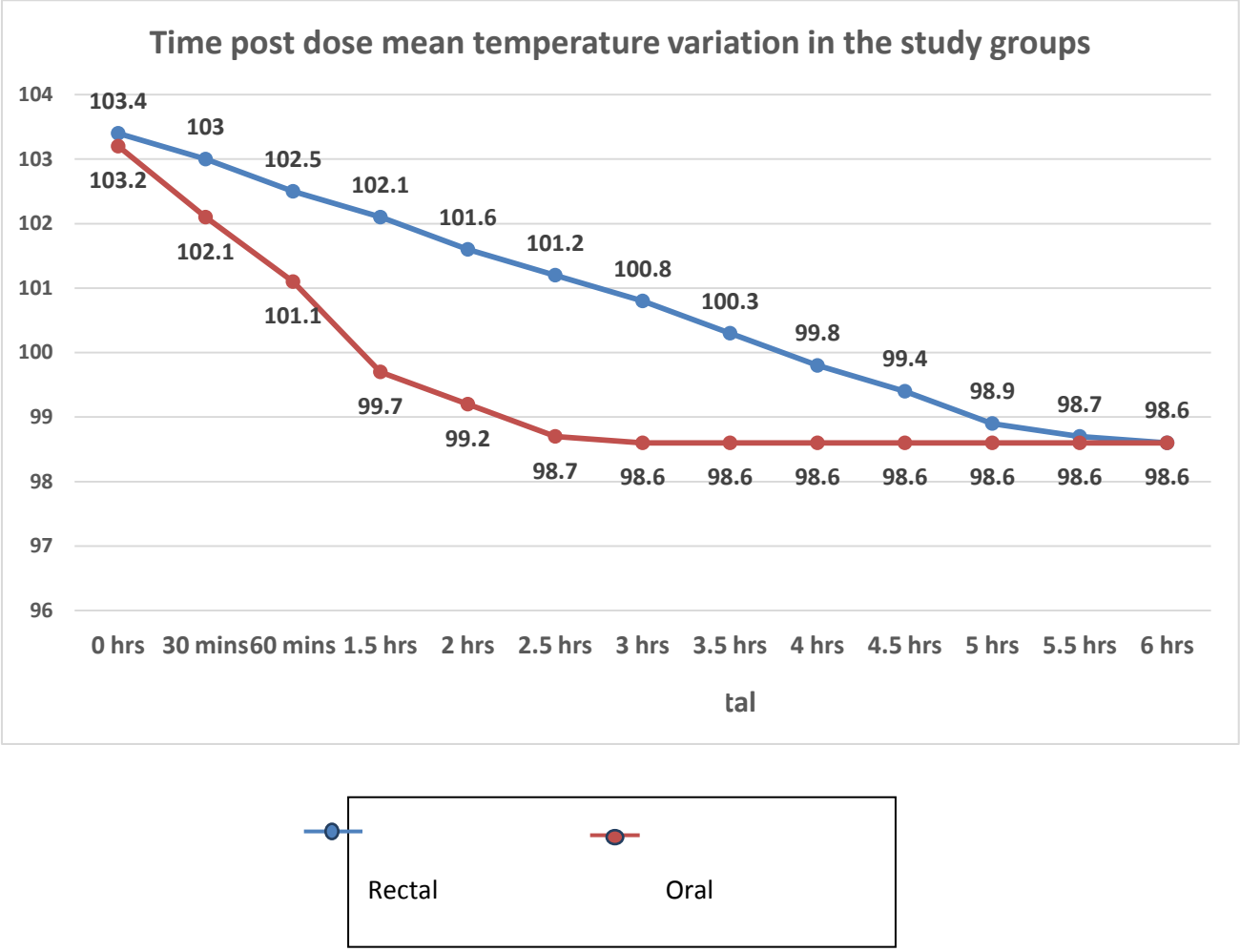

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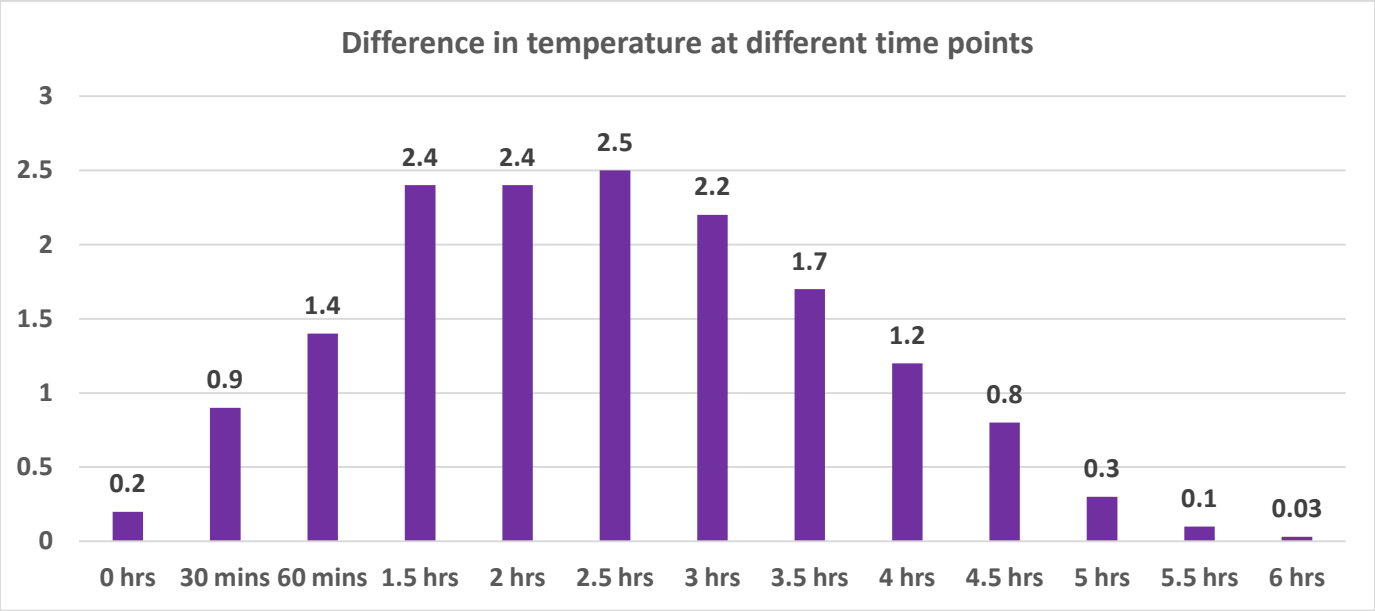
Figure 2:



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