Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr Index Copernicus value = 85.10

(e) ISSN Online: 2321-95 (p) ISSN Print: 2348-6805

Original Research

Intravenous acetaminophen versus oral acetaminophen in the management of fever in children

Mohd.Tahazzul

Assistant Professor, Dept. of Pediatrics, TS Misra Medical College, Lucknow, Uttar Pradesh, India

ABSTRACT:

Background: Fever is one of the commonest presenting symptoms in clinical medicine in all age group patients. The present study was conducted to compare antipyretic efficacy of intravenous (IV) acetaminophen versus oral (PO) acetaminophen in the management of fever in children. **Materials & Methods:** 62 patients of fever of both genders were randomly divided into 2 groups of 31 each. Group I received oral acetaminophen (15 mg/ kg/dose) and group II received IV acetaminophen (15 mg/kg/dose) as antipyretic. **Results:** There were 17 boys and 14 girls in group I and 13 boys and 18 girls in group II. The mean weight was 24.7 kgs in group I and 25.1 kgs in group II, heart rate was 114.6 beats/min in group I and 102.3 beats/min in group II and respiratory rate was 22.6 cycles/min in group I and 18.4 cycles/min in group II. Adverse events were dry mouth seen in 1 in group I and 5 in group II, itching 1 in group I and 7 in group II, constipation 1 in group I and 6 in group II and additional dose was required in 7 in group I and 4 in group II. **Conclusion:** A single dose of intravenous acetaminophen is safe and effective in reducing fever where patients are unable to tolerate oral administration.

Key words: acetaminophen, fever, constipation

Received: 13 March, 2018 Accepted: 21 April, 2018

Corresponding author: Mohd.Tahazzul, Assistant Professor, Dept. of Pediatrics, TS Misra Medical College, Lucknow, Uttar Pradesh, India

This article may be cited as: Tahazzul M. Intravenous acetaminophen versus oral acetaminophen in the management of fever in children. J Adv Med Dent Scie Res 2018;6(5):112-115.

INTRODUCTION

Fever is one of the commonest presenting symptoms in clinical medicine in all age group patients. It is defined as oral temperature of >37.2 °C (>98.9 °F) in the morning or >37.7 °C (>99.9 °F) in the evening.[1] Fever can be caused by a numerous ailments ranging from potentially serious conditions to very benign illness.[2] Treatment with antipyretics not only reduces fever but also improves the associated other symptoms (e.g., − arthalgia, myalgia, headache, nausea, vomiting). Both pharmacologic and non-pharmacologic methods like tepid sponging have been used to reduce body temperature in febrile patients.[3]

Acetaminophen is a synthetic, nonopioid, centrally acting analgesic and antipyretic agent. It has a well-established efficacy profile, a well-understood risk/benefit ratio, and a very low potential for harmful drug–drug interactions. In recommended doses, acetaminophen is considered safe for infants, children, and adults.[4] Although the exact site and mechanism of action of acetaminophen are not clearly defined, its effectiveness as an antipyretic agent has been attributed to its effect on the hypothalamic heat-regulating center.Worldwide, acetaminophen is the most widely used analgesic and antipyretic.[5] It has a well-established efficacy profile, a well understood risk/benefit ratio, and a very low potential for harmful drug–drug interactions. In recommended doses, acetaminophen is considered safe for all age strata, from infants to the elderly.[6]The present study was conducted to compare antipyretic efficacy of intravenous (IV) acetaminophen versus oral (PO) acetaminophen in the management of fever in children.

MATERIALS & METHODS

The present study comprised of 62 patients of fever of both genders. The consent was obtained from their parents.

Data such as name, age, gender etc. was recorded. They were randomly divided into 2 groups of 31 each. Group I received oral acetaminophen (15 mg/ kg/dose) and group II received IV acetaminophen (15 mg/kg/dose) as antipyretic. Baseline vital parameters

including mean arterial pressure using non-invasive blood pressure monitor by oscillometric technique were recorded. Axillary temperature was recorded with mercury thermometer for 5 min every ½ hourly, till 6 h. Children were monitored for any evidence of intolerance. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Groups	Group I	Group II
Status	Oral acetaminophen	iv acetaminophen
M:F	17:14	13:18

Table I shows that there were 17 boys and 14 girls in group I and 13 boys and 18 girls in group II.

Table II Baseline parameters

Parameters	Group I	Group II	P value
Weight (Kgs)	24.7	25.1	0.91
Heart rate (beats/min)	114.6	102.3	0.01
Respiratory rate (cycles/min)	22.6	18.4	0.04

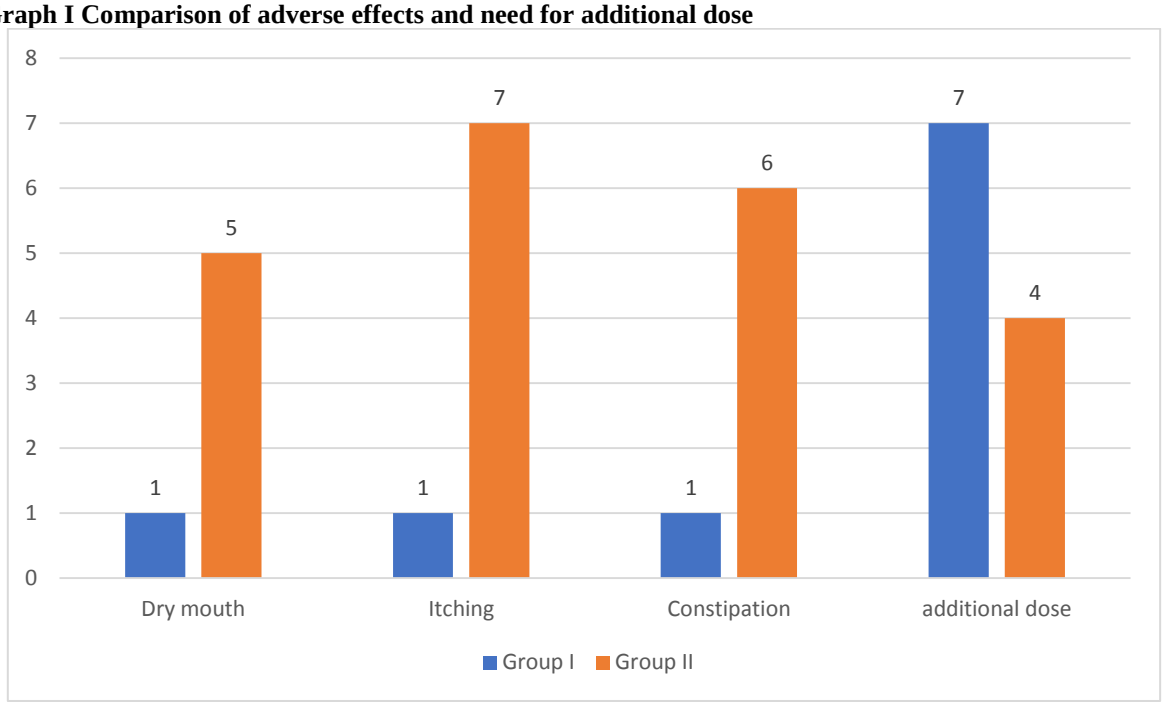
Table II shows that mean weight was 24.7 kgs in group I and 25.1 kgs in group II, heart rate was 114.6 beats/min in group I and 102.3 beats/min in group II and respiratory rate was 22.6 cycles/min in group I and 18.4 cycles/min in group II. The difference was significant (P< 0.05).

Table III Comparison of adverse effects and need for additional dose

Parameters	Group I	Group II	P value
Dry mouth	01	5	0.04
Itching	01	7	0.01
Constipation	01	6	0.03
additional dose	7	4	0.05

Table III, graph I shows that adverse events were dry mouth seen in 1 in group I and 5 in group II, itching 1 in group I and 7 in group II, constipation 1 in group I and 6 in group II and additional dose was required in 7 in group I and 4 in group II. The difference was significant (P< 0.05).

Graph I Comparison of adverse effects and need for additional dose



DISCUSSION

Acetaminophen is considered safest antipyretic as well as analgesic and is the most widely used antipyretic.[7] Per oral (PO) acetaminophen was first approved by the U.S. Food and Drug Administration (FDA) in the year 1951 and was marketed in 1953 in United States. Intravenous (IV) acetaminophen was first approved in Europe in 2001.[8] As of now acetaminophen has received approval for short-term management of fever as well as acute pain in about 80

countries besides United States.[9] Most of the available studies on acetaminophen were carried out in endotoxin-induced febrile models and in intensive care patients.[10] The present study was conducted to compare antipyretic efficacy of intravenous (IV) acetaminophen versus oral (PO) acetaminophen in the management of fever in children.

In present study, there were 17 boys and 14 girls in group I and 13 boys and 18 girls in group II. The mean weight was 24.7 kgs in group I and 25.1 kgs in group II, heart rate was 114.6 beats/min in group I and 102.3 beats/min in group II and respiratory rate was 22.6 cycles/min in group I and 18.4 cycles/min in group II. Roy et al[11] assessed the antipyretic efficacy of IV acetaminophen 15 mg/kg/dose vs. PO acetaminophen 15 mg/kg/dose over 6 h. Subjects were randomly assigned to receive either IV acetaminophen (n = 200) or PO acetaminophen (n = 200). Allergic reaction was found in 7 (3.5%) patients in IV acetaminophen group and was absent in PO acetaminophen group. Onset of constipation and dry mouth was found in 8 patients (4%) in IV acetaminophen group and was absent in PO acetaminophen group. Additional dose was required in 6 patients (3%) in intravenous acetaminophen group and 10 patients (5%) in oral acetaminophen group respectively. Statistically significant differences in the rate of fall in temperature through 180 min were observed in favor of the IV acetaminophen group when compared to those receiving PO acetaminophen. We observed that adverse events were dry mouth seen in 1 in group I and 5 in group II, itching 1 in group I and 7 in group II, constipation 1 in group I and 6 in group II and additional dose was required in 7 in group I and 4 in group II.Frank et al[12] assessed the antipyretic efficacy and safety of IV acetaminophen 1 g versus PO acetaminophen 1 g over 6 hours. Subjects who achieved a sufficient fever response to a test dose of reference standard endotoxin were randomly assigned to receive either IV acetaminophen and PO placebo (n = 54) or PO acetaminophen and IV placebo (n = 51). Of 105 subjects receiving study medication, 24 vomited within 2 hours postdose (PO acetaminophen, n = 15; and IV acetaminophen, n = 9) and were excluded from the modified intent-to-treat population that consisted of 36 and 45 subjects treated with PO and IV acetaminophen, respectively. While this was done to not confer an advantage to the IV formulation, a sensitivity analysis including these subjects did not change the overall efficacy results. Statistically significant results favoring IV acetaminophen were observed for the primary endpoint and also at each time point from T30 to T90 minutes, although the maximum mean observed temperature difference was only 0.3°C. The study drugs were well tolerated. The AE frequency was comparable between the IV and PO groups.

Kett et al[13] evaluated the antipyretic effect and safety of intravenous (i.v.) acetaminophen using an endotoxin-induced fever model. Subjects exhibiting sufficient fever response following administration of reference standard endotoxin (RSE) were randomly assigned to receive i.v. acetaminophen 1,000mg (n = 31) or matching placebo (n = 29). The primary efficacy end point was the weighted sum of temperature differences from baseline through 6h. Relative to placebo, i.v. acetaminophen administration produced a rapid decrease in temperature that persisted throughout the 6-h study period. The primary end point favoredi.v. acetaminophen over placebo ($P < 0.001$). Temperature differences from baseline reached statistical significance at T30 min after endotoxin administration (15min after completing the study medication infusion). Acetaminophen administered i.v. was well tolerated, and the frequency of adverse events was comparable to that after administration of i.v. placebo. This study shows that i.v. acetaminophen in a single 1,000-mg dose is safe and effective in reducing fever

CONCLUSION

Authors found that a single dose of intravenous acetaminophen is safe and effective in reducing fever where patients are unable to tolerate oral administration.

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