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RESEARCH ARTICLE

# A comparison of the antipyretic effect of Acetaminophen and Ibuprofen in febrile children hospitalized at Amir-al-Momenin Hospital in Semnan (Iran)

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**ABSTRACT**

Prolonged and high fever may cause various disturbances in children, and prompt lowering of fever is essential. Therefore, an appropriate treatment aimed at rapid lowering of fever and keeping the child afebrile is mandated. There have been various studies on different types of anti-pyretic treatment in children. The aim of our study was to compare the antipyretic effect of Acetaminophen and Ibuprofen.100 febrile patients aged 2 months-12 years, who were admitted into Amir-al-Momenin Hospital in Semnan in 2005, were randomly allocated into two groups consisting of 50 patients each. Acetaminophen (15 mg/kg/dose) was administered to one group and Ibuprofen (10 mg/kg/dose) to the other. Body temperature for each patient was recorded initially before the administration of each drug; and subsequently at 30 min., 1, 2, 3, 4, 5 and 6 hours after the drug use. There was no significant difference between the antipyretic effect of acetaminophen and ibuprofen until the end of the 3rd hour. Both drugs lowered fever markedly and proved to be equally effective. However during the $4^{th}$ ($p=0.029$), $5^{th}$ ($p=0.012$), and $6^{th}$ ($p=0.012$) hour after treatment, ibuprofen was more effective than Acetaminophen. In conclusion both acetaminophen and ibuprofen proved to be effective antipyretic agents. The antipyretic effects of both drugs as well as their efficacies were the same, but the duration of action of Ibuprofen was longer than Acetaminophen.

**Keywords:** *Fever, Acetaminophen, Ibuprofen, Febrile children*

Normal body temperature is 37°C (36°C - 37.5°C), and varies in a regular circadian fashion every day. This circadian rhythm, or diurnal variation, results in lower body temperatures in the early morning and temperatures approximately 1°C higher in the evening. Regulation of body temperature is mediated by the thermosensitive neurons located in the anterior hypothalamus that respond to changes in blood temperature as well as to cold and warm receptors located in skin and muscle. Fever is a controlled increase in body temperature over the normal values for an individual. Regardless of the cause of fever (i.e. infection, malignancy or rheumatologic disorders), the body's thermostat is reset in response to endogenous pyrogenes. The best studied mediator that acts as an endogenous pyrogen is the lipid prostaglandin E2 [1].

In humans, increased temperature (fever) is associated with decreased microbial reproduction and an increased inflammatory response, suggesting that it is an effective response and should be treated only in specific circumstances. Acetaminophen, Ibuprofen and Aspirin as inhibitors of hypothalamic cyclo– oxygenase inhibit PGE2 synthesis are all effective antipyretic agents, but because Aspirin has been associated with Reye's syndrome in children, its use is not recommended in febrile children. Acetaminophen, a para-aminophenol compound, at a dose of 10-15 mg/kg q 4 hr orally is a safe antipyretic and analgesic drug with hardly any significant side effects. However, prolonged use of this drug may lead to renal injury or hepatic failure [1].

Ibuprofen, a non-steroidal anti-inflammatory drug, given 10 mg/kg q 6 hr orally, may cause gastrointestinal hemorrhage, dyspepsia, reduced renal blood flow; and

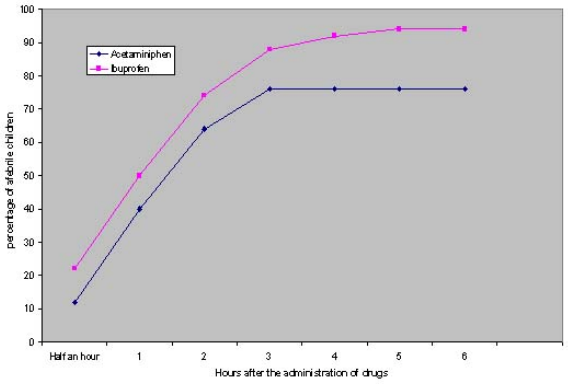


**Fig 1.** Percentage of afebrile patients during the following hours after administration of Acetaminophen and Ibuprofen

rarely, aseptic meningitis, hepatic toxicity or aplastic anemia [1]. There have not been any formal studies of the antipyretic effect of these two drugs in Iranian children to date. We therefore decided to compare the effectiveness of Acetaminophen and Ibuprofen as antipyretic agents in Iranian febrile children.

## MATERIALS AND METHODS

100 febrile patients aged 2 months to 12 years, admitted into Amir-al-Momenin Hospital of Semnan University of Medical Sciences from October 2004 to October 2005, were randomly allocated to two groups, each with 50 patients.

The patients selected were undergoing their first 24 hours of admission, had not received any medications, and were included in the study irrespective of their initial/provisional diagnosis.

Acetaminophen 15 mg/kg/dose were administered to the patients in the first group, and Ibuprofen 10mg/kg/dose to the patients in the second group. The patients' temperature was recorded before administration, and in 1/2, 1, 2, 3, 4, 5 and 6 hours after administration of the drugs. Both drugs were administered in syrup form and measured in ml (by a syringe); and the same Iranian brand of Acetaminophen and Ibuprofen were used during the study.

Recording of temperature and collection of data was carried out by pediatric ward nurses and interns. These professionals had received the same training for obtaining axillary temperature readings using a mercury thermometer for the specific purpose of the study, and entering the data in questionnaires which were used for statistical analysis.

## RESULTS

The average initial temperature (before administering the drugs) was $38.69 \pm 0.58^{o}C$ in the 1st (Acetaminophen) group, compared to $38.77 \pm 0.61^{o}C$ in the 2nd (Ibuprofen) group. There was no significant difference between the two groups in this respect, (P=0.481).

The average time between giving the drugs and the fall in temperature to normal, was $1.5 \pm 0.84$ hours in the 1st group, compared to $1.65 \pm 1.11$ hours in the 2nd group. There was not a significant difference between two groups from this point of view.

Half an hour after administering the drugs, 6 patients from the 1st group (12%) and 11 patients from the 2nd group (22%) had a normal temperature. One hour after treatment, 20 patients in the first group (40%) and 25 patients in the second group (50%) were afebrile. These findings show that the response rate does not have a significant difference in the two groups after half (p=0.183) and one hour (p=0.315).

At the end of the 2nd hour the number of afebrile patients was 32 (64%) in the 1st group and 37 (74%) in the 2nd group. At the end of the 3rd hour, this number was 37 (74%) and 44 (88%) for the 1st and the 2nd group respectively. Therefore, there was no significant difference between the response rate of patients in the two groups after 2 hours (p=0.280) and 3 hours (p=0.118).

However, 4 hours after administration of the drugs, 38 patients (76%) in the 1st group were afebrile compared to 46 patients (92%) in the 2nd group, demonstrating a significant difference between the response rates of patients in the two groups at the end of this period (p=0.029). 5 hours after administration of the drug, 38 patients in the 1st group (76%) and 47 patients in the 2nd group (94%) were afebrile (p=0.012), reflecting an approximately similar response rate compared to the 4th hour; and these figures stayed the same after 6 hours. These findings show a significant difference between the number of afebrile patients across the 1st and 2nd group at the end of the 5th (p=0.012) and 6th (p=0.012) hour, (Fig 1).

## DISCUSSION

The results reveal no significant difference between the antipyretic activity of Acetaminophen and Ibuprofen until the 4th hour after administering the drugs. Both drugs caused marked lowering of the fever. However, compared to Acetaminophen, Ibuprofen was effective in a larger number of patients during the 4th, 5th, and 6th hour after administration.

In the study carried out in Nottingham Hospital UK, 4 hours after administration of Ibuprofen (20 mg/kg/day) and Acetaminophen (50 mg/kg/day) the temperature decreased $1.8^{o}C$ and $1.6^{o}C$ respectively. Thus, the effectiveness of the two drugs was roughly similar [2]. Although we used a different dose of each drug in our study, our findings yielded the same results, demonstrating an approximate $1.69^{o}C$ and $1.77^{o}C$ decline in the temperature after taking Acetaminophen and Ibuprofen, respectively.

In another study at Saint-Vincent De Paul Hospital of Paris involving 116 febrile children, acetaminophen ($9.8 \pm 1.9$ mg/kg) and Ibuprofen ($10.3 \pm 1.9$ mg/kg) were given as single dose antipyretic drugs. The required time for lowering the temperature was $3.79 \pm 1.3$ hours for Ibuprofen and 3.84 1.22 hours for Acetamino-

phen [3]. In comparison to the Paris study, our results showed a shorter duration for the lowering of fever by both drugs ($1.5 \pm 0.84$ hours for Acetaminophen and $1.65 \pm 1.11$ hours for Ibuprofen).

In a multi centric study in Mumbai involving 175 febrile children aged 4 month-12 years; Acetaminophen at 8 mg/kg was given to 90 children and Ibuprofen at 7 mg/kg to another 85. The average decline in temperature in both groups was similar and no significant difference was recorded. Consequently, the antipyretic activity of Acetaminophen and Ibuprofen was concluded to be the same [4]. Although we did not use similar doses of the two drugs in our study, our results were compatible with the results of the Mumbai study.

In the Pediatric Department of Ohio University, a group of febrile patients aged 2 - 11 years was studied for the antipyretic effects of Acetaminophen (10 mg/kg) and Ibuprofen (10 mg/kg). The results showed Ibuprofen to be more effective than Acetaminophen [5]. The main distinguishing feature of our study was that we used a higher dose of Acetaminophen (15 mg/kg), while Ibuprofen was taken at a similar dose; which accounts at least in part, for the discrepancy between our results and those of Ohio University.

In a mini-review of the efficacy of Acetaminophen and Ibuprofen at the Florence Nightingale School of Nursing in London, the effectiveness of the two drugs was shown to be the same. However, 6 hours after administration, Ibuprofen showed a significantly better antipyretic effect than Acetaminophen. Overall, both drugs were effective, with Ibuprofen having a longer duration of activity [6]. Our study gave the same results and revealed a better antipyretic effect for Ibuprofen from the $4^{th}$ to $6^{th}$ hour after treatment.

In another study on 22 febrile children, Acetaminophen and Ibuprofen were given as antipyretic drugs, and the temperature was measured at 30 min, 1, 2, 3, 4, 5, 6, 8, and 12 hours after treatment. The findings showed Ibuprofen to be effective in a larger number of patients after the $6^{th}$ and $8^{th}$ hour [7]. These results were also comparable with our results.

In the Pediatric Department of Detroit University, 37 febrile patients aged 2-12 years were randomly given Acetaminophen (10 mg/kg) and Ibuprofen (10 mg/kg). The results showed Ibuprofen to have a more effective and longer antipyretic activity [8]. The dose of acetaminophen in the Detroit University was lower than that of our study, accounting at least partially for the difference between the results obtained.

## CONCLUSION

Both Acetaminophen and Ibuprofen proved to be effective antipyretic agents. The onset of action of both drugs was found to be the same, but the duration of action of Ibuprofen was longer than Acetaminophen. Therefore, with the overall antipyretic activity of Acetaminophen and Ibuprofen being similar, and with acetaminophen having lesser side effects; Acetaminophen appears to be the antipyretic drug of choice in children**.**

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