

COMPARISON BETWEEN THE EFFECT OF COMBINED PARACETAMOL AND  
IBUPROFEN WITH PARACETAMOL ALONE IN THE TREATMENT OF FEVER IN  
CHILDREN

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## ABSTRACT

**Background:** Fever is one of the most common clinical conditions in children and a frequent cause of healthcare visits. Paracetamol and ibuprofen are widely used antipyretics, and recent interest has focused on the potential benefit of combined therapy due to their different mechanisms of action. **Objectives:** To assess the effectiveness of combined paracetamol and ibuprofen therapy compared with monotherapy in reducing fever in children. **Methods:** An unblinded randomized clinical trial was conducted in Mosul General Hospital, including febrile children aged 1–6 years. Participants were allocated into three groups: paracetamol, ibuprofen, and combined therapy. Body temperature was measured at baseline, 1, 3, and 4 hours after drug administration. Data were analyzed using appropriate statistical methods, and a p-value <0.05 was considered significant. **Results:** Paracetamol showed a more rapid reduction in temperature at 1 hour, while combined therapy demonstrated significantly greater effectiveness at 4 hours. The success rate of fever reduction was highest in the combined therapy group compared to monotherapy. No statistically significant difference was observed between paracetamol and ibuprofen alone. No serious adverse effects were reported. **Conclusions:** Combined paracetamol and ibuprofen therapy is more effective than monotherapy in reducing fever after 4 hours, while paracetamol alone provides faster initial relief. Combined therapy may be beneficial in selected cases but should be used under medical supervision.

**KEYWORDS:** Antipyretics; Children; Combination therapy; Fever; Ibuprofen; Paracetamol.

## 1- INTRODUCTION

Fever is one of the most prevalent clinical presentations in children and a frequent reason for medical attention. Although it is a normal physiological response to infection, it is frequently connected with parental anxiety and may result in excessive or inappropriate usage of antipyretic drugs. Current pediatric practice emphasizes that the major goal of fever control is to improve the child's comfort, not to achieve normothermia.<sup>[1]</sup> The most often used antipyretic drugs are paracetamol (acetaminophen) and ibuprofen, which have proven effectiveness and safety profiles.<sup>[2]</sup>

Paracetamol's antipyretic effect is primarily mediated by central inhibition of prostaglandin synthesis in the hypothalamus, whereas ibuprofen, a non-steroidal anti-inflammatory drug, inhibits both central and peripheral cyclooxygenase.<sup>[3]</sup> These complementary processes resulted in increased interest in the use of combination therapy, with the hope that it may produce better antipyretic effects than monotherapy.<sup>[4]</sup>

Several recent controlled randomized trials and meta-analyses have examined the efficacy of combination paracetamol and ibuprofen therapy. Evidence suggests that combination therapy may result in a faster fall in body temperature and a greater proportion of afebrile

children within the first few hours of delivery than either agent alone.<sup>[5-6]</sup> Furthermore, several prospective trials have found superior clinical outcomes and faster symptom relief without a notable increase in side effects.<sup>[7]</sup> However, other studies have found no significant difference between combination therapy and monotherapy after the initial phase of treatment, implying that the clinical importance of combination therapy is uncertain.<sup>[8]</sup>

Furthermore, systematic reviews and clinical guidelines continue to raise questions about the routine use of combination or alternating antipyretic regimens. While certain benefits in temperature reduction have been seen, these must be balanced against potential concerns, including dosing errors and the increased risk of toxicity associated with complex dosing schedules.<sup>[4,9]</sup>

As a result, many guidelines recommend using combination therapy only when monotherapy fails to provide adequate symptomatic relief.<sup>[2]</sup>

Given the ongoing controversy and diversity in the current evidence, further studies is needed to determine the comparative efficacy of combined paracetamol and ibuprofen against monotherapy in lowering fever in children. Such an evaluation is essential to support clinical decision-making and ensure safe and evidence-based therapy of pediatric fever.

## 2-PATIENTS AND METHODS

An official agreement was obtained from the Ministry of Health and Directorate of Health in Mosul before conduction of the present study. A verbal consent was taken from the parents of the patients. The present study is conducted from 1<sup>st</sup> of May 2025 to the 1<sup>st</sup> of February 2026 using the design of unblinded randomized clinical trial, three hundred cases were collected from the emergency Department at Mosul General Hospital suffering from fever greater than 38 °C (axillary corrected). This Fever was due to many illnesses like acute gastroenteritis, urinary tract infection, respiratory tract infection, otitis media and etc. They were allocated in either group A receiving paracetamol syrup 15mg/kg/dose orally, group B receiving ibuprofen syrup

10mg/kg/dose orally. And group C receiving combined treatment (paracetamol 15mg/kg/dose and ibuprofen 10mg/kg/dose at same time orally). each group involved 100 cases.

The temperature of the patients was measured by the researchers used electrical thermometer from axilla region. The temperature was recorded at the time of dose in take at zero Hour, at 1- Hour, at 3- hour and at 4-hour after receiving treatment.

Drugs was given under supervision of the medical staff to ensure taking the medication if the patient vomits the drugs, he/she should take another dose of drugs.

The benefits and side effects of drugs and treatment and the nature of febrile illness were explained to the parents. Adverse effects including of allergic reaction (pruritic rash), and hepatotoxicity following overdose. Other side effects due to paracetamol administration would be asthma, rhino-conjunctivitis, eczema and atopy. Gastrointestinal bleeding and renal failure are serious side effects for Ibuprofen. Both paracetamol and ibuprofen have been shown that have equal role in children safety for fever treatment. There were no serious adverse events in the trials that were directly attributed to the medications used.

Data were analyzed using appropriate statistical methods. Continuous variables were expressed as mean values, and categorical variables as frequencies and percentages. Comparisons between groups were performed to assess differences in temperature reduction over time, and treatment effectiveness was evaluated using success rates and relative risk. Statistical significance was determined using p-values, with a threshold of less than 0.05 considered significant.

## 3-RESULTS

Out of 300 children in the study (38%) were boy, (62%) were girl. The mean of age for boys and girls were 2.38 ± 2.5 and 2.6±2.78 years, respectively. The average of temperature at the admission, 1, 3 and 4 hours after administration with paracetamol, ibuprofen and combination therapy are shown in Table 1.

**Table 1: The mean temperature level over time after the dose intake.**

Drugs	Mean Temperature at (0- Hour)	Mean Temperature at (1- Hour)	Mean Temperature at (3- Hour)	Mean Temperature at (4- Hour)
Paracetamol	38.96 <sup>0</sup> C	37.7 <sup>0</sup> C	37.5 <sup>0</sup> C	37.8 <sup>0</sup> C
Ibuprofen	38.95 <sup>0</sup> C	37.91 <sup>0</sup> C	37.41 <sup>0</sup> C	37.5 <sup>0</sup> C
combined	38.98 <sup>0</sup> C	38.2 <sup>0</sup> C	37.28 <sup>0</sup> C	37.14 <sup>0</sup> C

The average of temperature measured at 1 and 4 hours after drug intake in the three groups showed different. The average of temperature on admission, 1, 3 and 4 hours after drug intake in each group and was compared with each other. The results shows one hours after taking drug a significant difference between the mean of

temperature for paracetamol, ibuprofen and combination therapy in favour of paracetamol was observed. Moreover, 4 hours after taking drug a significant difference between the mean of temperature for paracetamol, ibuprofen and combination therapy in favour of combination therapy was observed.

**Table 2: The success rate at one hour, four hour.**

Drugs	Success rate after one hour	Success rate after four hour
paracetamol	95%	60%
Ibuprofen	80%	66%
Combined ( Paracetamol and Ibuprofen )	85%	88%

**Table 3: The result of comparing combined protocol with paracetol alone.**

Result of comparing combined protocol with paracetamol	
Relative Risk(RR)	0.20
95% CI	1.5945 to 15.6786
P value	< 0.001 ( significant result)

**Table 4: Result of comparing combined protocol with ibuprofen.**

Result of comparing combined protocol with ibuprofen	
Relative Risk(RR)	0.2353
95% CI	1.3335 to 13.5247
P value	< 0.05 ( significant result)

**Table 5: Result of comparing paracetamol with ibuprofen.**

Result of comparing paracetamol with ibuprofen drugs	
Relative Risk(RR)	0.8500
95% CI	0.3991 to 1.8105
P value	0.6736 ( not significant)

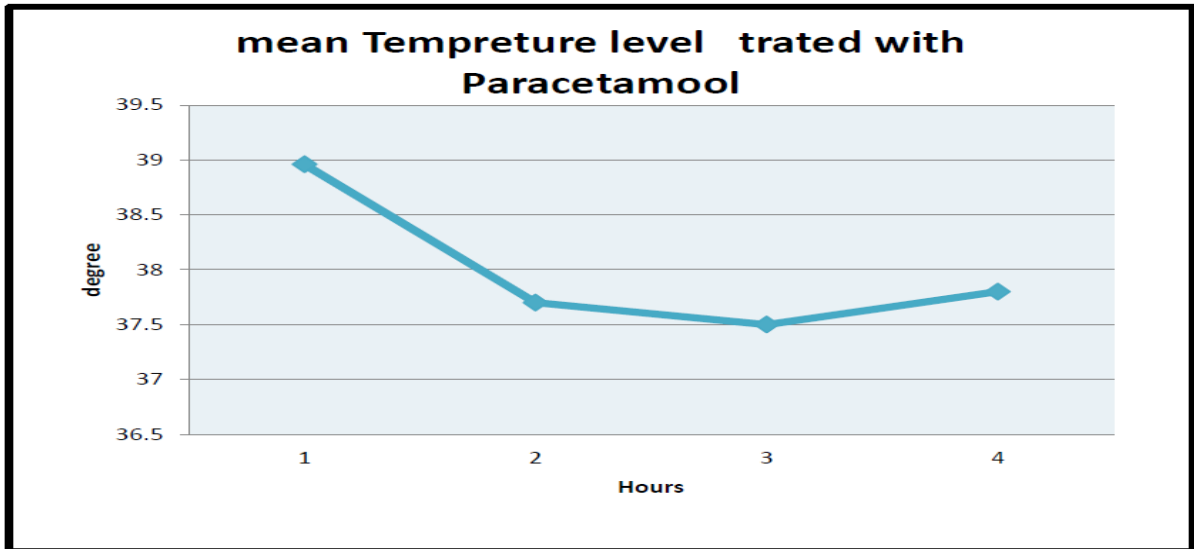


Figure 1: Mean temperature level treated with paracetamol.

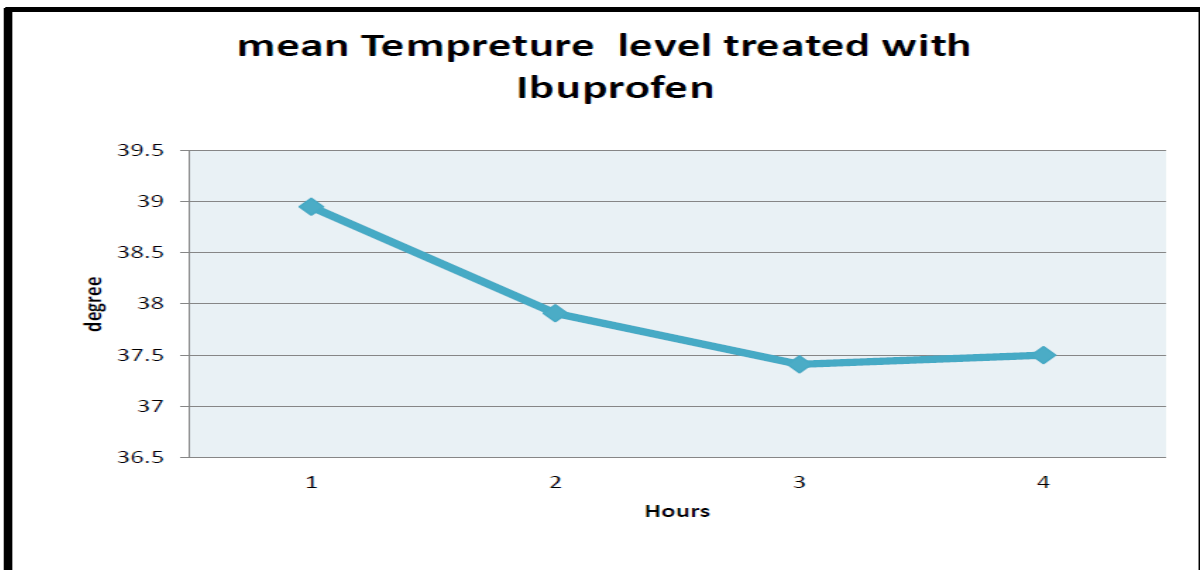


Figure 2: Mean temperature level treated with Ibuprofen.

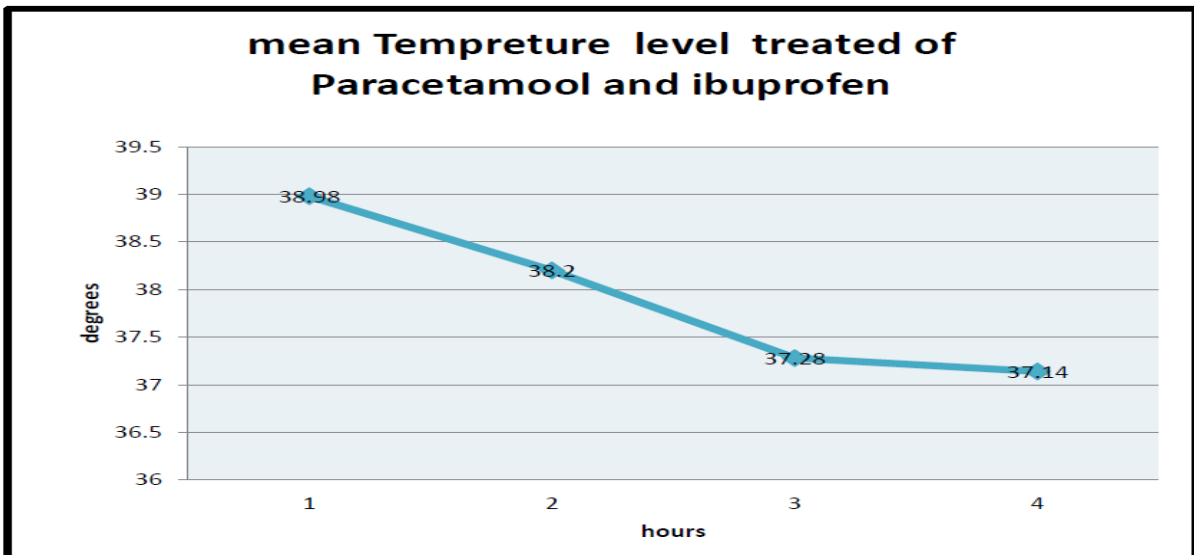


Figure 3: mean temperature level of combined treatment.

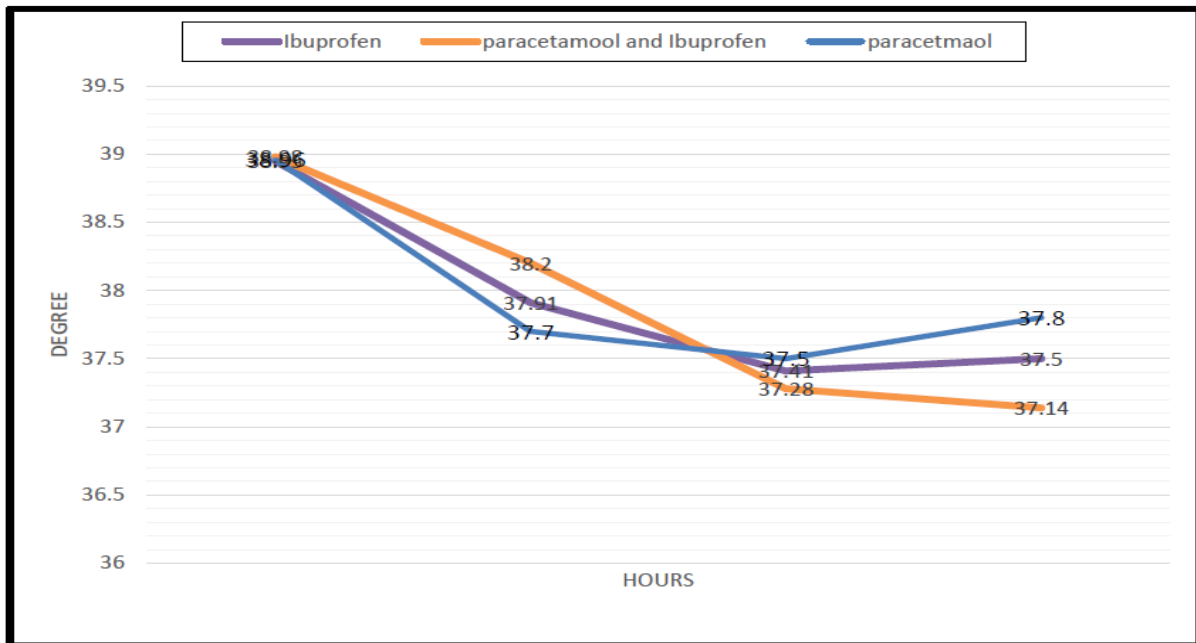


Figure 4: Comparison between mean Temperature levels treated of paracetamol, ibuprofen and combined treatment.

#### 4- DISCUSSION

The current study found that combined therapy with paracetamol and ibuprofen is more successful in lowering fever at 4 hours than monotherapy, with paracetamol having a faster onset of action at 1 hour. These findings are consistent with other previous studies showing that combination therapy improves antipyretic efficacy, especially in the early stages of treatment. A recent prospective study found that the combination of paracetamol and ibuprofen resulted in faster and greater temperature reduction than either treatment alone, with no significant increase in adverse effects.<sup>[10]</sup> Similarly, a randomized clinical study revealed that the combination group experienced the higher temperature reduction and proportion of afebrile children during the first 4 hours.<sup>[11]</sup>

In the current study, paracetamol exceeded ibuprofen in terms of one-hour effectiveness, which is consistent with its rapid central mechanism of action and faster onset. This finding is corroborated by prior study indicating that paracetamol reduces fever more immediately, although its duration of action may be shorter.<sup>[12]</sup> In contrast, meta-analyses have revealed that ibuprofen has a more prolonged antipyretic effect throughout time, notably between 4 and 24 hours, due to its extended half-life and peripheral anti-inflammatory activity.<sup>[13]</sup>

At 4 hours, the superior efficacy of combined therapy seen in the current study is consistent with recent systematic reviews and meta-analyses, which show that dual therapy may be more beneficial than monotherapy in terms of temperature reduction and afebrile status.<sup>[14]</sup> Pharmacologically, this can be explained by the two medications' complimentary modes of action: paracetamol works centrally, whilst ibuprofen has both central and peripheral actions, resulting in a synergistic

antipyretic response.<sup>[15]</sup> However, the evidence remains conflicted on the usual use of combination therapy. Some systematic evaluations have found that the increased effect of combination therapy over monotherapy is minimal and may not be clinically significant, particularly after the first few hours of treatment.<sup>[16]</sup> Furthermore, new evidence suggests that both paracetamol and ibuprofen alone have equivalent efficacy in many clinical contexts, with variations mostly related to onset and duration rather than total effectiveness.<sup>[17]</sup>

In terms of safety, the current study found no major adverse events, which is consistent with previous studies indicating that short-term use of both medications, either alone or in combination, is generally safe in children when administered at adequate doses.<sup>[10,13]</sup> Nonetheless, there are still worries about the potential dangers of combined or alternating therapy, including dosage errors and increased toxicity, prompting numerous guidelines to advocate careful usage under medical supervision.<sup>[14]</sup>

This study has some limitations. The unblinded design may have resulted in observer and measurement bias. The relatively short follow-up period (up to 4 hours) limits the ability to evaluate long-term antipyretic effects and fever recurrence. Furthermore, the study focused primarily on temperature decrease rather than standardized clinical comfort or distress levels. The variability in underlying causes of fever, as well as the lack of classification by diagnosis, may have influenced the outcomes.

#### 5- CONCLUSION AND RECOMMENDATION

Combined therapy with paracetamol and ibuprofen was more successful in lowering body temperature at 4 hours

than monotherapy, but paracetamol alone had a faster onset of action at 1 hour. Combined therapy may be considered in children who do not react well to monotherapy or who have persistent or recurrent fever, but it must be used under physician supervision to avoid dose errors and side effects. More large-scale, blinded randomized studies with longer follow-up and clinical outcome measures are needed to determine the efficacy and safety of combination antipyretic medication.

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