Efficacy & Safety of Ketoprofen 25mg vs. Paracetamol 1g intravenous preparations in the management of fever in adults: A pilot, double-blind, parallel-group, randomized controlled trial

Dr. Omar S. Tabbouche, M.Sc, D.Sc, Pharm.D
Head of Pharmacy Department
New Mazloum Hospital
Tripoli, Lebanon
Research Journey

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**INTRODUCTION**

One of the four primary vital signs\(^1\)

**Standard of Fever Management: Paracetamol & Ibuprofen**

- **Paracetamol:**
  - A small overdose (25%\(>\) MDD) is considered hepatotoxic\(^2\)
  - Most common cause of Acute Liver Failure in the Western World\(^3\)

- **Ketoprofen:**
  - Crosses the Blood-Brain Barrier (BBB)\(^4\)
  - 25% of the standard dose
  - Central effect with minimal peripheral effects\(^5\)
  - Lower cost

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RATIONALE

• To compare the antipyretic efficacy & safety of Ketoprofen 25mg to Paracetamol 1g intravenous preparations

• “Pioneer RCT” - No previous studies have investigated the difference between the two antipyretic medications per the intravenous route
OBJECTIVES

• PRIMARY OUTCOME:
  – Mean Reduction in Core Body Temperature (CBT) 30 minutes after the end of the I.V. infusion “CBT30”

• SECONDARY OUTCOMES:
  – Mean Reduction in CBT 15 minutes after the end of the I.V. infusion “CBT15”
  – Rate of Adverse Drug Events in both groups
  – Severity Level of the Adverse Drug Events
MATERIALS & METHODS

1. Setting:
   - New Mazloum Hospital, in collaboration with Queen’s University Belfast, UK

2. Study Design:
   - Double-blind Randomized Controlled Trial “RCT”
3. **Sample Population:**

a. **Power** 0.05, CI 95%, **Effect size** 0.4, **Error** 0.8 (162 pat.)

b. **Sample size:** 180 patients equally divided into the two treatment arms (90 patients/arm)

c. **Inclusion & Exclusion criteria**

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult patients (12-70 years)</td>
<td>Pediatric patients &lt; 12 years old</td>
</tr>
<tr>
<td>Males &amp; Females</td>
<td>Geriatric patients &gt; 70 years old</td>
</tr>
<tr>
<td>Fever of infectious origin (proof of infection)</td>
<td>Female pregnant women in the 3rd trimester</td>
</tr>
<tr>
<td>Fever &gt;38.5°C</td>
<td>Hypersensitivity to any of the two studied drugs</td>
</tr>
<tr>
<td>Wards: ER, Internal Medicine, cardiology, &amp; ICU</td>
<td>Fever of neurologic origin and/or fever of unknown origin</td>
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<td></td>
<td>Active gastric or cerebro-vascular bleeding</td>
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<tr>
<td></td>
<td>History of peptic ulcer</td>
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<tr>
<td></td>
<td>Severe Hepatic &amp;/or Renal insufficiency</td>
</tr>
</tbody>
</table>
### 3. Sample Population:

**d. Characteristics of the sample population**

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>KEToprofen</th>
<th>PARacetamol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>Age</td>
<td>42.86 +/- 14.983</td>
<td>48.91 +/- 17.594</td>
</tr>
<tr>
<td>Male : female ratio</td>
<td>1.72</td>
<td>1.14</td>
</tr>
<tr>
<td>Initial Body Temperature (°C)</td>
<td>38.888 +/- 0.4598</td>
<td>38.754 +/- 0.5635</td>
</tr>
<tr>
<td>Infections (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>34.5</td>
<td>36.4</td>
</tr>
<tr>
<td>Upper airway</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Gastro-intestinal</td>
<td>14.5</td>
<td>5.6</td>
</tr>
<tr>
<td>Urinary</td>
<td>20</td>
<td>20.6</td>
</tr>
<tr>
<td>Skin</td>
<td>13.3</td>
<td>13.3</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>8.9</td>
<td>0</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>0</td>
<td>1.1</td>
</tr>
<tr>
<td>Unknown</td>
<td>8.9</td>
<td>13</td>
</tr>
<tr>
<td>PPI therapy (%)</td>
<td>67.8</td>
<td>94.4</td>
</tr>
<tr>
<td>Departments (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>77.8</td>
<td>78.9</td>
</tr>
<tr>
<td>Cardiology</td>
<td>12.2</td>
<td>11.1</td>
</tr>
<tr>
<td>ER</td>
<td>5.6</td>
<td>5.6</td>
</tr>
<tr>
<td>ICU</td>
<td>3.3</td>
<td>4.4</td>
</tr>
</tbody>
</table>
4. **Protocol:**

Sample population $n=180$

- Paracetamol 1g I.V. infusion over 10 min ($n=90$)
  - Body temperature 15 minutes after administration
  - Body temperature 30 minutes after administration

- Ketoprofen 25mg I.V. infusion over 10 min. ($n=90$)
  - Body temperature 15 minutes after administration
  - Body temperature 30 minutes after administration

5. **Statistics:**
   
   a. Univariante Analysis of Variance “ANOVA”
   
   b. Software: IBM SPSS v.21
RESULTS

- **PRIMARY OUTCOME “DBT30”**:  
  - DBT30 of Ketoprofen “1.448 ± 0.3233”, Paracetamol “1.163 ± 0.4575”  
  - Ketoprofen reduced CBT by 0.285°C more than Paracetamol  
  - 24.5% more reduction in CBT
RESULTS

- **SECONDARY OUTCOMES “DBT15”:**
  - DBT15 of Ketoprofen “0.8067 ± 0.294”, Paracetamol “0.6567 ± 0.365”
  - Ketoprofen reduced CBT by 0.15°C more than Paracetamol
  - 22.8% more reduction in CBT

\[ p = 0.002 \]
RESULTS

• SECONDARY OUTCOMES “RATE OF THE ADVERSE DRUG EVENTS”:

- Nausea
- Vomiting
- Dyspepsia
- Increase in Bld Pressure
- Elevation in Hepatic Enzymes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ketoprofen</th>
<th>Paracetamol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>0.0%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.2%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>2.2%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Increase in Bld Pressure</td>
<td>1.1%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Elevation in Hepatic Enzymes</td>
<td>1.1%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>
RESULTS

• SECONDARY OUTCOMES “SEVERITY OF THE ADVERSE DRUG EVENTS”:

ADE CLASS

CONCLUSION

• Ketoprofen 25mg I.V. reduced the fever more potently than did Paracetamol 1g (p=0.012)

• Ketoprofen 25mg I.V. achieved a faster antipyretic response

• The safety profiles of both medications were almost similar

• Ketoprofen 25mg I.V. is a much more cost-efficient antipyretic medication than Paracetamol 1g I.V.
REFERENCES


