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

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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*

1. O'Grady et al. *Crit. Care Med.* 2008;36(4): 1330-1349.
2. US FDA. 1999. http://www.fda.gov/ohrms/dockets/dailys/04/mar04/033104/78n-0036L-rc00002-04-Tab-C-vol137.pdf.
3. Hawkins LC et al. *Drug Saf.* 2007;30(6):465-479.
4. Kokki H. *Paed. Drugs.* 2010;12(5):313-329.
5. Kokki H. *Clin Drug Invest.* 2010; 30(4): 251-258.

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"

MATERIALS & METHODS

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

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

MATERIALS & METHODS

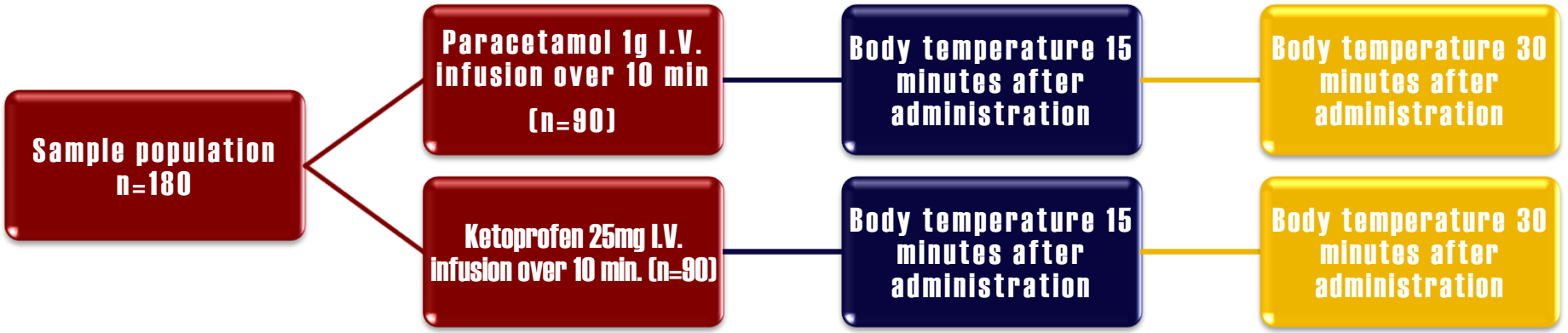
3. Sample Population:

d. Characteristics of the sample population

CHARACTERISTICS	KETOPROFEN	PARACETAMOL
Number of patients	90	90
Age	42.86 +/- 14.983	48.91 +/- 17.594
Male : female ratio	1.72	1.14
Initial Body Temperature (°C)	38.898 +/- 0.4598	38.754 +/- 0.5635
Infections (%)		
Pulmonary	34.5	36.4
Upper airway	0	10
Gastro-intestinal	14.5	5.6
Urinary	20	20.6
Skin	13.3	13.3
Prostatitis	8.9	0
Hepatitis A	0	1.1
Unknown	8.9	13
PPI therapy (%)	67.8	94.4
Departments (%)		
Internal Medicine	77.8	78.9
Cardiology	12.2	11.1
ER	5.6	5.6
ICU	3.3	4.4

MATERIALS & METHODS

4. Protocol:



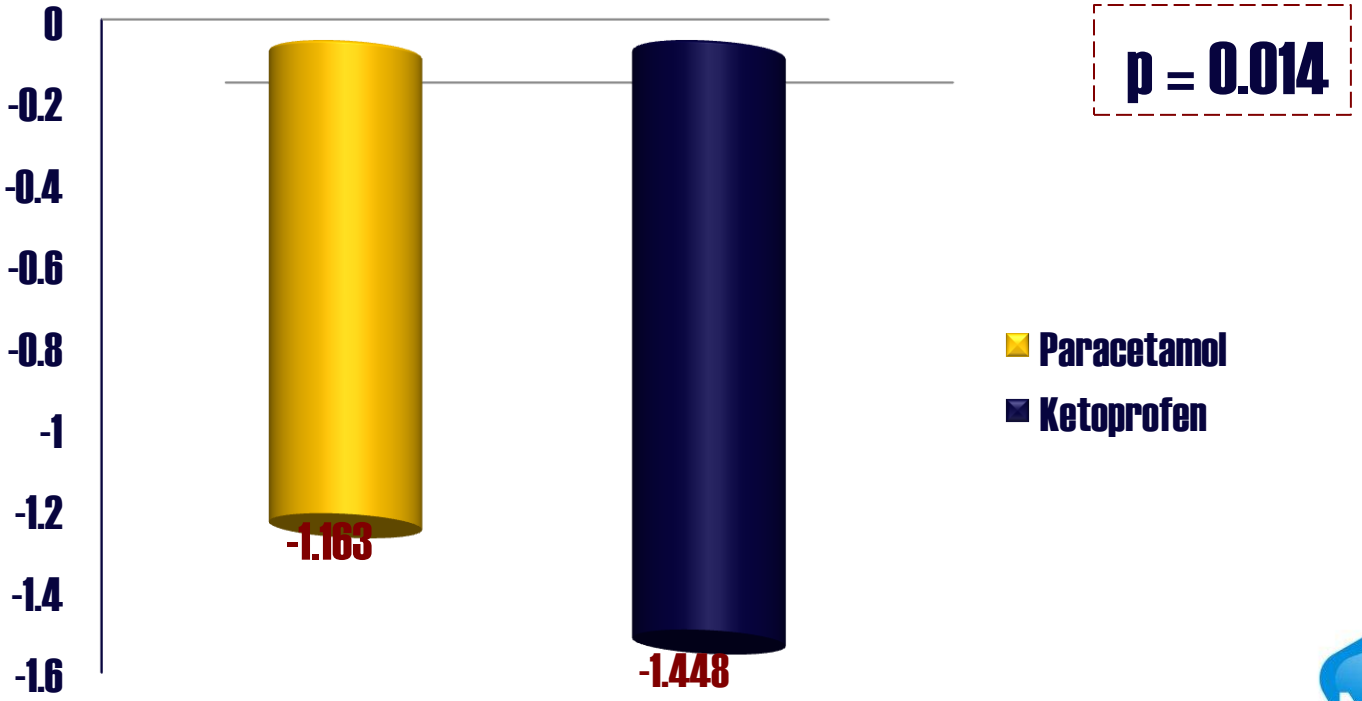
5. Statistics:

a. Univariate Analysis of Variance "ANOVA"

b. Software: IBM SPSS v.21

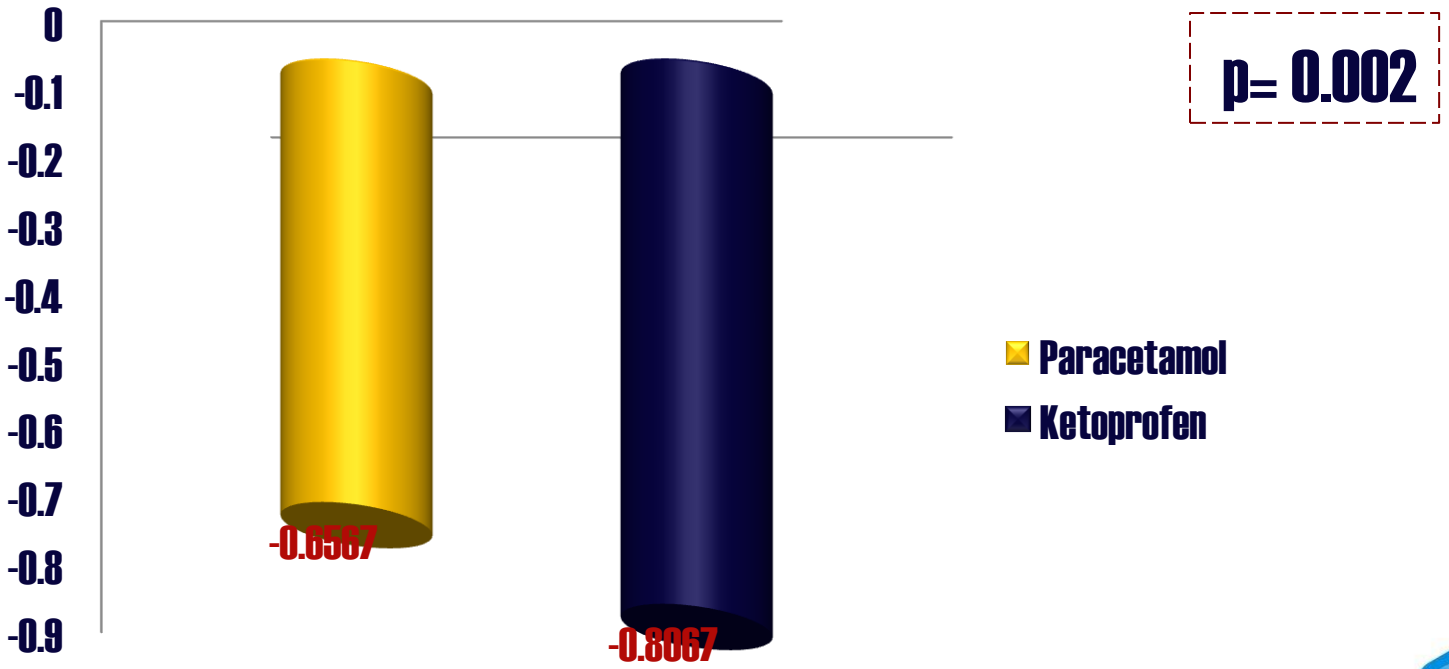
RESULTS

- **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

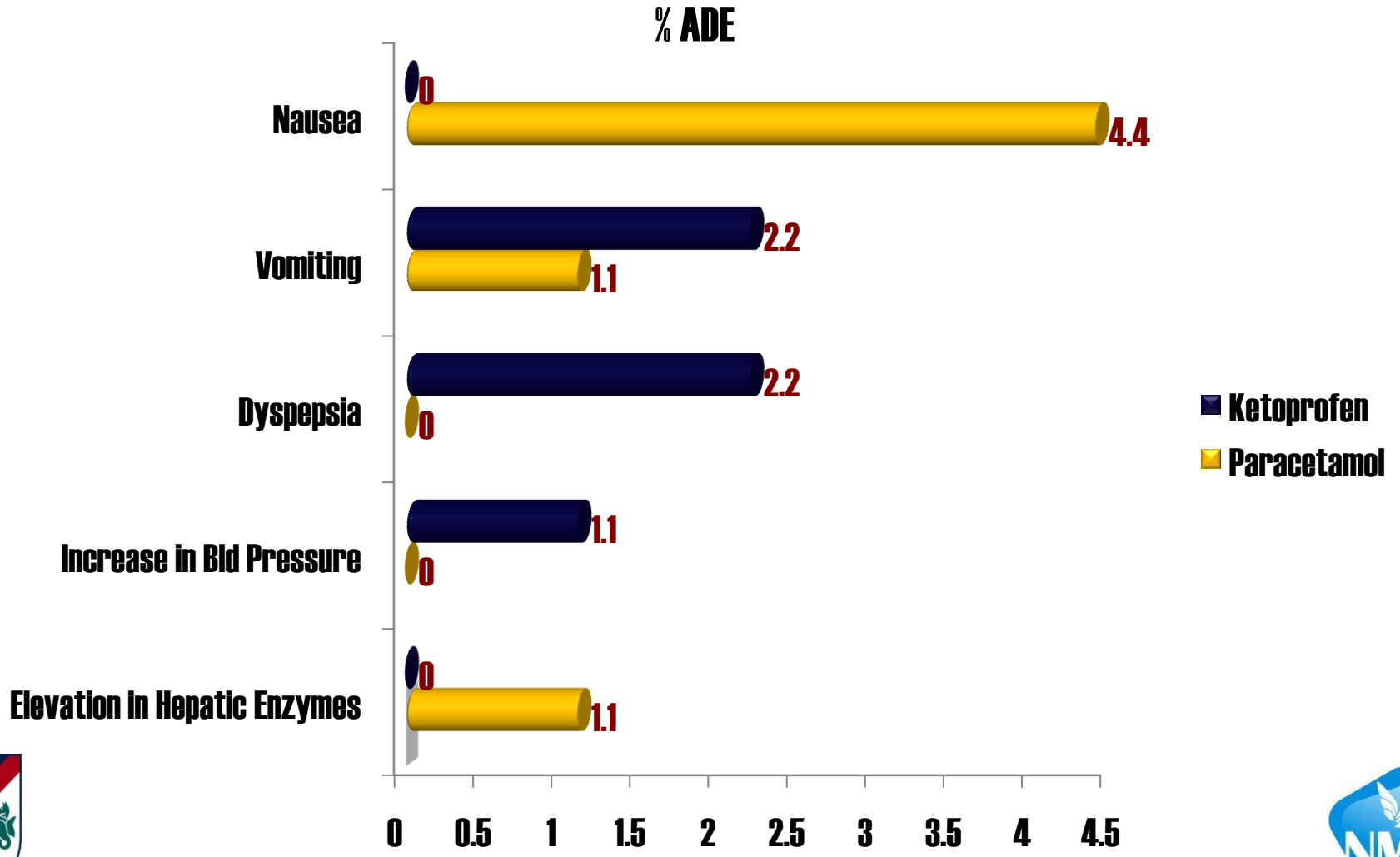
- **SECONDARY OUTCOMES "DBT15":**
  - DBT15 of Ketoprofen "0.8067 ± 0.294", Paracetamol "0.6567 ± 0.365"
  - Ketoprofen reduced CBT by 0.15°C more than Paracetamol
  - 22.8% more reduction in CBT



p= 0.002

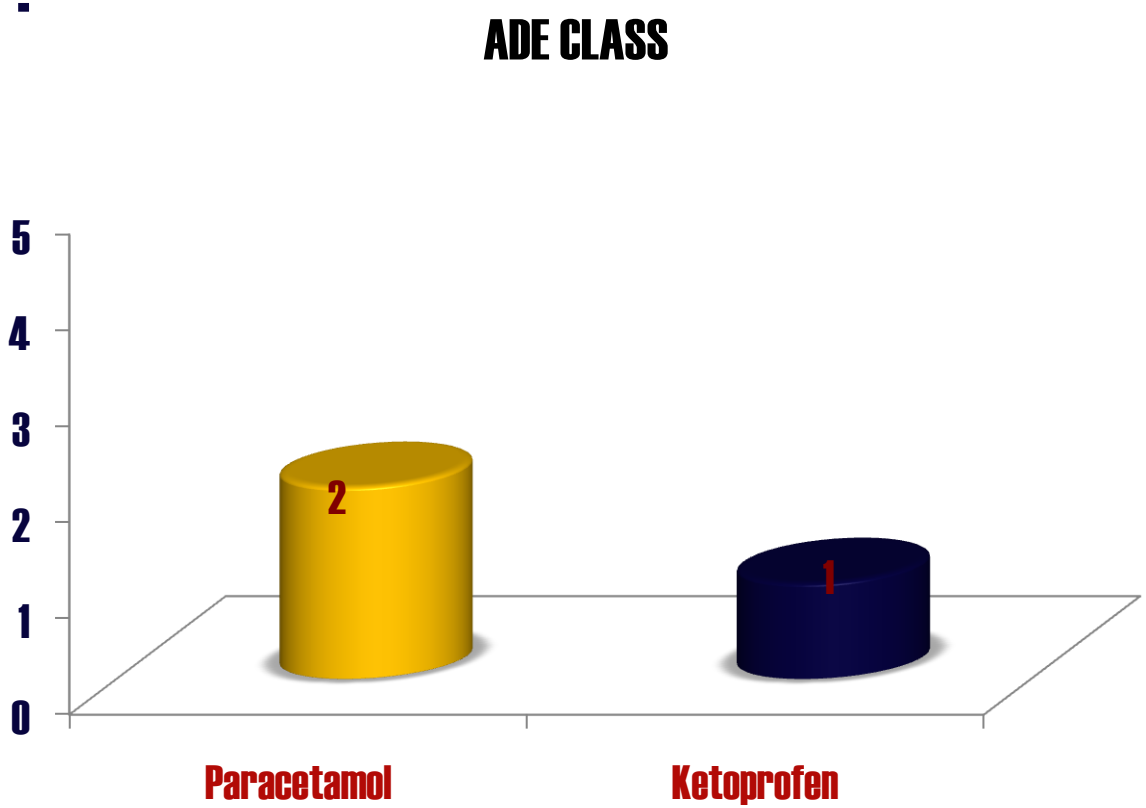
RESULTS

- **SECONDARY OUTCOMES "RATE OF THE ADVERSE DRUG EVENTS":**



RESULTS

- SECONDARY OUTCOMES "SEVERITY OF THE ADVERSE DRUG EVENTS":



Common Toxicity Criteria. US FDA. 1999. http://www.fda.gov/ohrms/dockets/dailys/04/mar04/033104/78n-0036L-rc00002-04-Tab-C-vol137.pdf

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.

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