

DOI: <http://dx.doi.org/10.18203/2319-2003.ijbcp20200708>

Original Research Article

A comparative single dose study of oral acetaminophen 650 mg to its standard 500 mg dose in adult pyrexia patients in a tertiary care hospital

Pradeepkumar B. T.^{1*}, Jayanthi C. R.², Raveendra K. R.³, Ramya Y. S.²

¹Department of Pharmacology, Annapoorna Medical College and Hospital, Salem, Tamil Nadu, India

²Department of Pharmacology, ³Department of General Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

Received: 28 January 2020

Revised: 12 February 2020

Accepted: 13 February 2020

*Correspondence:

Dr. Pradeepkumar B. T.,

Email: pradeepkumar6@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Acetaminophen commonly called as paracetamol is the most used ‘over-the-counter’ analgesic for headache, musculoskeletal pain, dysmenorrhoea etc. It is the best drug to be used as antipyretic for fever due to any cause and safest to be prescribed in all age groups. Antipyretic dose of acetaminophen is 325 to 650 mg; 3 to 4 times a day and is available in the strength of 650 mg and 500 mg tablets. This study was conducted to analyse the antipyretic efficacy and safety profile of two different doses of acetaminophen in patients with low grade fever.

Methods: 300 hospitalised patients aged more than 18 years, in department of General Medicine, having low grade fever (38° to 39° C) were randomly allocated into two groups of 150 each, group A received 500 mg and group B received 650 mg of single oral dose of acetaminophen tablets. Oral temperature was measured before dosing, 30 minutes after dosing, one hour, two hourlies thereafter for 6 hours after the dose. Safety was assessed by monitoring for adverse effects during the study and 24 hours after administration of the assigned drug.

Results: There was a statistically significant decrease in temperature in group B patients from baseline 39.06±0.87° C to 37.02±0.89° C at the end of 6th hour as compared with 39.18±0.80° C to 38.03±0.77° C in Group A patients (p=0.031).

Conclusions: Our study concluded that acetaminophen in a dose of 650 mg is highly efficacious antipyretic drug compared to acetaminophen 500 mg with no adverse effects.

Keywords: Acetaminophen, Antipyretic, Cyclooxygenase

INTRODUCTION

Acetaminophen (paracetamol) is an effective antipyretic belonging to the class of nonsteroidal anti-inflammatory drugs (NSAIDs). It is also an effective analgesic for relieving mild to moderate pain.¹ The mechanism of antipyretic action is not completely understood although it is thought to act primarily through inhibition of the prostaglandin synthetase in the brain.² It is of particular

value when other NSAIDs are contraindicated, perhaps by known hypersensitivity or a history of gastric ulceration or bleeding.³ Recent studies have showed that acetaminophen is a reversible inhibitor of hypothalamic cyclooxygenase-3 (COX-3) enzyme, which is a splice variant of cyclooxygenase-1 (COX-1).⁴ It has a short half-life of around 2 to 3 hours which necessitates frequent dosing. The UK recommended regimen is between 500 mg to 1000 mg every 4 to 6 hours.⁵ Acetaminophen is

commonly available in strength of 650 mg and 500 mg. This comparative study is intended to systematically analyse the antipyretic and safety profile of a single dose of 650 mg and 500 mg acetaminophen in patients with low grade fever (38° to 39° C).

METHODS

This was a single centre, open label, comparative study conducted in the inpatients of department of General Medicine Bangalore Medical College and Research Institute attached to Victoria Hospital Bangalore, India between October 2014 to December 2014.

Inclusion criteria

Patients willing to consent for the study and patients aged ≥ 18 years of either sex with low grade fever (38° to 39° C) recorded by measuring oral temperature by a thermometer were included.

Exclusion criteria

Patients aged < 18 years, patients not consenting for the study, patients with cirrhosis, end stage liver failure and stroke, patients who have taken acetaminophen in the preceding 4 hrs of start of the study were excluded.

After obtaining clearance from the institutional ethics committee the patients who fulfilled the inclusion criteria were enrolled in the study. Demographic data, history, clinical examination and details of drug prescription by the treating physician were recorded in the study proforma.

300 hospitalised patients aged more than 18 years, in the department of General Medicine, having a low-grade fever (38° to 39° C) were randomly allocated into two groups to receive either 650 mg or 500 mg of single oral dose of acetaminophen. Group A received acetaminophen tablet in a dose of 500 mg and group B received acetaminophen 650 mg tablet.

Primary efficacy parameter (antipyretic activity) were measured by recording changes in body temperature. Oral temperature was measured before dosing, 30 minutes after dosing, one hour and two hourly thereafter for 6 hours after the dose (baseline, 30 mins, 1, 2, 4 and 6 hrs).

Assessment of safety was done by monitoring for adverse effects during the study and 24 hours after administration of the assigned drug.

Statistical analysis

Parametric variables were analysed using student t test and z test. Non-parametric variables were analysed using Fischer exact test and Chi-square test.

RESULTS

The present study was done at Victoria hospital, department of General Medicine, Bangalore medical college and research institute revealed the following results. Totally 300 patients having low grade fever 38° C to 39° C were evaluated. All the 300 patients completed the study and there were no dropouts.

In the present study both the treatment groups matched with respect to age, gender, diet, habits, co-morbid conditions and area of distribution.

Group A received the tablet acetaminophen 500 mg and group B received tablet acetaminophen 650 mg.

The baseline values of temperature, heart rate, respiratory rate and blood pressure of the study participants are mentioned in the Table 1.

Table 1: Baseline parameters of the study subjects.

Variables	Group A	Group B	P value
	Mean \pm SD	Mean \pm SD	
Temperature	39.18 \pm 0.80	39.06 \pm 0.87	0.021
HR	94.93 \pm 1.54	94.80 \pm 1.74	0.048
RR	26.14 \pm 0.81	26.26 \pm 0.91	0.022
SBP	185.71 \pm 5.23	184.61 \pm 5.67	0.082
DBP	84.59 \pm 8.29	85.09 \pm 4.19	0.050

The baseline temperature was recorded before intake of tablet in both the groups. The mean baseline temperature in group A was 39.18° C and in group B was 39.06° C (Table 1). Temperature was recorded after administration of tablets to both the groups at the end of 30 minutes, 1st hour, 2nd hour, 3rd hour, 4th and 6th hour.

The mean reduction in the temperature after administration of two different doses of acetaminophen in both the groups are given in the Table 2.

Table 2: Mean temperature recordings in both the treatment groups.

Temperature	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	39.18	0.80	39.06	0.87	0.021
30 minutes	38.97	0.74	38.86	0.80	0.020
1 hr	38.74	0.77	38.69	0.84	0.056
2 hr	38.41	0.90	38.33	1.04	0.051
4 hr	38.15	0.77	38.06	0.85	0.041
6 hr	38.03	0.77	37.02	0.89	0.031

The mean temperature at the end of 6th hour in group A was 38.03 \pm 0.77° C whereas in group B the mean temperature at the end of 6th hour was 37.02 \pm 0.89° C. There was a statistically significant decrease in temperature in group B (acetaminophen 650 mg) when

compared to group A (acetaminophen 500 mg) (p=0.031) as shown in Table 2.

The changes in heart rate in both the treatment group is given in Table 3. The mean change in heart rate at the end of 24 hour was 86.08±2.46 beats per minute in group B compared to 88.31±3.17 beats per minute in group A. There was a statistically significant reduction in heart rate in group B compared to group A with p value 0.04.

Table 3: Comparison of heart rate in both the groups.

Heart rate	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	94.93	1.54	94.80	1.74	0.048
4 hr	93.52	1.69	93.42	1.69	0.073
8 hr	92.49	1.80	92.28	1.69	0.057
12 hr	91.93	2.22	90.10	2.05	0.051
24 hr	88.31	3.17	86.08	2.46	0.048

Table 4: Comparison of respiratory rate in both the groups.

Respiratory rate	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	26.26	0.81	26.14	0.91	0.022
4 hr	25.05	0.81	24.99	0.83	0.096
8 hr	24.54	0.89	23.53	0.91	0.094
12 hr	22.33	0.96	22.35	1.05	0.081
24 hr	20.75	1.60	18.75	1.22	0.049

The changes in the respiratory rate in both the treatment groups are given in Table 4. There was statistically significant reduction in respiratory rate in group B 18.75±1.22 breaths per minute when compared to 20.75±1.60 breaths per minute in group A with p value 0.049.

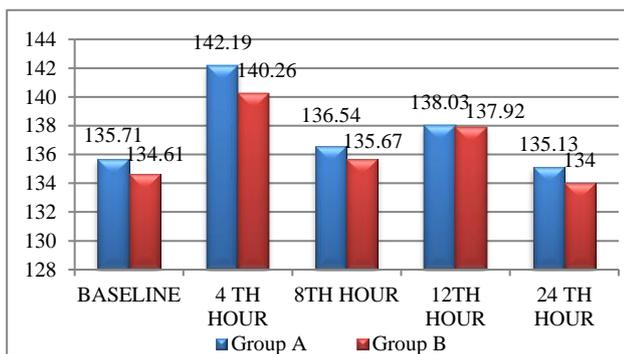


Figure 1: Comparison of systolic blood pressure in both the groups.

The mean systolic blood pressure (SBP) in both the groups are shown in the Figure 1. The mean SBP in group B at 24th hour was 134±2.46 mm of Hg and in group A was 135.13±2.16 mm of Hg. There was no statistically significant difference in reduction of SBP in both the groups with p value 0.136.

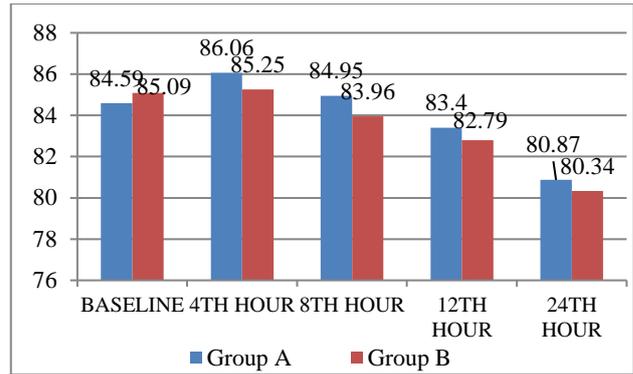


Figure 2: Comparison of diastolic blood pressure in both the groups.

The changes in the diastolic blood pressure (DBP) in both groups are shown in the Figure 2. The mean diastolic blood pressure at 24th hour in group B was 80.34±2.97 mm of Hg and in group A was 80.87±4.26. There was no statistically significant difference in reduction of DBP in both the groups with p value 0.164.

DISCUSSION

Acetaminophen (paracetamol) is one of the most commonly used drugs for fever over the counter. Initially the single dose of paracetamol was 1000 mg which was later reduced to 650 mg by US FDA in 2009 and the total daily dose for an adult to 2600 mg in place of 4000 mg.

Since the acetaminophen is also available in 500 mg dosage formulation, this study was conducted to analyse whether 650 mg dosage is superior or equally efficacious in terms of reducing fever with 500 mg dosage.

In our study the mean reduction in temperature at the end of the 6th hour with acetaminophen 650 mg tablet was 37.02±0.89° C when compared to 38.03±0.77° C with acetaminophen 500 mg tablet which is statistically significant (p=0.031). This indicates that the need for next dose of acetaminophen was at the end of the 6th hour in group A patients who took 500 mg tablet, whereas in group B patients with acetaminophen 650 mg the temperature came down to normal level which does not necessitate the further dosing. This is also supported by statistically significant reduction in heart rate and respiratory rate in group B patients compared to group A suggesting acetaminophen in a dose of 650 mg has got better antipyretic effect when compared to 500 mg dosage formulation.

In a study conducted by Qi et al has showed that there is statistically significant reduction in post-surgical dental pain with acetaminophen 1000 mg when compared to 650mg.⁶ In another study conducted by Toms et al has shown that acetaminophen in a dose of 650 mg is effective in relieving postoperative pain in adults.⁷ In a study done by Barden et al single doses of acetaminophen is a good analgesic in relieving acute post-operative pain.⁸

But there was no evidence found on the comparative clinical efficacy of different doses of acetaminophen for the management of fever. Our study has showed that acetaminophen in a dose of 650 mg is a better antipyretic compared to 500 mg.

Acetaminophen is well tolerated in therapeutic doses but can produce mild elevation in hepatic enzymes, with larger doses dizziness, excitement and disorientation, rashes and other allergic reactions are seen.^{9,10} An overdose of acetaminophen (>2.6 grams) leads to cellular and oxidative damage which results in acute hepatic necrosis.¹¹ However, in our study no adverse drug reactions has been noted in both the treatment groups which indicates that acetaminophen is safer at both the doses.

CONCLUSION

In our study it has been observed that in majority of the patients who received acetaminophen in a dose of 650 mg the temperature dropped to normal range within 6 hours which was not achieved with 500 mg dosage. Hence, we conclude that acetaminophen in a dose of 650 mg is better to prescribe for patients with pyrexia than 500 mg.

ACKNOWLEDGEMENTS

The authors would like to thank all the staff, department of Pharmacology and General Medicine, Bangalore Medical College and Research Institute, Bangalore, for their constant valuable support and guidance in making the study successful.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Moore A, Collins S, Carroll D, Mc Quay H, Edwards J. Single dose paracetamol with or without codeine, for post-operative pain, Cochrane database Syst rev. 2000;2:CD001547.
2. Rod JR. Anti-inflammatory and immunosuppressant drugs. In: Rang HP, Dale MM, Ritter JM, eds. Rang & Dale's Pharmacology, 4th ed. Elsevier; 2007: 229-247.
3. Nguyen AM, Graham DY, Gage T, Griffiths GR. Nonsteroidal anti-inflammatory drug use in dentistry, gastrointestinal implications. Gen Dent. 1999;47:590-6.
4. Sharma HL, Sharma KK. Nonsteroidal Anti-inflammatory Agents, Drugs for Gout and Antirheumatoid Drugs. In: Sharma HL, Sharma KK, eds. 3rd ed. Sharma & Sharma's Principles of Pharmacology; 2017: 371-389.
5. British Medical association and royal pharmaceutical society of Great Britain. British national formulary. Oxon Pharma Press. 2000;39:205-8.
6. Qi DS, May LG, Zimmerman B, Peng P, Atillasoy E, Brown JD, et al. A randomized, double-blind, placebo-controlled study of acetaminophen 1000 mg versus acetaminophen 650 mg for the treatment of postsurgical dental pain. Clin Ther. 2012;34(12):2247-58.
7. Toms L, McQuay HJ, Derry S, Moore RA. Single dose oral paracetamol (acetaminophen) for postoperative pain in adults. Cochrane Database Syst Rev. 2008;(4):CD004602.
8. Barden J, Edwards J, Moore A, McQuay H. Single dose oral paracetamol (acetaminophen) for postoperative pain. Cochrane Database Syst Rev. 2004;(1):CD004602.
9. Furst DE. Nonsteroidal Anti-Inflammatory Drugs, Disease-Modifying Antirheumatic Drugs, Nonopioid Analgesics, & Drugs Used in Gout. In: Bertram G. Katzung, Susan B Masters, Anthony J Trevor, eds. Basic and Clinical Pharmacology. 12th ed. New York, NY: McGraw-Hill; 2012: 635-657.
10. Grosser T. Analgesic-antipyretic agents; pharmacotherapy of gout. In: Brunton L, Chabner B, Knoll B, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics, 12th ed. New York, NY: Mc-Graw-Hill; 2011: 959-1001.
11. David M. Pharmacology of Eicosanoids. In: Golan E, Tashjian H, eds. Principles of Pharmacology. 3rd ed. Wolters Kluwer; 2012: 742-759.

Cite this article as: Pradeepkumar BT, Jayanthi CR, Raveendra KR, Ramya YS. A comparative single dose study of oral acetaminophen 650 mg to its standard 500 mg dose in adult pyrexia patients in a tertiary care hospital. Int J Basic Clin Pharmacol 2020;9:388-91.