

Effect of analgesics from different groups on renal functions of healthy male albino rats

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Abstract

Objective: 1. To determine the extent of affection of renal functions of analgesics from different groups and to compare the drugs with relation to the renal parameters. 2. To determine the least nephrotoxic drugs among the groups based on affection of renal parameters. **Material and Methods:** With prior approval from animal ethical committee four groups of Adult Male albino rats weighing 160-200 g with 6 in each group were selected. The normal urinary output for 24 hrs and urinary protein excretion for 24 hrs, urine creatinine, and routine urine examination are observed for each animal keeping it in a metabolic cage for 24 hrs. Blood was drawn from the lateral tail vein of rat and Blood urea, serum creatinine are estimated. Then the same animal was administered with the test drugs indomethacin (8 mg/kg) etorcoxib (9 mg/kg) Paracetamol (25 mg/kg), Ibuprofen (15 mg/kg) respectively for 3 days with appropriate dose and 24 hrs of urine output is observed and all the above test are repeated for each drug on the 4th day. The observations were tabulated and results are statistically analysed. **Results:** The results showed significant changes in pH (*P=0.001), Urea (*P=0.05), creatinine (*P=0.02) levels in case of Paracetamol, etorcoxib showed prominent changes in urinary creatinine level (*P=0.035). P values showed Positive significance with regards to paracetamol and etorcoxib. With regards to drug ibuprofen and indomethacin significant changes were in serum creatinine and urine creatinine levels (*P=0.05). P values showed Negative significance in case of indomethacin and ibuprofen. **Conclusion:** Blood urea and serum creatinine are important parameters with regards to assessment of renal functions. The drugs paracetamol, etorcoxib, administered to albino rats for a short duration of 3 days clearly demonstrated a decline in the renal function parameters. Paradoxically drugs Indomethacin and ibuprofen have demonstrated a beneficial effect on the parameters of renal functions.

Keywords: Paracetamol, Indomethacin, Etorcoxib, Ibuprofen, Renal parameters.

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INTRODUCTION

The Most common presentation of a patient to a Doctor is pain and inflammation¹. Drugs in clinical use as analgesics belong to Narcotic or Morphine Group and Analgesic Antipyretic group (Non steroid Antiinflammatory Group (NSAIDs))². NSAIDs are among the largest pharmaceutical agents all over the world. In

contrast to opioids they do not depress CNS, do not produce physical dependence, but they are commonly associated with untoward adverse effects³. They produce renal effects by one of the following mechanisms COX-1 dependent decrease in renal blood flow and GFR, COX-2 dependent oedema due to sodium and water retention and renal papillary Necrosis⁴. Renal functions are best assessed by renal parameters such as 24 hr urine output, 24 hr urinary protein excretion, urine creatinine, Blood Urea and creatinine⁵. Hence in this study an earnest attempt is made to determine the extent of affection of renal function of different analgesics using these parameters in Healthy Albino rats.

MATERIALS AND METHODS

Source: Four groups of Adult Male albino rats weighing 160-200 g with 6 in each group are selected from central animal house of Velammal Medical college Madurai after obtaining prior approval from institutional animal ethical

committee. This study was conducted in assistance with Department of Biochemistry VMC Madurai at the central animal house VMC Madurai.

Inclusion Criteria: Healthy adult male albino rats weighing 160-200 g.

Exclusion Criteria: Female rats and diseased animals

Materials

Four groups of adult male albino rats (6 in each group). Drugs with appropriate solvent (sterile water). Metabolic cage. Feeding tubes for rat. Reagent bottles for sample collection

Drugs (Analgesics)	Groups	Dose/kg of body weight
Paracetamol	Para amino Phenol Derivative	25 mg
Ibuprofen	Propionic acid derivative	15 mg
Etoricoxib	Selective cox 2 inhibitor	9mg ⁶
Indomethacin	Acetic acid Derivative	8 mg ⁶

Methodology

The normal urinary output for 24 hrs and urinary protein excretion for 24 hrs, urine creatinine, and routine urine examination were observed for each animal keeping it in a metabolic cage for 24 hrs. Blood was drawn from the lateral tail vein of rat and Blood urea, serum creatinine are estimated. Then the same animal was administered with the test drugs respectively for 3 days with appropriate dose and 24 hrs of urine output was observed and all the above test are repeated for each drug on the 4th day. The observations are tabulated. Applying appropriate statistical methods the results were analysed by SPSS Version 21. And the conclusion was derived.

Investigations

1. Urine output for 24 hrs,
2. Protein in 24 hrs urine collection,
3. Urinary creatinine,
4. Routine urine examination,
5. Blood urea,
6. Serum creatinine.

RESULTS AND OBSERVATIONS

Table 1: Shows the statistical analysis (paired t test) of paracetamol administration on the mean values of the renal parameters in male albino rats.

Parameter	Mean values before drug administration	Mean values after drug administration
Ph	7.87	8.37
Specific gravity	1.022	1.023
Albumin	3.25	2.75
Microprotein	263.25	327.50
Urea creatinine	158.75	125
Blood urea	65.32	96.25
Serum creatinine	0.85	1.55

Table 2: Shows the statistical analysis of the effect of paracetamol on renal parameters using paired sample correlation (ANOVA).

Parameters	*P value (≤ 0.05 is significant)
Ph	0.001
Blood urine	0.05
Serum creatinine	0.02

Table 3: shows the statistical analysis (paired t test) of Ibuprofen administration on the mean values of the renal parameters in male albino rats.

Parameter	Mean values before drug administration	Mean values after drug administration
Ph	8.5	8.62
Specific gravity	1.001	1.003
Albumin	3.5	3.5
Microprotein	272.5	366.0
Urea creatinine	102.5	134.5
Blood urea	95.75	88.0
Serum creatinine	2.52	0.67

Table 4: Shows the statistical analysis of the effect of Ibuprofen on renal parameter using paired sample correlation (ANOVA)

Parameters	*P value (≤ 0.05 is significant)
Serum creatinine	0.003

Table 5: Shows the statistical analysis (paired t test) of Indomethacin administration on the mean values of the renal parameters in male albino rats.

Parameter	Mean values before drug administration	Mean values after drug administration
pH	8.9	8.87
Specific gravity	1.003	1.002
Albumin	4	3.75
Microprotein	132	103.25
Urea creatinine	226.5	87.06
Blood urea	75.75	55.75
Serum creatinine	1.37	1.07

Table 6: Shows the statistical analysis of the effect of Indomethacin on renal parameter using paired sample correlation (ANOVA)

Parameters	*P value (≤ 0.05 is significant)
Urine creatinine	0.05

Table 7: Shows the statistical analysis (paired t test) of Etoricoxib administration on the mean values of the renal parameters in male albino rats

Parameter	Mean values before drug administration	Mean values after drug administration
pH	8.75	8.87
Specific gravity	1.003	1.005
Albumin	4.0	4.0
Microprotein	33.75	87
Urea creatinine	52.12	88.25
Blood urea	26.75	9.5
Serum creatinine	0.82	1.32

Table 8: Shows the statistical analysis of the effect of Etoricoxib on renal parameter using paired sample correlation (ANOVA)

Parameters	*P value (≤ 0.05 is significant)
Urine creatinine	0.035

DISCUSSION

Statistical analysis of paracetamol administration (table.1) shows that there is a considerable difference (increase) in the mean values of blood urea and serum creatinine with a significant *P value of ≤ 0.05 (table.2). This result is in accordance with the study which showed 'c-s lyase mediated final metabolism of paracetamol -s conjugates which might be responsible for its nephrotoxicity⁷. Also it shows a increase in the mean pH value (after administration) of urine to a reasonable extent which confirms the fact that weakly acidic drugs are better excreted in alkaline pH. Table.3 shows that there is a little change in the mean values of the before and after administration of Ibuprofen with respect to urinary pH and blood urea. At the same time there is a remarkable decrease in the mean after value of serum creatinine (from 2.52 to 0.67) with a significant *P value of ≤ 0.05 (table.4) which means a favourable effect on the renal functions. This result is in accordance with the study which demonstrated that evaluation of renal functions failed to demonstrate adverse effect when ibuprofen administered within 48 hrs in patients with sepsis⁸. The mean values of the after administration of indomethacin (table.5) shows that there is a greater reduction in the following parameters: urine creatinine, blood urea and serum creatinine suggesting that they may have a favourable effect on the renal functions. The 'P' value of urea creatinine is significant (table.6). The result is in accordance with the study which clearly

demonstrated renoprotective effect of indomethacin at a dose of 5 mg /kg in mice⁹ Finally, statistical analysis of etoricoxib (table.7) shows that there is a significant raise in the urea creatinine (table.7) with very minimal changes in the other parameters of renal functions (*P ≤ 0.05 , table.8)

CONCLUSION

Blood urea and serum creatinine are important parameters with regards to assesment of renal functions. The drugs paracetamol, etoricoxib, administered to albino rats for a short duration of 3 days clearly demonstrated a decline in the renal function parameters. Paradoxically, Indomethacin and ibuprofen have demonstrated a beneficial effect on the parameters of renal functions. Since data based on animal studies cannot be extrapolated on human, further human studies have to be conducted on these parameters. The results of this study will be helpful to find the least nephrotoxic drugs among the four groups.

REFERENCES

1. Anderson WAD. Inflammation and Healing. Pathology, 9th Edition, C.V Mosby co; 1990; 1:67
2. Gupta SK, Analgesic drugs, chapter 32. Drug Screening Methods; 2009, 2ND Edition; Jaypee Brothers medical Publishers: 466-467.
3. Rang HP, Dale MM, Ritter JM. Antiinflammatory and immunosuppressant drugs, chapter 26. Rang and Dale's Pharmacology, 7th edition. Elsevier Publications; 2008: 318-334
4. Murray TG, Goldberg M "Analgesic-associated nephropathy in the U.S.A.: epidemiologic, clinical and pathogenetic features". Kidney Int. 1978; 13 (1): 64-71.
5. Nanra RS, Stuart-Taylor J, de Leon AH, White KH "Analgesic nephropathy: etiology, clinical syndrome, and clinicopathologic correlations in Australia". Kidney Int. 1978; 13 (1): 79-92.
6. M.C.F. Azoubel¹, A.M.A. Menezes¹, D. Bezerra¹, R.B. Oriá² "Comparison of etoricoxib and indomethacin for the treatment of experimental periodontitis in rats Braz". J Med Biol Res, January 2007; Volume 40(1) 117-125.
7. Hartman W, Siegers-CP "Mechanistic and therapeutic aspects". Journal of Applied toxicology, April 1991; vol 11 (2) 141-146.
8. Gordon R, Arthur P E "Effect of Ibuprofen on physiology and survival of patients with sepsis" N Eng J Med 1997; 33(6): 912-918.
9. Zhungh -Hong, Jia -Li "Protective Effect of Indomethacin in renal ischemia -reperfusion injury in mice Jzhezhang univ sci B. 2014 Aug; 15(8) :735-742.

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