Comparative Evaluation of the Renal Profile of Some Propionic Acids (NSAIDs) in Male Albino Rats

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ABSTRACT

Introduction: Propionic acids (NSAIDs) are associated with renal toxicity; therefore, this study comparatively evaluated the renal profile of propionic acids (NSAIDs) in adult male albino rats.

Materials and Methods: Adult male albino rats were orally treated with ibuprofen(IF)(250mg/kg) naproxen (NX) (140 mg/kg), ketoprofen (KF) (30mg/kg) and fenoprofen (FF) (170mg/kg) for 14 days. Animals were sacrificed, serum extracted and evaluated for urea (UR), creatinine (CR), uric acid (UA), total protein (TP), albumin (AB) and electrolytes ($N a^{+}$, K^{+}, Ca^{+}, Cl^{-} and $HCO3^{-}$). Also, kidneys were harvested and evaluated for malondialdehyde(MDA), superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), glutathione peroxidase (GPX), glutathione transferase (GST), and glutathione reductase (GR).

Results: Treatments with these agents did not produce significant ($p<0.05$) effects on absolute kidney weight, body weight and kidney/body weight ratio when compared to the control. Also, effects on serum electrolytes produced by these agents were insignificant ($p>0.05$) when compared to the control. Serum UR, CR, UA levels were significantly ($p<0.05$) increased while TP and ABlevels were decreased by these agents when compared tothe control.Increases in UR (173, 89, 79 and 144%), CR (152, 85, 81 and 109 %) and UA (157, 87,83and 127 %) respectively were obtained with IF, FF KF and NX treatments. Kidney MDA level was significantly ($p<0.05$) increased while CAT, GSH, SOD, GPX, GST and GR levels were decreased when compared to the control. Decreases in CAT (80, 60, 47 and 65%), GSH (79, 51, 50 and 69 %), SOD (76,45, 44 and 66%) GPX (78, 55, 52 and 68%), GST (80, 60, 55 and 70%) and GR (89, 54, 51 and 70) levels respectively were observed with IF, FF, KF and NX treatments.

Conclusion; This study shows adverse renal effects ofthese evaluated propionic acids may be ranked in this order; IF->NX> FF > KF

Keywords: Propionic Acids, Kidney, Antioxidants, Toxicity, Rats

INTRODUCTION

Propionic acids are non-steroidal anti-inflammatory drugs (NSAIDs) which are widely used. These agents share anti-inflammatory, analgesic, and antiplatelet properties and also have many side effects in common. They are used for the treatment of musculo-skeletal disorders, such as rheumatoid arthritis, osteo-arthritis, ankylosing spondylitis and postoperative pain.[2] The uses of propionic acids have been associated with renal toxicity attributed to inhibition of cyclooxygenase.Inhibition of COX (Cyclooxygenase) can alter the metabolism of eicosanoids, includingprostaglandins(PGs), thromboxane, and leukotrienes, which are derived from arachidonic acid. Cyclooxygenase is the rate-limiting enzyme for the conversion of arachidonic acid to the labile intermediate PGH2, which serves as a substrate for other PGs, such as PGE2 and PGD2.[2] The inhibition of prostaglandins synthesis from arachidonic acid by NSAIDS could leadto vasoconstriction and a decrease in glomerular capillary pressure, resulting in a prompt decline in glomerular filtration rate.[4] Also, oxidative stress characterized by decreased kidney antioxidants hasbeen implicated in drugs induced renal toxicity and may be a factor in NSAIDs renal toxicity. Oxidative stress can stimulate the formation of vasoactive mediators that can initiate renal vasoconstriction or decrease the glomerular capillary ultrafiltration coefficient; and thus reducing glomerular filtration rate.[5]

Pripionic acids and other NSAID-related renal syndromes include fluid and electrolyte disorders, acute renal dysfunction, nephrotic syndrome/interstitial nephritis, and renal papiliary necrosis. NSAIDs are a known cause of acute kidney injury (AKI) which may remain undiagnosed because it maybe moderate, asymptomatic, transitory, and non-anuric.[7] AKI can occur from NSAID induced renal interstitial inflammation, resulting in acute interstitial nephritis.[8] Also, acute renal dysfunction occurs with the short term used of NSAIDs which might progress to acute tubular necrosis and substantial loss of renal function up to the point of requiring dialysis supportwith continuation of NSAIDs therapy.[9] Interstitial

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nephritis and renal papillary necrosis which are markers of chronic renal failure occur with the chronic use of NSAIDS due to high dose administration over a long period.[10] Due to the frequent use of propionic acids and reported renal toxicity; therefore, this study comparatively evaluated the renal profile of propionic acids (NSAIDs) in male albino rats. Comparative evaluation of the adverse renal profile of propionic acids will enhance their rational selection, decrease nephrotoxicity and add to therapeutic benefits.

MATERIALS AND METHODS

Materials

Ibuprofen (Ranbaxy Pharm India),Naproxen (Ranbaxy Pharm India), Ketoprofen (Nicholas Piramal India)and Fenoprofen (Ranbaxy Pharm India). All other chemicals used for this study were of analytical grade

Animals

Thirty adult male rats of average weight 310±5g were used for this study. Animals were obtained from the animal house of the Department of Pharmacology and Toxicology, Madonna University Elele, Rivers State. Animals were grouped in cages and were allowed to acclimatize for 14 days and had free access to food and water *ad libitum.*

Grouping of animals and drug administration

Animals were divided into 6, groups A -F of 5 animals each. Animals in group A (placebo control) and group B (solvent control) orally received water and normal saline respectively. Animals in groups C-F received oral doses of ibuprofen (250mg/kg) naproxen (140 mg/kg), ketoprofen (30mg/kg) and fenoprofen (170mg/kg)for 14 days respectively. Doses used for this study represent 10 times theirclinical doses.[11] Higher doses were used for this studybecause laboratory animals metabolize and excrete drugs faster than humans and to simulate toxic levels of the drugs in the animals.[12]

Collection of Samples

At the end of drug therapy animals were sacrificed with the aid diethyl ether, blood sample was collected in a non-heparinized sample container via cardiac puncture. The Blood sample was allowed to clot, centrifuged and serum was collected and evaluated for biochemical parameters. Animals were dissected, kidneys were collected and washed in an ice cold 1.15% KCL solution. Kidneys were then homogenized with 0.1M phosphate buffer (pH 7.2). The resulting homogenate was centrifuge at 2500rmp speed for 15 minutes then it was removed from the centrifuge and the supernatant was decanted and stored at -20°C until analysis.

Evaluation of Renal Function Parameters

Total protein and albumin were evaluated as reported by Ibiam et al., 2013[13] while serum creatinine, urea, and uric acid were evaluated as reported by Prabu et al., 2010.[14]

Evaluation of Kidney Oxidative Stress Markers

Glutathione (GSH), Superoxide Dismutase (SOD), Catalase (CAT) Glutathione peroxidase, Glutathione S-transferase and Glutathione reductase were evaluated as reported by Prabu et al., 2010[14] while malondialdehyde was evaluated as reported by Ahmed et al., 2013[15]

STATISTICAL ANALYSIS

All the tested parameters were subjected to statistical analysis. Statistical analysis was done by One-way Analysis of Variance (ANOVA) and means were compared by Dunnettes comparison.

RESULTS

Treatments with these agents did not produce significant effects ($p<0.05$) on body weight, absolute kidney weight and kidney/body weight ratio when compared to the control. (Table1). These agents produced significant ($p<0.05$) increases in serum creatinine, urea and uric acid levels with decreases in serum albumin and total protein levels when compared to the control. Observed increases in serum urea levels by IF, FF, KF and NX treatments represent 173, 89, 79 and 144% respectively. Also, observed increases in serum creatinine levels by IF, FF, KF and NX represent 152, 85, 81 and 110 % respectively. Furthermore, uric acid levels were increased by IF, FF, KF and NX treatments to 156, 87, 83 and 127% respectively. In this study, observed changes produced by these agents on serum electrolytes were insignificant ($p>0.05$) when compared to the control (Table 2 and 3).Observation in this study shows significant ($p<0.05$) deceases in kidney SOD,CAT GSH, GPX,GST and GR levels with increase in MDA level in animals treated with these agents when compared to the control. Observed decreases in GSH levels by IF, FF, KF and NX treatments represent 79, 51, 50 and 69% respectively. Also, IF, FF, KF and NX induced increases in CAT levels represent 80, 60, 47 and 65% respectively. Fur-

Drugs	Initial body Weight (g)	Final body weight (g)	Kidney weight (g)	Kidney/body weight ratio
Control	310.0±1.02	370.6±1.10	0.88±0.02	0.0024±0.09
Ibuprofen	297.2±1.11	320.1±2.15	0.90±0.01	0.0028±0.03
Ketoprofen	300.0±1.15	335.6±3.10	0.85±0.09	0.0025±0.07
Fenoprofen	330.1±2.00	352.2±2.14	0.80±0.02	0.0023±0.01
Naproxen	320.4±1.75	340.7±1.16	0.87±0.07	0.0027±0.06

Table-1: Effects of propionic acids (NSAIDs) on the body weight, absolute kidney weight and kidney weight/body weight ratio of male albino rats

thermore, treatments with IF, FF, KF and NX produced the following decreases in SOD (74, 46, 44 and 66%), GPX (78, 55, 52 and 68%) and GST (80, 60, 55 and 70%) respectively. Kidney malondialdehyde level was significantly ($P<0.05$) increased to 1.23±0.01, 0.910±0.03, 0.87±0.05 and 1.04±0.08 nmole / mg protein in IF, FF, KF and NX treated animals respectively (Table 4).

DISCUSSION

Kidneys receive about 25% of the cardiac output and are the major organ for drugexcretion; hence the renal arterioles and glomerular capillaries are vulnerable to the effects of drugs.[16] Propionic acids are non-steroidal anti-inflammatory drugs (NSAIDs) that are most commonly used as over-the-counter medications and are known to have adverse effects on kidney function.[17] This study comparatively evaluated the adverse renal effects of propionic acids (ibuprofen, fenoprofen, ketoprofen and naproxen) in male albino rats. Effects were evaluated on serum electrolytes (Na^{+}, K^{+}, Cl^{-}, Ca^{+}, $HCo3^{-}$), creatinine, urea uric acid levels. Also, effects were evaluated on kidney MDA, GSH, CAT, SOD, GPX, GR, GST, and GR levels. In this study, treatments with propionic acids (NSAIDs) increased serum creatinine, urea and uric acid levelswith decreases in total protein and albumin levels. This observation is consistent with previous studies which reported changes in these parameters with the uses of NSAIDs.[18,19] Maximal effects on these parameters were observed in ibuprofen treated animals followed by naproxen, fenoprofen and ketoprofen. Effects observed on serum levels of these parameters suggest signs of kidney damage because serum concentrations of these evaluated parameters are commonly used as surrogate markers of renal toxicity.[20] Serum electrolytes are regulated by the kidney and their serum levels are fundamental indices for renal toxicityand adverse cardiovascular events.[21] This study observed changes in serum electrolytes in animals treated with propionic acids. This is in agreement with previous reports that associated the uses of NSAIDs with electrolytes and acid-base disturbances.[22] Furthermore, kidney MDA level was increased while antioxidants (GSH, CAT, SOD, GPX, GR, GST, and GR) were decreased by these agents. Increases observed in kidney MDA levels with decreases in kidney antioxidants were maximal in ibuprofen treated animals. This study observed that adverse renal profile of these propionic acids may be ranked in this order; ibuprofen > naproxen > fenoprofen > ketoprofen. This connotes that ibuprofen will produce more adverse renal effect while ketoprofen will produce the least effect.

In this study, observed increases in serum creatinine, urea

Drugs	Urea (mg/dL)	Creatinine (mg/dL)	Uric acid (mg/dl)	Total protein (g/dl)	Albumin (g/dl)
Control	20.1±0.06	1.65±0.02	1.46±0.02	6.30±0.20	3.71±0.03
Ibuprofen	54.9±0.03[a]	4.15±0.23[a]	3.75±0.06[a]	3.00±0.01[a]	1.10±0.07[a]
Fenoprofen	37.9±0.04[b]	3.05±0.01[b]	2.63±004[b]	4.21±0.01[b]	2.71±0.01[b]
ketoprofen	35.9±0.06[b]	2.98±0.09[b]	2.67±0.01[b]	4.28±0.07[b]	2.75±0.06[b]
Naproxen	49.0±0.08	3.44 ±0.06[c]	3.31±0.09[c]	3.24±0.08[c]	1.17±0.08[c]

Values represent means ±S.EM, n= 5. Values with different superscript in the same column are significantly different at ($p<0.05$).

Table-2: Effects of treatment with propionic acids (NSAIDs) on serum renal function parameters of male albino rats

Dose	Na^{+} (mmol/l)	K^{+} (mmol/l)	Cl^{-} (mmol/l)	Ca^{2+} (mg/dl)	HCO_3^{-} (mmol/l)
Control	120.0±2.06	3.42±0.06	122.6±3.02	10.2±0.01	20.2±0.03
Ibuprofen	135.2±2.11	3.86±0.09	135.0±2.61	11.8±0.12	19.1±0.01
fenoprofen	130.0±1.28	3.69±0.07	124.2±0.06	10.9±0.16	19.9±0.06
ketoprofen	127.1±3.15	3.61±0.04	127.7±0.15	10.4±2.00	20.0±0.03
Naproxen	132.4±1.43	3.70±0.06	130.0±0.09	11.0±0.36	18.7±0.09

Values represent means ±S.EM. n= 5

Table-3: Effects of treatment with propionic acids (NSAIDs) on serum electrolytes in male albino rats

Parameters	Control	Ibuprofen	Fenoprofen	ketoprofen	Naproxen
MDA	0.51±0.06	1.23±0.01 [a]	0.90±0.03[b]	0.87±0.05[b]	1.04±0.08[c]
GSH	9.65±0.02	2.00±0.06 [a]	4.72±0.06[b]	4.82±0.09[b]	3.00±0.04[c]
CAT	30.2±1.08	6.16±0.12[a]	12.1±0.35[b]	15.9±0.20[b]	10.6±0.16[c]
SOD	15.6±0.03	3.82±0.08[a]	8.47±0.06[b]	8.71±0.02[b]	5.20±0.27[c]
GPX	9.80±0.19	2.11±0.01[a]	4.38±0.01[b]	4.70±0.03[b]	3.10±0.04[c]
GST	10.7±0.05	2.10±0.26[a]	4.27±0.01[b]	4.82±0.01[b]	3.20±0.12[b]
GR	0.87±0.06	0.10±0.01[a]	0.40±0.01[b]	0.43±0.07[b]	0.26±0.04[c]

MDA: Malondialdehyde, (nmol/mg protein), GSH: Glutathione, CAT: Catalase, SOD: Superoxide dismutase (Unit/mg protein), GST: Glutathione-s-transferase (µmol/min mg protein) GR: Glutathione reductase (nmol/min mg protein), GSP: Glutathione peroxidase (µg/min mg protein). Values represent means ±S.EM, n= 5. Values with different superscript in the same row are significantly different ($p<0.05$).

Table-4: Effects of treatments with propionic acids (NSAIDs) on kidney oxidative indices of male albino rats

and uric acid may be due to reduced renal plasma flow caused by inhibition of prostaglandins (PG) synthesis by these agents. Studies have shown that prostaglandins regulate renal function by modulating both intrarenal vascular tone, salt and water excretion. In particular, PGE2 contributes to the regulation of renal perfusion and glomerular filtration rate in virtue of its vasodilation property, which counteract the actions of vasoconstrictive substances such as angiotensin II, catecholamines, vasopressin, and endothelin.[23,24] Also, increases in serum creatinine, urea and uric acid levels may be due to oxidative stress induced by these agents in the kidneys of treated animals. Because oxidative stress can promote the formation of vasoactive mediators that can affect renal function directly by initiating renal vasoconstriction or decreasing the glomerular capillary ultrafiltration coefficient; and thus reducing glomerular filtration rate.[25] Changes in serum electrolytes observed in this study are common adverse effects of NSAIDs characterized by decrease sodium, water and potassium excretion and edema. The NSAIDs attenuate the release of renin mediated by prostaglandins which may reduce the formation of aldosterone and, as a consequence, decrease the excretion of potassium. Furthermore, in the presence of decreased glomerular flow, the opposition to the natriuretic and diuretic effects of prostaglandins by the NSAIDs can increase sodium and water reabsorption in the renal tubule, with a decrease in the Na+-K+ exchange in the distal nephron.[26]

Observe increase in kidney MDA level with decreases in antioxidants in animals treated with these agents may be due to oxidative stress induced by these agents. Antioxidants scavenge free radicals and prevent biomolecules from oxidative damage.[27,28] Studies have shown that decreases in the levels of antioxidants suggest signs of oxidative stress.[29] Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxidation in cells. It is a known marker of oxidative stress and antioxidant status[30]; hence increase in malondialdehyde level observed in this study is a sign of lipid peroxidation. Pronounced renal toxicity observed in ibuprofen treated animals may be due to the ability of ibuprofen to inhibit prostaglandin synthesis and/or induce oxidative stress more than other propionic acids evaluated in this study. Findings in this study may be further validated by evaluating the effects of these agents on urine levels of creatinine, urea, uric acid, albumin, total protein, and electrolytes. Also, effects on free radicals generation in the kidney may be evaluated.

CONCLUSION

The adverse renal profile of propionic acids evaluated in this study may be ranked in this order; ibuprofen> naproxen>fenoprofen> ketoprofen.Pronounced renal toxicity observed with ibuprofen treatment may be due to inhibition of prostaglandins synthesis and/orinduction of kidney oxidative stress more than other propionic acids evaluated in this study.

REFERENCES

1. Higgs, G, K. Eakin, S. Moncada and J. Vane, The effects of nonsteroidal anti-inflammatory drug on leucocyte migration in carrageenin induced inflammation. Euro J. Pharmcol., 1980: 66: 81-86.
2. Adams, D, J. Michael, and P. Bacon, A. Howie, et al., Nonsteroidal anti-inflamatory drugs and renal failure. Lancet, 198611: 57-60.
3. Fries S, Grosser T. The cardiovascular pharmacology of COX-2 inhibition. In: Fries S, Grosser T, eds. Hematology. Washington, DC: American Society of Hematology Education Program; 2005:445–451.
4. Ejaz P, K. Bhojani, VR. Joshi. NSAIDs and kidney. J Assoc Physicians India. 2004;52:632-40
5. Recknagel R. O., EA. Glende, JA. Dolak, RL. Waller Mechanisms of carbon tetrachloride toxicity. Pharmacol Ther., 1989; 43: 139-154.
6. Whelton A. Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications. Am J Med. 1999; 106: 13S-24S.
7. John, R, AM. Herzenberg, Renal Toxicity of Therapeutic Drugs. J Clin. Pathol. 2009, 62,505-515
8. Clarkson, M, L. Giblin, F. O'Connell, P. Kelly, J. Walshe, P. Conlon, P et al Acute interstitial nephritis: clinical features and response to corticosteroid therapy. Nephrol. Dial. Transplant. 2004, 19, 2778-2783.
9. Blackshear, H, JS. Napier, M. Davidman, T.M, Stillman, Renal complications of nonsteroidal anti-inflammatory drugs; identification and monitoring of those at risk. Semin. Arthritis Rheum. 1985, 14, 163-175.
10. Murray MD, and DC Brater. Renal toxicity of the nonsteroidal anti-inflammatory drugs. Annu Rev Pharmacol Toxicol. 1993;33:435-65.
11. British national formulary 1999 pp 437-440
12. Laumann H, R. Lullmann-Rauch, O. Wassermann. Drug induced phospholipidosis. Crit Rev Toxicol 1995;4:185-218.
13. Ibiam AU, E. I. Ugwuja, C. Ejeogo, and O. Ugwu Cadmium-Induced Toxicity and the Hepatoprotective Potentials of Aqueous Extract of Jessiaea Nervosa Leaf Adv Pharm Bull. 2013; 3: 309–313.
14. Prabu M, S, K. Shagirtha, J. Renugadevi Quercetin in combination with vitamins (C and E) improves oxidative stress and renal injury in cadmium intoxicated rats European Review for Medical and Pharmacological Sciences, 2010; 14: 903-914
15. Ahmed AM, and KMA Hassanein,. Cardioprotective effects of *Nigella sativa* oil on lead induced cardiology; Antiinflammatory and antioxidant mechanism Jour Physio and Patho. 2013; 24; 5; 72-80
16. Allah, AM, The Side Effects Of The Nonst eroidal Anti-Inflammatory Drug (NSAID) Ketoprofen On Histological And Ultrastructural Aspects Of The Kidneys Of Albino Rats The Egyptian Journal of Hospital Medicine 3: 161 -176
17. Onay, O.S, HS. Ercoban, US, Bayrakci, E. Melek, N.

Cengiz, E. Baskin. Acute, reversible nonoliguric renal failure in two children associated with analgesic-antipyretic drugs. Pediatr.Emerg. Care 2009, 25, 263-266
18. Jennifer L Ng, D.J R Morgan, N. K M Loh, S. K Gan, P. L Coleman, G. S Y Ong and D. Prentice, Life-threatening hypokalaemia associated with ibuprofen-induced renal tubular acidosis MJA 2011; 194: 313-316
19. Krummel T, Y Dimitrov, B Moulin, T Hannedouche Acute renal failure induced by topical ketoprofenBMJ 2000;320:93
20. Traynor J, CC. Geddes, JG. Fox. How to measure renal function in clinical practice. BMJ. 2006;333:733-7.
21. Adikwu E, R. O. Igbans and N. Brambaifa Toxicological Assessment of Co-treatment with Rifampicin and Tenofovir on Serum Electrolytes and Kidney Histology of Albino Rats Afr. J. Pharmacol. Ther. 2015: 124-129
22. Kim S and K W. Joo, Electrolyte and Acid-Base Disturbances Associated with Non-Steroidal Anti-Inflammatory Drugs Electrolyte Blood Press. 2007; 5: 116–125.
23. Langhendries JP, and B. van Overmeire. Prostaglandines, anti-inflammatoires non steroidiens (AINS) et reinperinatal: un subtil compromis. In: Guignard JP (ed). Nephrologie Perinatale. Vol. 4. Paris: Elsevier; 2001:36-58.
24. Antonucci R, L. Cuzzolin, A. Arceri, V. Fanos. Urinary prostaglandin E2 in the newborn and infant. Prostaglandins Other Lipid Mediat 2007; 84: 1-13
25. Garcia-Cohen E. C., J. Marin, LD, Diez-Picazo, AB. Baena, M. Salaices, MA, Rodriguez-Martinez: Oxidative stress induced by tert- butylhydroperoxide causes vasoconstriction in the aorta from hypertensive and aged rats: role of cyclooxygenase- 2 isoform J Pharmacol Exp Ther 2000; 293;1: 75-81
26. Blum M, Aviram A. Ibuprofen-induced hyponatremia. Rheumatol Rehab. 1980; 19: 258-9
27. Zini RA, A. Berdeaux, D. Morin,. The differential effects of superoxide anion, hydrogen peroxide and hydroxyl radical on cardiac mitochondrial oxidative phosphorylation. Free Radic Res, 2007; 41: 1159-1166.
28. Patil SB, M.V Kodliwadmath, S M. Kodliwadmath study of oxidative stress and enzymatic antioxidants in normal pregnancy, Indian Journal of Clinical Biochemistry, 2007 / 22; 135-137
29. Ramamoorthy,H, P. Abraham,B. Isaac. Oxidative stress, decreased activities of anti-oxidant enzymes, and neutrophil infiltration contribute to Tenofovir disoproxil fumarate induced renal damage in rats, International Research of Pharmacy and Pharmacology 2012; 1:10; 259-270
30. Gaweł S, M. Wardas, E. Niedworok, P. Wardas W. Lekarskie. Malondialdehyde (MDA) as a lipid peroxidation marker]. Wiad Lek 2004; 57: 453-455.

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