Comparative Study on the Toxic Effects of Some Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in Rats

Ukwueze C. S., Ukwueze C. O. and Nweze E. C.


DOI: 10.5455/jva.20141208030829

Online version is available on: [www.grjournals.com](http://www.grjournals.com)
Comparative Study on the Toxic Effects of Some Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) in Rats

*1Ukwueze C. S., 2Ukwueze C. O. and 3Nweze E. C.

1Department of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike. Abia State, Nigeria.
2Department of Veterinary Surgery and Theriogenology, Michael Okpara University of Agriculture, Umudike. Abia State, Nigeria.
3Department of Veterinary Physiology and Pharmacology, Michael Okpara University of Agriculture, Umudike. Abia State, Nigeria.

Abstract

A comparative study was carried out on the toxic effects of some non-steroidal anti-inflammatory drugs [NSAIDs]; Paracetamol (acetaminophen), Ibuprofen (Julifen) and Nimesulide (Usteinim) in rats. The parameters used in determining the level of toxicity were body weight, blood sugar level, haematological and biochemical changes. The rats were randomly divided into four groups (A, B, C and D) of six rats each. Group A served as the control, Group B was treated with Paracetamol at the dose of 14mg/kg, Group C was treated with Ibuprofen at the dose of 11mg/kg and Group D was treated with Nimesulide at the dose of 3mg/kg. All drugs were orally administered once daily with a stomach tube for a period of three weeks. The mean body weight and blood sugar level did not show any significant (P>0.05) different in all the treated groups when compared with the control. The mean PCV and HB concentrations significantly (P<0.05) decreased in group treated with Paracetamol and the total WBC counts significantly (P<0.05) increased in group treated with Nimesulide. ALT levels increased significantly (P<0.05) in all the treated groups. The urea level increased significantly (P<0.05) only in the group treated with Ibuprofen. There was no significant (P>0.05) different in Albumin and Creatinine levels in all the treated groups when compared with the control. The result of this study shows that all NSAIDs used were toxic to the rats within the period of study. Paracetamol and Nimesulide caused hepatic impairment, whereas Ibuprofen caused both hepatic and renal impairment. Paracetamol had effect on the haematology and is capable of inducing anaemia. It was concluded from the study that prolonged use of NSAIDs is harmful to the body system and leads to organ damage.

Keywords: Toxicity, NSAIDs, Paracetamol, Ibuprofen and Nimesulide.
Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are non-narcotic agents that provide analgesic (pain killing) and antipyretic (fever reducing) effects and in higher doses anti-inflammatory effects (Hanson and Meddoson 2008; Hunter et al., 2011). NSAIDs are classified by their chemical structure as well as by their specific inhibitory activity for enzymes (Hunter et al., 2011). NSAIDs produce their therapeutic effects through the inhibition of prostaglandins synthesis (Gillman et al., 1985; Klassen 2001) and are usually used for treatment of acute or chronic conditions where pain and inflammation are present (Hunter et al., 2011). NSAIDs block the formation of colon cancer in experimental animals and there is epidemiological evidence that NSAID usage decreases the incidence of colorectal cancer in humans (Gupta and Dubois 1998). The most prominent of this group of drugs includes aspirin, ibuprofen and naproxen, which are available over the counter in most countries (Warden 2010).

NSAIDs are commonly ingested in overdose in humans and animals in many areas in the world (Hunter et al., 2011). Ibuprofen is the most widely used NSAID. In an acute over dose renal impairment has been reported in patients with underlying renal and cardiovascular diseases (Court et al., 1981; Perry et al., 1987). The majority of patients with acute NSAIDs over dose will remain asymptomatic or develop minor self-limiting gastrointestinal symptoms. However, serious clinical consequences that have been reported in some patients include convulsion, metabolic acidosis, coma and renal failure (Hall et al., 1986; Hunter et al., 2011). The management of these serious clinical features is largely supportive and there is no specific antidote for acute NSAIDs toxicity. The widespread use of NSAIDs has made the adverse effects increasingly prevalent (Hunter et al., 2011). Thus this work was designed to compare the haematological and biochemical changes in acute toxicity of Paracetamol, Ibuprofen and Nimesulide.

Materials and Methods

Experimental Animals

Twenty four (24) albino rats weighing between 160-200g were used in the study. They were kept in clean rat cages and in well ventilated fly proof experimental animal house. The animals were humanely cared for in compliance with the principles of laboratory animal care. They were fed with commercial broiler ration and water was supplied to them ad libitum.

Experimental Procedure

The rats were allowed to acclimatize for two weeks before the commencement of the study. They were randomly divided into four groups (A, B, C and D) of six rats each. Group A served as the control, Group B was treated with Paracetamol (Emzor Pharmaceutical Industries LTD) at the dose of 14mg/kg, Group C was treated with Ibuprofen (ZIM Laboratories LTD) at the dose of 11mg/kg and Group D was treated with Nimesulide (Gemicon Healthcare & Exports) at the dose of 3mg/kg. All drugs were orally administered once daily with a stomach tube for a period of three weeks. The animals were observed daily in their cages for clinical signs. At the end of the experimental period, the animals were anaesthetized using diethyl ether and blood obtained by cardiac puncture for haematological and serum biochemical analysis.

Determination of Haematological and Biochemical Parameters

Packed cell volume (PCV) was determined by microhaematocrit method (Coles 1986), haemoglobin by cyanomethaemoglobin method (Kachmar 1970), red blood cells RBC and total white blood cell WBC counts using improved neubauer chamber counting technique (Shalm et al., 1975). Albumin (ALB), Alanine aminotransferase (ALT), Creatinine level and Blood urea nitrogen (BUN) were determined using commercial reagents kits (Randox, Laboratory LTD, UK).

Determination of Weight and Blood Sugar Level

The weight was determined using electronic weighing balance and the fasting blood glucose
level was determined using glucometer ACCU-CHEEK.

Statistical Analysis

The data obtained were expressed as mean ± standard error (SE). Statistical significance was assessed using one way analysis of variance (ANOVA) and Duncan’s multiple range test with SPSS version 18 software package. P values < 0.05 were considered significant.

Results

Weight and Haematological Parameters

No significant different was observed in the mean weight (P>0.05) in all the treated groups when compared with the control. The mean PCV and HB concentrations significantly (P<0.05) decreased in group treated with Paracetamol and the total WBC counts significantly (P<0.05) increased in group treated with Nimesulide (Table 1).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Paracetamol</th>
<th>Ibuprofen</th>
<th>Nimesulide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean weight (kg)</td>
<td>199.22±5.86</td>
<td>193.30±10.33</td>
<td>195.62±15.62</td>
<td>202.30±11.77</td>
</tr>
<tr>
<td>PCV (%)</td>
<td>41.00±2.00</td>
<td>35.60±0.88*</td>
<td>37.00±2.08</td>
<td>38.33±0.88</td>
</tr>
<tr>
<td>HB (g/dl)</td>
<td>13.66±0.66</td>
<td>11.88±0.29*</td>
<td>12.22±0.77</td>
<td>12.77±0.29</td>
</tr>
<tr>
<td>RBC (10^6 cells/mm³)</td>
<td>10.01±7.50</td>
<td>9.48±4.05</td>
<td>10.15±7.36</td>
<td>10.30±0.28</td>
</tr>
<tr>
<td>WBC (10^3/µL)</td>
<td>11.68±10.24</td>
<td>9.05±17.60</td>
<td>11.21±7.40</td>
<td>17.90±23.37*</td>
</tr>
</tbody>
</table>

*Indicates significant (P<0.05) different when compared with the control.

Blood Sugar Level and Serum Biochemical Parameters

No significant difference was observed in the blood sugar level (P>0.05) in all the treated groups when compared with the control. ALT levels increased significantly (P<0.05) only in the group treated with Ibuprofen. There was no significant (P>0.05) different in Albumin and Creatinine levels in both the treated and untreated (Table 2).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Paracetamol</th>
<th>Ibuprofen</th>
<th>Nimesulide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood sugar level (g/dl)</td>
<td>83.00±4.93</td>
<td>87.00±5.03</td>
<td>87.00±1.73</td>
<td>76.66±1.35</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.29±0.10</td>
<td>2.93±0.23</td>
<td>3.38±0.16</td>
<td>3.36±0.28</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>19.66±2.66</td>
<td>32.33±1.66*</td>
<td>29.33±2.60</td>
<td>31.00±3.00*</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.68±0.00</td>
<td>0.65±0.02</td>
<td>0.68±0.00</td>
<td>0.90±0.22</td>
</tr>
<tr>
<td>Urea/dl (mg)</td>
<td>19.81±0.25</td>
<td>20.54±1.63</td>
<td>26.13±2.05*</td>
<td>22.60±2.55</td>
</tr>
</tbody>
</table>

*Indicates significant (P<0.05) different when compared with the control.

Discussion

The non-steroidal anti-inflammatory drugs (NSAIDs) are widely abused because of their analgesic, anti-inflammatory and antipyretic effects and their availability over the counter (Gilman et al., 1990; Hunter et al., 2011). The result of this study shows that NSAIDs may be potentially toxic, when improperly used and could serve a source of harm to both humans and animals.
parameters. The total WBC increased significantly (P<0.05) in Nimesulide treated group. This result supports the findings of Ahmad et al., (2013) in a similar study. However, the administration of these drugs did not cause a significant (P>0.05) change on the body weight.

The blood sugar level was not significant (P>0.05) in all the treated groups. This shows that the drugs did not have effect on blood sugar level of the animals. Mork and Robertson (1983) in a similar study did not observe any significant change in the plasma glucose level of diabetic patients treated with Ibuprofen and other NSAIDs. Serum ALT levels increased significantly (P<0.05) in all the treated groups. This increase may be an indication of liver damage (Kankeno 1985; Bush 1991). Abaten et al., (2013) in a similar work has reported increase in ALT levels in rats treated with NSAID. The BUN increased significantly (P<0.05) in the group treated with Ibuprofen. This increment is suggestive of renal impairment (Bauer 1982).

The result shows that Ibuprofen caused more toxic effects taking into consideration the result of haematological and biochemical parameters mentioned. NSAIDs are weakly acidic and extensively protein bound, with a low volume of drug distribution. Metabolisms occur mainly by oxidation and conjugation in the liver and renal elimination of less than 10-20% parent NSAID (Ellenhorn et al., 1997). Prolonged use of NSAIDs especially Ibuprofen has a variety of effects on the liver and kidney. Sever adverse renal effects may partly be due to vasoconstriction consequent upon inhibition of renal prostaglandin-mediated vasodilatation, decreasing renal blood flow and resulting in a reduction in glomerular filtration rate (Whelton et al., 2003) Prostaglandins also play an integral role in maintaining gastrointestinal mucosal integrity and in platelet aggregation (Elomeba et al., 2006). These effects are responsible for many of the adverse effects seen with the therapeutic doses of some NSAIDs. NSAIDs induced renal failure and hepatic dysfunction depends largely on the drug, dose and pharmacologic effects and the health status of the patient (Whelton and Hamilton 1991).

It was concluded from the study that, none of the drugs were safe for continuous use for a period of three weeks. To minimize the risk of NSAIDs toxicity, the lowest dose should be used for the shortest duration possible. Patients on NSAIDs medication for a long time should be monitored with regular laboratory tests to avoid adverse effects on the haemopoetic system and organ damage.

References


