Effect of arsenic trioxide poisoning on hematological parameters, liver marker enzymes and kidney of male albino rats

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ABSTRACT

Arsenic is a notorious human toxicant that is derived from the natural environment. The incidence of arsenic contamination of ground water used for both irrigation as well as for human consumption or industrial activities has taken the dimension of an epidemiological problem. The present investigation was therefore undertaken to study the effect of arsenic trioxide on the hematological parameters, liver and kidney of male albino rats. 20 male albino rats were divided into two groups of 10 rats per group: Groups A (control) received no poisoning while group B received arsenic trioxide (20mg/Kg body weight twice a day for seven days). They were acclimatized for one week before administration of arsenic trioxide commenced.  The WBC count in group B animals administered with arsenic trioxide (P<0.05) were significantly increased compared to group A animals (control group). The results of this study show that HGB, RBC and HCT values were significantly reduced (P<0.05) in group B administered with arsenic trioxide compared to the healthy control group. Arsenic trioxide significantly reduced (P<0.05) total protein and albumin while total bilirubin increases in group B compared to group A. The result of this study indicates that arsenic trioxide induced marked renal and liver damage characterized by a significant increase (P<0.05) in plasma urea, creatinine, AST, ALT, and ALP values in group B compared to group A.

Keywords: Arsenic trioxide, Hematological parameters, kidney function test and Liver marker enzymes.

Introduction

Arsenic is a chemical substance that behaves like a metal because it is an element that is present in the environment and does not deteriorate. Arsenic is a toxic element for humans and it is commonly associated with serious health disruptions (Brookes 1998).

Arsenic compounds are released from the earth's crust via natural processes and from certain human activities. Natural processes involve volcanoes, weathering of arsenic containing minerals from the area and from human activities (via industrial processes); such as mining, in the glass industry as a clarifier as a wood preservative (copper arsenite), in the production of semiconductor (Gallium arsenide), coal-fired power plants and as a product of smelting of non ferrous metals, particularly gold and copper. Environmental contamination also occurred because it is used in agricultural pesticides. Humans may come in contact with arsenic in contaminated dusts, fumes, or mists. They may eat food either contaminated with arsenical pesticides or grown with arsenic-contaminated water or in arsenic-rich soils (Nriagu and Azcue, 1990). Many epidemiological studies have revealed that people are more likely to have vascular diseases when living for many years in areas where well water are contaminated with inorganic arsenic (as arsenite and arsenate) (Lilienfeld, 1988; Engel et al.,1994; and Chiou et al., 1997). Inorganic arsenic compounds are well recognised human carcinogens (IARC 1980 and 1987). Arsenic poisoning is second to lead as the most frequently reported heavy metal toxicant. Arsenic exposure causes both acute and chronic toxicity in humans. Human arsenic exposure is related to severe health problems such as skin cancer, diabetes, liver, kidney and CNS disorders (Neiger et al, 1985). Arsenic occurs in different forms and some is transported between different parts of the environment where it may change its form. Arsenic in weathered rock or soil can be picked up and moved by the wind and arsenic compounds bind to soil and only move short distances when water percolates down through the soil it also bind with water. If arsenic is released into the atmosphere by industrial processes or volcanic activity, it attaches to particles that are dispersed by the round and fall back to the ground. Microbes in soil and sediment also release substances containing arsenic into the atmosphere. Arsenic is of great environmental concern due to extensive contamination of groundwater thereby causing carcinogen toxicity poisoning to millions of people as well as animals.

Methodology

Experimental animals and treatments

Male albino rats weighing between 140-160g were acclimatized for one week to Laboratory condition (23 ± 2 OC). They were bred and housed in the animal house of the department of science laboratory, school of technology, Lagos State Polytechnic, Ikorodu, Lagos, Nigeria. They were
kept in wire meshed cages and fed with commercial rat chow and supply with water *ad-libitum*.

**Animal grouping and arsenic trioxide administration**

Twenty rats were divided into two groups of ten rats per group as follows:

**Group A**: Control group: Animals fed with normal diet and water *ad-libitum* without arsenic trioxide for a period of seven days.

**Group B**: Animals administered with dose of arsenic trioxide (20mg/Kg body weight of arsenic trioxide with concentration of 2.5g/100ml of water), twice a day for seven days.

**Collection of blood samples for plasma analysis**

The rats were sacrificed by cervical dislocation. Blood samples were collected by ocular punctures into heparinized tubes. The blood was later centrifuged for 10mins at 3000rpm using a centrifuge. The clear supernatant was used for the estimation of lipid profiles and liver function tests.

**Determination of hematological parameters**

The total red blood cell (RBC), hemoglobin concentration (HGB), white blood cell count (WBC), lymphocyte and other hematological parameters were determined using ADVIA 60 Closed Tube (CT) Automated Hematology System in Yaba psychiatric hospital in Lagos, Nigeria.

**Determination of total protein, total bilirubin and albumin.**

The plasma total protein, total bilirubin and albumin were determined using Randox diagnostic kits.

**Determination of liver and kidney function test**

Plasma enzymes like alkaline phosphatase (ALP), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined using Randox diagnostic kits. The urea and creatinine levels were also determined in the plasma using Randox diagnostic kits.

**Data analysis**

Data analysis was done using the GraphPad prism computer software. Students 't'-test and one-way analysis of variance (ANOVA) were used for comparison. A P-value < 0.05 was considered significant.

**Results**

**Table I**: Effect of arsenic trioxide on hematological parameters of male albino rats.

<table>
<thead>
<tr>
<th>Hematological Parameters</th>
<th>Group I</th>
<th>Group II</th>
</tr>
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<tbody>
<tr>
<td>WBC (×10⁹/L)</td>
<td>6.99 ± 1.08</td>
<td>9.36±2.74</td>
</tr>
<tr>
<td>HGB g/dl</td>
<td>14.20 ± 1.20</td>
<td>9.70 ± 1.40</td>
</tr>
<tr>
<td>RBC (×10¹²/L)</td>
<td>7.50 ± 1.6</td>
<td>5.40 ± 1.30</td>
</tr>
<tr>
<td>HCT %</td>
<td>43.50 ± 5.3</td>
<td>30.90± 4.20</td>
</tr>
<tr>
<td>MCH pg</td>
<td>18.90 ± 1.20</td>
<td>18.10 ± 2.10</td>
</tr>
<tr>
<td>MCHC g/dl</td>
<td>34.50 ± 2.10</td>
<td>34.2 ± 1.10</td>
</tr>
<tr>
<td>MPV fl</td>
<td>7.3 ± 0.6</td>
<td>7.3 ± 0.7</td>
</tr>
<tr>
<td>PCT %</td>
<td>0.464 ±0.0541</td>
<td>0.413 ± 0.065</td>
</tr>
</tbody>
</table>

The values are the Means ± SD for ten rats in each group. White blood count (WBC), Hemoglobin (HGB), Red blood count (RBC), Hematocrit (HCT), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), Mean platelet volume (MPV) and Plateletcrit (PCT)
Table II. Effect of arsenic trioxide on kidney function test and liver marker enzymes of male albino rats.

<table>
<thead>
<tr>
<th></th>
<th>GROUP A</th>
<th>GROUP B</th>
</tr>
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<tbody>
<tr>
<td>Urea mg/dl</td>
<td>2.0±0.8</td>
<td>2.9±2.5</td>
</tr>
<tr>
<td>Creatinine µmol/l</td>
<td>63.6±8.30</td>
<td>99.41±7.94</td>
</tr>
<tr>
<td>AST U/L</td>
<td>9.45±2.30</td>
<td>15.4±2.0</td>
</tr>
<tr>
<td>ALT U/L</td>
<td>7.60±2.10</td>
<td>10.70±4.70</td>
</tr>
<tr>
<td>ALP U/L</td>
<td>75.40±12.30</td>
<td>148.10±15.60</td>
</tr>
</tbody>
</table>

The values are the Means ± SD (range) for ten rats in each group. Significant differences from the control P<0.05.

Discussion

Arsenic is a notorious human toxicant that is derived from the natural environment. The incidence of arsenic contamination of ground water used for both irrigation as well as for human consumption or industrial activities has taken the dimension of an epidemiological problem. Hematological and biochemical indices have been reported to be a reliable parameter for assessment of the health status of humans and animals with arsenic poisoning (Sexena et al. 2011) and Ohaeri et al. (2011). There is a significant increase (P < 0.05) in the WBC count in group B compared to group A (Table I). This shows that there was thrombocytosis in all the animals in group B compared to the healthy group (Group A). Therefore, it may be that arsenic trioxide causes the release of thrombopoietin which lead to an increase in WBC count (Erslev and Gabuzda, 1979). Table I shows clearly that there is a significant decrease (P<0.05) in HGB, RBC and HCT in the group administered with arsenic trioxide compared to the healthy group (group A). The significant reduction of HGB, RBC and HCT may be attributed to the cytotoxic effect of arsenic compounds. This observation is supported by a report stating that anemia is characterized by decreased values of HGB, RBC and HCT (Aleksandro et al 2009 and Eyong et al., 2004). The primary reason for assessing the RBC is to check anemia and to evaluate normal erythropoiesis. HGB levels indicate the amount of intracellular iron, while HCT represents the volume of RBC in 100ml of blood, which helps to determine the degree of anemia or polycythaemia. The mean cell hemoglobin level is a significant index for folic acid and/or Vit B12 need (Ganong, 1999). Arsenic trioxide may have an effect on bone marrow, kidney and hemoglobin metabolism. Young and Maciejewski, 1997 showed clearly that any substance which significantly affects the values of red blood cells and associated parameters would have effects on the bone marrow, kidney and haemoglobin metabolism. Other hematological parameters like MCH, MCHC, MPV and PCT showed no significant differences both in group A and B.
Group B shows significant reduction (P<0.05) in total protein and albumin values compared to group A (Figure I and 2). This is an indication that arsenic trioxide destroys the total protein and albumin. Figure 3 shows that animals administered with arsenic trioxide show a significant increase (P<0.05) in total bilirubin compared to control group (group A). An increase in bilirubin may be a metabolic disturbance in liver involving defective conjugation or excretion of bilirubin (Mankani et al., 2005). Secondly, a rise in plasma level of bilirubin may suggests liver cell damage, since liver cells are responsible for removing bilirubin from serum (Nelson and Cox, 2005).

The results from this study showed significant increase (P<0.05) in activities of liver damage marker enzymes- AST and ALT in group administered with arsenic trioxide. (Table II). This increase indicates cellular leakage and failure of functional integrity of liver cell membranes. ALP is involved in the transport of metabolites across membrane, synthesis of certain enzymes and proteins, secretory activities and glycogen metabolism. Significant increase (P<0.05) in the ALP values of animals in group B compared to group A animals may imply that damage occurs in the liver cells of the rats administered with arsenic trioxide (Table II), since the activities of these enzymes are reported to be increased in liver damage. However the increase in this enzyme activity may not be unconnected with a disturbance in the transport of metabolites or alteration in the synthesis of certain enzymes as in other hepatotoxic conditions. The increase in these liver marker enzymes (AST, ALT and ALP) in the liver homogenate is responsible for the hepatotoxicity of the liver in the group administered with arsenic trioxide. The significant increase (P<0.05) in the urea and creatinine values of albino rats administered with arsenic trioxide compared to the healthy rats (group A) indicate that group B animals have renal impairment (Table II).

Conclusion

The result of this study shows clearly that administration of arsenic trioxide is hepatotoxic and causes renal impairment and kidney damage.

References


