HAEMATOLOGICAL CHANGES INDUCED BY DIMETHOATE IN RAT

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Received June 1, 1988.

Chronic effects of a sublethal dose (150 mg/kg body weight) of dimethoate, an organophosphorus insecticide, on blood constituents were investigated in rats after exposure of 15 and 30 days. A significant decrease was observed in haemoglobin concentration, total RBC and WBC counts and in haematocrit values. After 30 days of exposure, the levels of blood glucose, cholesterol, urea, total bilirubin and the activities of glutamic-oxalacetic transaminase, glutamic-pyruvic transaminase and amylase markedly increased, but the activities of acid phosphatase and cholinesterase significantly decreased. There was no effect on total plasma protein content. The rats exposed to dimethoate for 30 days showed more prominent changes in all the blood constituents than those exposed for 15 days.

The insecticides are among the most widespread pollutants. They create difficult problems from the point of view of environmental protection and pose hazards to human health. The use of organophosphorus insecticides, because of their rapid biodegradability, is preferred to that of more persistent chlorinated hydrocarbon insecticides (1). In recent years their production has noted a manifold increase. Thus, the pharmacological and toxicological effects of organophosphorus insecticides have become a matter of serious concern.

A variety of metabolic disorders, including hyperglycaemia and glycosuria are known to be induced by organophosphorus insecticides (2), which also act as potent inhibitors of cholinesterase activity in the blood and other tissues (3–5). Although a great deal of information is available on their effects on aquatic organisms (6–9), the haematological and biochemical changes produced by these insecticides in mammals have received little attention. However, the effects of malathion on different systems in rats have been reported (10,11). The mutagenicity of dimethoate was observed in Drosophila by Velazquez and co-workers (12). The genotoxicity of the same compound was also studied in rats (13). The present report deals with the chronic effect of dimethoate, an organophosphorus insecticide and acaricide on the blood constituents of rat.
MATERIAL AND METHODS

Thirty adult male albino rats (Rattus rattus albinus), 90 days old, weighing 100 ± 10 g were randomly selected from the laboratory stock and placed into three groups of 10 rats each. The rats were housed individually in plastic cages with galvanized iron wire bar tops. They were provided pellet diet (Lipton India Ltd., Bangalore) and tap water ad libitum. Rats in Groups I and II were injected dimethoate (150 mg/kg body weight, dissolved in 0.5 ml of physiological saline), intraperitoneally, on alternate days, for a period of 13 and 30 days respectively. Rats from Group III received an equal volume of physiological saline and served as controls. Dimethoate (99.5%) is a polar compound (soluble in water 25 g/l at 21 °C) and rather stable in aqueous media at acidic or neutral pH. It was provided as a gift from Chemicova, A/S (Harboore, Denmark).

After scheduled treatment, the rats were starved overnight and decapitated. Blood samples were collected from the aorta and analysed for total RBC and WBC counts and for haemoglobin (14) and haematocrit values (15). To estimate other components, the blood was first allowed to clot, and was then centrifuged. The clear serum was collected and analysed for glucose (16), cholesterol (17), total bilirubin, amylase (18) and urea (19). The activities of glutamic-oxalacetic and glutamic-pyruvic transaminases, alkaline and acid phosphatases and cholinesterase were determined (20). Total plasma proteins were estimated using bovine serum albumin as standard (21). The statistical significance between control and experimental values was calculated by means of Student’s t-test (22).

RESULTS AND DISCUSSION

The rats exposed to dimethoate for 30 days exhibited more conspicuous changes in the chemical composition of blood than those treated for 13 days (Table 1). Haemoglobin, RBC, WBC and haematocrit values were significantly decreased in rats exposed to dimethoate. The percentage of inhibition increased with the duration of exposure. The total plasma protein content remained unchanged. Blood glucose, cholesterol, total bilirubin and urea levels increased significantly after 30 days of exposure to the insecticide. On the other hand there was no significant change in the level of glucose, cholesterol or total bilirubin in the blood of rats treated with dimethoate for 15 days. An elevation was also recorded in the activities of glutamic-oxalacetic transaminase, glutamic pyruvic transaminase, alkaline phosphatase and amylase. Maximum elevation was found in the activity of glutamic-pyruvic transaminase after 30 days of treatment. The activities of acid phosphatase and cholinesterase were reduced.

According to present results dimethoate induced gross changes in experimental rats in terms of haematological indices (Table 1). Several indices such as haemoglobin, RBC and haematocrit values were significantly decreased indicating the presence of dimethoate-induced anaemia. These results are in agreement with those reported for fish (23). Total plasma protein content remained constant indicating no change in blood volume.

The elevated blood glucose level in rats exposed to dimethoate supported the findings of Dybing and Sognes (24) who observed significant variations in the blood sugar levels of rats exposed to diazinon, another organophosphorus insecticide. The condition
Table 1

Alteration in haematological parameters induced by dichloroacetate in rats

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Control</th>
<th>Experimental</th>
<th>% Alter.</th>
<th>% Alter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 days</td>
<td>30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>13.48 ± 0.8</td>
<td>9.60 ± 1.0*</td>
<td>28.8(−)</td>
<td>8.00 ± 1.0**</td>
</tr>
<tr>
<td>RBC (10⁶/mm³)</td>
<td>6.81 ± 0.5</td>
<td>4.92 ± 0.7*</td>
<td>27.8(−)</td>
<td>3.50 ± 0.7**</td>
</tr>
<tr>
<td>WBC (10⁹/mm³)</td>
<td>8.28 ± 0.9</td>
<td>6.89 ± 0.8*</td>
<td>16.0(−)</td>
<td>4.32 ± 0.8*</td>
</tr>
<tr>
<td>Haematocrit (g/dl)</td>
<td>39.30 ± 1.0</td>
<td>28.20 ± 2.1**</td>
<td>28.6(−)</td>
<td>22.60 ± 2.1**</td>
</tr>
<tr>
<td>Total plasma protein (g/dl)</td>
<td>6.68 ± 0.9</td>
<td>6.60 ± 1.0</td>
<td>10.2(−)</td>
<td>6.50 ± 0.6</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>93.60 ± 3.3</td>
<td>100.10 ± 5.7</td>
<td>4.7(+)</td>
<td>120.81 ± 5.5**</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>230.00 ± 8.9</td>
<td>220.16 ± 5.0</td>
<td>4.3(−)</td>
<td>268.20 ± 5.1**</td>
</tr>
<tr>
<td>Urea (mg of Urea N/dl)</td>
<td>16.2 ± 2.1</td>
<td>38.00 ± 3.3***</td>
<td>133.8(+)</td>
<td>50.50 ± 3.0**</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>0.32 ± 0.1</td>
<td>0.42 ± 0.0</td>
<td>31.2(+)</td>
<td>0.58 ± 0.1*</td>
</tr>
<tr>
<td>GGT (IU)</td>
<td>40.00 ± 3.3</td>
<td>46.00 ± 2.7</td>
<td>15.0(+)</td>
<td>54.55 ± 3.0**</td>
</tr>
<tr>
<td>GPT (IU)</td>
<td>12.00 ± 2.0</td>
<td>26.50 ± 2.4**</td>
<td>130.8(+)</td>
<td>38.12 ± 2.7**</td>
</tr>
<tr>
<td>Alkaline phosphatase (µ mol P⁰⁰/min/litre)</td>
<td>47.02 ± 3.7</td>
<td>50.00 ± 4.1</td>
<td>6.3(+)</td>
<td>39.28 ± 2.9*</td>
</tr>
<tr>
<td>Acid phosphatase (µ mol P⁰⁰/min/litre)</td>
<td>28.30 ± 4.0</td>
<td>18.55 ± 3.0*</td>
<td>34.4(−)</td>
<td>10.00 ± 20**</td>
</tr>
<tr>
<td>Amylase (Somogyi units/ml)</td>
<td>65.00 ± 2.2</td>
<td>90.00 ± 5.0**</td>
<td>38.4(+)</td>
<td>110.20 ± 7.0**</td>
</tr>
<tr>
<td>Cholinesterase (µM acetylcholine hydrolysed/mg protein)</td>
<td>40.00 ± 2.5</td>
<td>28.45 ± 2.9*</td>
<td>28.9(−)</td>
<td>19.02 ± 2.5**</td>
</tr>
</tbody>
</table>

All values are means ± SEM of five observations; (±), % stimulation; (−), % inhibition; IU, International Units; P⁰⁰, p-nitrophenol; Values are significant at *P < 0.05; **P < 0.01; ***P < 0.001 (Fisher's 'T' test).
of hyperglycaemia indicated disrupted carbohydrate metabolism which might have been due to enhanced breakdown of liver glycogen, possibly mediated by adrenocorticotropic (ACTH) and glucagon hormones and reduced insulin activity.

The elevated blood cholesterol level (25) may have been due either to the animal's hypermetabolic state or to impaired liver function. The rise in urea level suggested kidney damage. Increased bilirubin level was a sign of malfunctioning of the liver (conjugation of bilirubin) or of haemolytic anaemia.

The increased activity of serum enzymes, alkaline phosphatase, glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase also indicated liver damage and disruption of normal liver function. Elevated blood transaminases induced by organophosphates have also been reported (26). Rouiller (27) attributed the increase in the blood alkaline phosphatase activity to the leakage of this enzyme to circulating medium from hepatocytes. The increase in serum amylase activity may be attributed to pancreas damage. In all the experimental rats, cholinesterase activity was significantly inhibited.

Acknowledgement – We thankfully acknowledge the financial assistance from UGC and CSIR, New Delhi.

REFERENCES

HEMATOLOŠKE PROMJENE IZAZVANE DIMETOATOM U ŠTAKORA

Kronični učinci subletalne doze organskosforsfornog insekticida dimetoata (130 mg/kg tjelesne težine injiciranog intraperitonealno svakog drugog dana, na sastojke krvi u štakora proučavan su nakon 15 do 30 dana tretmana. Značajno pad zamijećen je u postotku hemoglobina, broju eritrocita, leukocita i vrijednosti hematokritna. Nivo glutam-kolesalacetat transaminaze, glutaminpiruvičke transaminaze i aminotransferaznje značajno su porasli nakon 30 dana izloženosti, ali aktivnost kiselih fosfataze se značajno smanjila. Učinak nije zamijećen na sadržaju protein plazme. Štakori izlagani dimetoatu 30 dana pokazali su uočljivu promjencu u svim sastojcima krvi negoli oni izlagani samo 15 dana.

Odjel za biologiju i biotehnologiju, Sveučilište u Roorkeetu, Roorkee, Indija