GLYCEMIC EFFECT OF VENOM FROM THE SCORPION

BUTHUS MINAX (L. KOCH)

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Abstract—The venom from the scorpion Buthus minax caused hyperglycemia in rats. Tolazoline and specific antivenom prevented or abolished this effect while propranolol did not modify the hyperglycemic response. Liver glycogenolysis seems to be the major contributing factor for this rise in blood glucose.

INTRODUCTION

Scorpion venoms produce hyperglycemia (Mohamed, 1950; Freire-Maia et al., 1959; Freire-Maia and Ferreira, 1961). Glycogenolysis and gluconeogenesis were postulated as possible mechanisms of this hyperglycemia, although the analysis was complicated by the presence of serotonin in the venom (Mohamed et al., 1972). Venom from the scorpion B. minax contains very little or no serotonin (El-Asmar et al., 1973b). Similarly, Ismail et al. (1973) showed that this venom produced its effects through autonomic nerve stimulation, with a predominance of sympathetic stimulation, and release of tissues catecholamines. In view of the low serotonin content of this venom, it was thought worthwhile to investigate the mechanism of its hyperglycemic effect.

METHODS

Male albino rats (200-250 g) were allowed food and water ad libitum. Venom was obtained from mature B. minax by electrical stimulation of the telson as described by El-Asmar et al. (1973a, 1973b).

B. minax antivenom was prepared in goats using a modification of the method described by El-Asmar et al. (1973a). Male goats were hyperimmunized according to the following schedule: two injections of 300 μg each in the first week, three injections of 500 μg each in the second week, one injection of 500 μg on each of the fourth and fifth weeks, and one injection of 1000 μg in each of the following 6 weeks. Each dose was emulsified in 0.5 ml complete Freund's adjuvant (Difco Laboratories, Detroit, Mich.). Five days later, blood samples were withdrawn from the marginal ear veins and tested for positive precipitin bands. Goats showing positive precipitin bands were injected with 1000 μg venom and were bled 6 days later. At the end of the hyperimmunization period the goats weighed between 6 and 8 kg. Serum was separated and kept at —20°C until used.

With the exception of those treated with reserpine, all rats were anaesthetized with intraperitoneally injected urethane (1.5 g/kg body weight). This was necessary to minimize

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the irritability of the animals after venom injection (EL-ASMAR et al., 1973a, 1973b). The rats were divided into 10 groups, each consisting of 5 animals. Tolazoline (2 mg/kg) or propranolol (1 mg/kg) were injected intraperitoneally 10 min before the venom while reserpine (5 mg/kg) was injected intraperitoneally 24 hr before the venom. A mixture of antivenom plus venom (8 ml/mg venom) was incubated for 1 hr at 37°C before injection. The venom was injected in a dose of 200 µg/kg body weight. Control animals receiving the same drug treatment were injected with saline in place of venom. All animals were sacrificed 10 min following injection of venom or saline. Blood was collected in citrated tubes and glucose was determined according to the method of NELSON-SOMOGYI (1944). Blood lactate was determined in control and venom treated animals by the BARKER and SUMMERSO method (1941).

RESULTS AND DISCUSSION

As shown in Table 1 a sublethal dose of B. minax venom (EL-ASMAR et al., 1973b) caused a significant elevation of the blood glucose level ($P<0.01$). Pretreatment of the rats with tolazoline, an $\alpha$-adrenergic receptor blocking agent, completely prevented the hyperglycemic effect of the venom; tolazoline alone caused a significant ($P<0.005$) lowering of the blood glucose level (NICKERSON, 1970). On the other hand pretreatment with propranolol, a $\beta$-adrenergic receptor blocking agent, did not prevent the hyperglycemic effect of the venom, nor did propranolol itself have any effect on the blood glucose level. It would appear that $\alpha$- but not $\beta$-adrenergic receptors are responsible for the hyperglycemic response to the catecholamines, perhaps through inhibition of insulin release and hepatic glycogenolysis (NICKERSON, 1970). Since B. minax is known to release catecholamines (ISMAIL et al., 1973), the effectiveness of tolazoline in preventing the venom induced hyperglycemia might be due to blockade of the $\alpha$-adrenergic receptors in the liver. Treatment with B. minax venom did not result in any significant change in the blood lactate level. The average control level in mg/100 ml blood was $54 \pm 8$, while that of the venom treated rats

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Blood glucose (mg/100 ml ± SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>$120 \pm 6.9$</td>
</tr>
<tr>
<td>Venom</td>
<td>$162 \pm 9.6^*$</td>
</tr>
<tr>
<td>Tolazoline + saline</td>
<td>$87 \pm 2.5$</td>
</tr>
<tr>
<td>Tolazoline + venom</td>
<td>$83 \pm 5.5$</td>
</tr>
<tr>
<td>Propranolol + saline</td>
<td>$115 \pm 6.3$</td>
</tr>
<tr>
<td>Propranolol + venom</td>
<td>$141 \pm 3.8^*$</td>
</tr>
<tr>
<td>Reserpine + saline</td>
<td>$71 \pm 4.8$</td>
</tr>
<tr>
<td>Reserpine + venom</td>
<td>$105 \pm 8.8^*$</td>
</tr>
<tr>
<td>Antivenom + saline</td>
<td>$106 \pm 14$</td>
</tr>
<tr>
<td>Antivenom + venom</td>
<td>$111 \pm 4.9$</td>
</tr>
</tbody>
</table>

*Those venom blood glucose values which are significantly different ($P < 0.01$) from corresponding saline value.

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was 50 ± 5. This is in agreement with the results reported by MOHAMED et al. (1972). As muscle glycolysis leads to lactate formation and the latter could be converted to glucose through gluconeogenesis, it could be argued from our results that this is not a significant factor in the venom induced hyperglycemia.

Injection of the venom in reserpine-treated rats caused a significant rise in blood glucose level (P<0.01), although reserpine alone caused a marked hypoglycemia (P<0.01). Reserpine depletes catecholamine stores of the adrenergic nerve endings; however, the adrenal medulla is less susceptible to its action (NICKERSON, 1970). It is possible that B. minax venom by releasing the residual catecholamines of the adrenal medulla increases the blood glucose through increased glycogenolysis.

The hyperglycemic effect of the venom was prevented by incubation with the specific antivenom, showing that the hyperglycemic factor(s) are antigenic and inactivated by the specific antivenom. These hyperglycemic factor(s) appear to be nondialyzable, since dialyzed venom prepared as described by EL-ASMAR et al. (1973b) produced the same degree of hyperglycemia.

REFERENCES