Rev. Inst. Med. trop. São Paulo
11(6):387-389, novembro-dezembro, 1969

UDC 616-099

EXPERIMENTAL TREATMENT OF NECROSIS PRODUCED BY PROTEOLYTIC SNAKE VENOMS. II — ACTION OF DEXAMETHASONE

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SUMMARY

Subcutaneous injection of proteolytic snake venom (*Bothrops jararaca*) in non treated mice caused 96.7% necrosis; the incidence in those treated only with antivenin was of 86.7%; with Dexamethasone alone it was of 62.5%; combined treatment with Dexamethasone and antivenin was somewhat less effective, resulting in 73.3% necrosis. Probably, the favorable effect of Dexamethasone was due to the vital stimulation produced in the animals and as a consequence, the mobilization of the venom, thus decreasing its concentration at the site of the injection.

INTRODUCTION

The problem of preventing necrosis produced by the bite of snakes with proteolytic venom is still recquiring experimental research, since antivenin therapy avoids death more easily than necrosis [1]. With this purpose the action of Isoxsuprine was investigated by ROSENFELD et al. [3] and it proved to be an efficient therapeutic means to reduce the incidence of necrosis produced by *Bothrops jararaca* venom in mice. Probably, by the vasodilator action of this drug, which enhances the circulation of the venom, decreasing its concentration at the site of the injection.

The investigation of the action of Dexamethasone on the lethal activity of some animal venoms (ROSENFELD & LANGLADA [2]) allowed parallel observation on the hormone's ability to prevent necrosis. Results obtained are discussed in the present paper.

MATERIAL AND METHODS

Mice — Four groups of 120 animals weighing from 20 to 35 g were used.

Venom — Desiccated venom of *Bothrops jararaca*, 1 mg in 1 ml saline solution prepared just before inoculation. 0.01 mg per g body weight were injected subcutaneously in the external surface of the thigh, corresponding to a proportion of 10.0 mg/kg.

Antivenin — Polyvalent anti-*Bothrops* serum from the "Instituto Butantan" with a potency of 2 units per ml was injected intravenously, in an amount neutralizing the venom dose, 15 minutes after the venom.

Dexamethasone — Dexamethasone-21-phosphate, di-sodium salt (*), in a dose of 0.1 mg was injected intramuscularly in each animal, 15 minutes and 8 hours after the venom, at the same site.

Observation of necrosis — Necrosis appearing as a sharp black scar was observed during 48 hours after injections.

RESULTS

All numerical results for the different experiments are shown in Table I, and their statistical analysis is shown in Table II.

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(1) Fellowship from the National Council of Research (CNPq) (Head of Research)

(*) Provided by Merck Sharp & Dohme S. A. under the name of "Decadron" injectable

ROSENFELD, G.; LANGLADA, F. G. de & KELEN, E. M. A. — Experimental treatment of necrosis produced by proteolytic snake venoms. II — Action of dexamethasone. *Rev. Inst. Med. trop. São Paulo* **11**:387-389, 1969.

TABLE I

Necrosis in mice injected subcutaneously with 0.5 mg snake venom (*Bothrops jararaca*) in the right thigh. Intramuscular injection of 0.1 mg Dexamethasone at the same site of the venom, 15 minutes and 8 hours after the venom. Specific antivenin injected intravenously, an amount neutralizing one venom dose, 15 minutes after the venom. Necrosis observed after 48 hours

Experiment no.	Group 1 Venom	Group 2 Venom + Dexamethasone	Group 3 Venom + Antivenin	Group 4 Venom + Antivenin + Dexamethasone
	Necrosis no./total	Necrosis no./total	Necrosis no./total	Necrosis no./total
128 A	18/20	15/20	16/20	16/20
128 C	18/20	15/20	16/20	7/20
129 B	20/20	15/20	15/20	9/20
129 C	20/20	10/20	19/20	20/20
130 B	20/20	10/20	19/20	16/20
130 C	20/20	10/20	19/20	20/20
Total	116/120	75/120	104/120	88/120
%	96.7	62.5	86.7	73.3

TABLE II

Statistical comparison of necrosis between groups treated with antivenin and Dexamethasone

Groups compared	Result	Chi^2 n = 1	Probability P
Group 1 — Venom × Group 2 — Venom and Dexamethasone	Highly significant High protective effect of Dexamethasone	43.11	$P << 0.1\%$
Group 1 — Venom × Group 3 — Venom and Antivenin	Very significant Protective effect of Antivenin	7.85	$1\% > P > 0.1\%$
Group 2 — Venom and Dexamethasone × Group 4 — Venom, Dexamethasone and Antivenin	Significant The protective effect of Dexamethasone alone is better than its association with antivenin	5.10	$5\% > P > 2\%$
Group 3 — Venom and Antivenin × Group 4 — Venom, Dexamethasone and Antivenin	Very significant Association with Dexamethasone protects better than antivenin alone	6.66	$1\% > P > 0.1\%$

Group 1 was only inoculated with venom, group 2 with venom and Dexamethasone, group 3 with venom and antivenin, and group 4 with venom, and treated with antivenin and Dexamethasone. One experiment always included all 4 groups simultaneously. The reason for such procedure was explained previously [3].

Dexamethasone alone reduced the incidence of necrosis from 96.7% to 62.5%, and the statistical analysis showed the hormone's efficiency.

Treatment only with antivenin reduced the percentage of necrosis to 86.7%. Statistically, this difference is significant but was less efficient than Dexamethasone.

Combined treatment with antivenin and Dexamethasone reduced the number of necrosis to 73.3%, showing a better effect than antivenin alone, but not as efficient as Dexamethasone when used as a single therapeutic agent.

DISCUSSION

Practically, Dexamethasone had neither favorable protective nor unfavorable effect against the lethal activity of *Bothrops jararaca* venom, as was demonstrated by ROSENFELD & LANGLADA [2]. However, its action on necrosis was effective as shown by the present results. The mechanism of action might be the vital stimulation produced by the hormone. This effect was manifested as restlessness, and a tendency to polyphagia, and also making the animal attack those where necrosis was detected after 24 hours. This stimulation probably activated circulation, resulting in a more rapid mobilization of the venom, and consequent diminishing of concentration at the site of the injection.

The protective action of Dexamethasone against necrosis was not as good as that of Isoxsuprine [3], what makes assume that Dexamethasone treatment does not seem to be advisable to protect from necrosis in envenomations by proteolytic venoms.

RESUMO

Tratamento experimental da necrose produzida por veneno ofídico proteolítico. II — Ação da Dexamethasona

Camundongos injetados por via subcutânea com veneno ofídico proteolítico (*Bothrops jararaca*), não tratados, apresentaram 96,7% de necroses; tratados sòmente com soroterapia antiveneno, a incidência foi de 86,7%; tratados ùnicamente com Dexamethasona, houve 62,5% de necroses, e o tratamento combinado de Dexamethasona e soroterapia foi um pouco menos eficiente, resultando em 73,3% de necroses. Provàvelmente, o efeito benéfico da Dexamethasona foi devido ao estímulo vital provocado nos animais que, com maior movimentação, contribuiu para mobilizar mais ràpidamente o veneno, diminuindo sua concentração no local da inoculação.

REFERENCES

1. ROSENFELD, G. — Symptomatology, Pathology and Treatment of Snake Bites in South America. *In*: BÜCHERL, W.; BUCKLEY, E. E. & DEULOFEU, V. — *"Venomous Animals and their Venoms"*. Vol. II, Chapter 4. New York, Academic Press. (In press).

2. ROSENFELD, G. & LANGLADA, F. G. de — Corticosteroid and ACTH in experimental poisoning with animal venoms. *Mem. Inst. Butantan* 31:171, 1964.

3. ROSENFELD, G.; LANGLADA, F. G. de & KELEN, E. M. A. — Experimental treatment of necrosis produced by proteolytic snake venoms. I — Action of Isoxsuprine. *Rev. Inst. Med. trop São Paulo* 11:383-386, 1969.

Recebido para publicação em 10/6/1969.