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CORTICOSTEROID AND ACTH IN EXPERIMENTAL POISONING WITH ANIMAL VENOMS *

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Corticosteroids or ACTH have been utilized in the treatment of human beings bitten by poisonous snakes. Some authors have attributed beneficial activity to these hormones, while other workers have found not only unsatisfactory results, but also have concluded that these drugs provoke inhibition of the activity of antivenom serum. Russel and Emery (6) made a report on the concerning literature. Schöttler (7) utilized ACTH, cortisone and hydrocortisone in mice, injected simultaneously with DL50 of snake venoms (*Bothrops jararaca* or *Crotalus durissus terrificus*) and did not observe change as concern either mortality or local reaction of the bothropic venom. Doses form 2,5 to 25 mg/kg of adrenocorticotropic hormone (ACTH) and cortisone and 2 mg/kg of hydrocortisone were used. Deichmann and others (2) made experiments with venom of *Crotalus adamanteus* in dogs, having observed the reduction of mortality with injections from 200 to 650 mg of hydrocortisone; the results were more satisfactory when immediate treatment was applied and were still favourable, but not so good when corticoid was injected 4 hours after the venom. Russel and Emery (6) employed methylprednisolone and hydrocortisone in doses from 5 to 500 mg/kg in mice, injecting venom of *Ancistrodon contortrix*, they concluded that, not only there was no protection, but also that the treatment seemed to produce unfavourable results, either due to the venom action or to the suppression of the immunizing mechanism of defense.

As the existing discrepancies were so numerous, both in clinical observations and experimental works, it seemed necessary once more to test the action of corticoids on animals injected with snake, spider and scorpion venoms, associating or not the treatment with specific antivenom serum. The chosen venoms were each diverse from another, so that it would be possible to come to a greater generalization than the referred past works.

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Material and methods

Venoms of Rattlesnake (*Crotalus durissus terrificus*) and Jararaca (*Bothrops jararaca*), extracted by pressing the glands, were utilized. The spider (*Phoneutria fera*) and scorpion (*Tityus serrulatus*) venoms were obtained by electric shock of the preys. All venoms were dried out in the vacuum and kept dry protected from light, they were always a pooling obtained from a large number of animals and the solution was made on the same day they were injected.

Albino mice weighing from 20 to 35 g were used. Venom and corticoids were injected intravenously in the tail or intramuscularly into a thigh in order to have a 3 mm penetration of the injected needle in all cases. They were kept under observation several days and were fed in the usual way. The results here reported concern the animal survival after one or two days, because no modification of greater importance was observed after these periods. For each experiment, on the same day, four groups of mice were used. The first group received only venom and served as control for the second group which was injected with venom and hormone; the third group received venom and specific antivenom serum for controlling the fourth group which was injected with venom, antivenom serum and hormone.

Antivenom sera were specific for each inoculated venom and the ones utilized were of routine production in the Instituto Butantan. These sera are purified by pepsin hydrolysis and precipitation of the antibody-carrying fraction. The injected doses corresponded to one the capacity of in vitro neutralization of the corresponding inoculated doses of venom, and were introduced subcutaneously or intravenously at the same time as the first injection of the hormones.

Zinc ACTH of long action or Dexamethasone-phosphate were used for intramuscular or intravenous injections, with variable doses repeated after 4, 8, 12 or 24 hours. With the greater doses of corticoid, some agitation could be noticed in mice. They also showed polyphagia and a tendency to attack other animals presenting necrosis after the first day (inoculated with bothropic venom).

Results

Table 1 presents the results obtained in experiments done with snake, spider and scorpion venoms and the respective treatment with antivenom serum and ACTH.

Table 2 presents the results obtained in experiments with the same venoms and treatment with antivenom serum and Dexamethasone.

In Table 3 all results of Table 1 were accumulated and the data of each group were compared with each other to analyse the significance of the different treatments. ACTH has significantly diminished the mortality, when spider venom

was injected without serumtherapy, but produced a negative effect increasing the mortality when antivenom serum was given with the same venom. No effect was observed with crotalic, bothropic or scorpionic venom with or without serumtherapy.

In Table 4 all results of Table 2 were reported and analysed in the same manner as in Table 3. Dexamethasone has significantly diminished the mortality when spider and scorpion venoms were inoculated and antivenom was not given, but increased the mortality when crotalic or spider venoms were injected and serumtherapy was given. No effect was seen with crotalic or bothropic venom without serumtherapy and also with bothropic an scorpion venom when antivenom serum was given.

In all experiments the results have shown a very significant protective activity of the specific antivenom sera which were injected 15, 30 or 60 minutes after the venom (Tables 3 and 4).

Discussion

Apparently results are contradictory, but a more careful analysis permits a better understanding. Table 5 summarizes favourable, unfavourable and absence of effects of hormone treatments according to their significance measured by the Chi-square test.

ACTH did not have any significant activity as to mortality in experimental envenomation of mice with venoms of *Crotalus durissus terrificus* and *Bothrops jararaca* associated or not to treatment with specific antivenom serum. These results agree with that of Schöttler (7) who studied the same venoms and with Minton (4) who experimented the venom of *Ancistrodon contortrix* in mice, but neither of them did associate serumtherapy. However, it was not the same for spider venom (*Phoneutria fera*) and scorpion venom (*Tityus serrulatus*). Mortality was significantly diminished by ACTH in animals injected only with the spider venom (*P. fera*) while a markedly unfavourable result was obtained when serumtherapy was associated. The beneficial activity in the first case is possibly due to a favourable action of the hormone on the pain stress caused by this venom which is of great intensity in human cases. In the second case, the negative action could be attributed to an eventual neutralization of the serum effect as it was suggested by Knyvett and Molphy (3) in human cases bitten by snakes having neurotoxic and hemolytic venom, or by Chang and Veinstein (1) in experiments with tetanus toxin and cortisone associated or not to serumtherapy.

On the other hand, in experiments with the scorpion venom (*T. serrulatus*) ACTH had a slight protective action but not significant when not associated to serumtherapy; this venom likewise that one of *P. fera* provokes intense pain, nevertheless there was no negative action of ACTH by its association with serum.

TABLE 1 — MORTALITY OF MICE TREATED WITH VENOMS OF SNAKES, *Crotalus durissus terrificus* (C.d.t.), *Bothrops jararaca* (B.j.), SPIDER *Phoneutria fera* (P.f.) AND SCORPION *Tityus serrulatus* (T.s.), ALONE OR IN ASSOCIATION WITH A CORRESPONDING DOSES OF SPECIFIC ANTIVENOM SERUM AND/OR ACTH. OBSERVATIONS MADE AFTER 48 HOURS

Experiment	TREATMENT								RESULTS GROUPS				
	Venom innoculated			Hormone injected ACTH				Antivenom serum	1 Venom	2 Venom and ACTH	3 Venom and Antivenom	4 Venom Antivenom and ACTH	
Nº	Specie	Amount γ/gm	Route	Doses Units	Route	Time after venom min.	Repetition hours	Route	Deaths Total	Deaths Total	Deaths Total	Deaths Total	
103	C.d.t.	0,2	IV	0,02	IM	30	4	SC	10/20	12/20	7/20	5/20	
106	"	"	"	0,20	"	30	4	"	15/25	16/25	5/25	7/25	
102	"	"	"	2,00	"	60	8	"	10/20	5/20	3/20	9/20	48 h
									35/65	33/65	15/65	21/65	
3	B.j.	10,0	IM	1,00	IM	15	24	IV	14/20	15/20	7/20	3/20	
4	"	"	"	1,00	"	30	"	"	13/20	13/20	0/20	3/20	
1	"	"	"	1,00	"	60	"	"	9/20	14/20	3/20	2/20	
2	"	"	"	1,00	"	90	"	"	19/20	18/20	14/20	17/20	48 h
									55/80	60/80	24/80	25/80	

121	P.f.	1,0	SC	0,2	IM	15	24	SC	18/20	19/20	5/20	14/20	
122	"	"	"	0,2	"	15	8	SC	20/20	18/20	3/20	12/20	
42	"	"	"	2,0	"	15	8	IV	15/20	11/20	2/20	7/20	
41	"	"	"	2,0	"	30	24	IV	18/20	14/20	12/20	14/20	48 h
43	"	"	"	2,0	"	60	24	IV	19/20	16/20	13/20	14/20	
									90/100	78/100	35/100	61/100	
111	T.s.	1,5	SC	0,2	IM	15	8	SC	20/20	16/20	14/20	10/20	
112	"	"	"	0,2	"	15	8	"	17/20	15/20	12/20	8/20	
123	"	"	"	0,2	"	15	8	"	17/20	15/20	6/20	7/20	
124	"	"	"	0,2	"	15	8	"	17/20	14/20	3/20	7/20	
39	"	"	"	2,0	"	15	24	"	18/20	19/20	7/20	3/20	48 h
40	"	"	"	2,0	"	30	24	"	17/20	13/20	3/20	4/20	
38	"	"	"	2,0	"	60	24	"	16/20	18/20	11/20	13/20	
									122/140	110/140	56/140	52/140	

TABLE 2 — MORTALITY OF MICE TREATED WITH VENOMS OF SNAKES, *Crotalus durissus terrificus* (C.d.t.), *Bothrops jararaca* (B.j.), SIPDER *Phoneutria fera* (P.f.) AND SCORPION *Tityus serrulatus* (T.s.), ALONE OR IN ASSOCIATION WITH A CORRESPONDING DOSES OF SPECIFIC ANTIVENOM SERUM, AND/OR DEXAMETHASONE. OBSERVATIONS MADE AFTER 24 HOURS

	TREATMENT								RESULTS GROUPS				
Experiment	Venom innoculated			Hormone injected Dexamethasone				Antivenom serum	1 Venom	2 Venom and Dexamet.	3 Venom and Antivenom	4 Venom, Antivenom and Dexamet.	
Nº	Species	Amount γ/gm	Route	Doses mg	Route	Time after venom min.	Repetition hours	Route	Deaths Total	Deaths Total	Deaths Total	Deaths Total	
108	C.d.t.	0,2	IV	0,02	IM	15	8	SC	10/20	10/20	5/20	6/20	
107	"	"	"	0,02	"	15	8	SC	9/20	11/20	4/20	5/20	
101	"	"	"	0,10	"	30	8	SC	14/20	12/20	8/20	7/20	
104	"	"	"	0,002	"	30	8	SC	15/25	21/25	7/25	16/25	24 h
16	"	"	"	0,025	IV	60	12	IV	14/20	15/20	5/20	15/20	
10	"	"	"	0,10	IV	60	12	IV	16/20	15/20	10/20	16/20	
									78/125	84/125	39/125	65/125	
13	B.j.	10,0	IM	0,025	IV	30	12	IV	18/20	19/20	5/20	10/20	
12	"	"	"	0,05	"	"	"	"	15/20	16/20	5/20	0/20	
14	"	"	"	0,05	"	"	"	"	13/20	17/20	1/20	1/20	
11	"	"	"	0,10	"	"	"	"	16/20	17/20	6/20	6/20	
109	"	"	"	0,02	IM	15	8	SC	17/25	14/25	7/25	15/25	
110	"	"	SC	0,02	"	15	"	"	18/25	13/25	5/25	10/25	
99	"	"	"	0,50	"	30	"	"	7/10	3/10	4/10	3/10	24 h

98	"	"	"	0,50	"	30	"	"	3/10	4/10	4/10	4/10	
126	"		"	0,02	"	15	"	"	20/20	17/20	11/20	10/20	
127	"		"	0,02	IV	15	"	IV	20/20	19/20	11/20	13/20	
128	"		"	0,10	IM	15	"	"	15/20	15/20	2/20	12/20	
129	"		"	0,10	"	15	"	"	14/20	17/20	11/20	10/20	
130	"		"	0,10	"	15	"	"	19/20	18/20	11/20	12/20	
									195/250	189/250	83/250	103/250	
113	P.f.	1,0	SC	0,02	IM	15	8	SC	11/20	6/20	6/20	2/20	
114	"	"	"	0,02	"	"	"	"	14/20	6/20	6/20	4/20	
115	"	"	"	0,02	"	"	"	"	10/20	8/20	1/20	3/20	
116	"	"	"	0,02	"	"	"	"	9/20	7/20	3/20	4/20	
117	"	"	"	0,02	"	"	"	"	10/20	9/20	4/20	3/20	48 h
22	"	"	"	0,05	IV	"	12	"	18/20	18/20	1/20	19/20	
18	"	"	"	0,05	IV	30	12	"	6/20	6/20	0/20	11/20	
21	"	"	"	0,05	IV	60	8	"	10/20	6/20	2/20	3/20	
									88/160	66/160	23/160	49/160	
119	T.s.	1,5	SC	0,02	IM	15	8	SC	20/20	16/20	13/20	8/20	
120	"	"	"	"	"	"	"	"	18/20	12/20	2/20	2/20	
118	"	"	"	"	"	"	"	"	17/20	10/20	3/20	5/20	
20	"	"	"	0,05	IV	"	12	IV	19/20	18/20	11/20	15/20	
24	"	"	"	"	"	30	"	"	16/20	12/20	8/20	13/20	
17	"	"	"	"	"	"	"	"	15/20	15/20	14/20	13/20	
19	"	"	"	"	"	60	"	"	16/20	12/20	9/20	13/20	
									121/140	95/140	60/140	69/140	

TABLE 3 — GROUPED DATA OF TABLE 1 WITH MORTALITY FOR EACH VENOM OF ACTH TREATED MICE AND CALCULATIONS OF CHI-SQUARE IN A 2×2 TABLE UNDER THE HYPOTHESIS OF INDEPENDENCE

TREATMENT				Cumulative results	COMPARISON BETWEEN GROUPS				Treatment effect *
Group	Venom	Hormone	Specific antivenom	Death/Total	Groups	−1 degree of freedom P=0,001 10,827	P=0,01 6,635	P=0,05 3,841	
1	*C. durissus terrificus*	—	—	35/65					
2	*C. durissus terrificus*	ACTH	—	33/65	1 with 2		0,123		None
3	*C. durissus terrificus*	—	Serum	15/65	1 with 3		13,000		Effective +++
4	*C. durissus terrificus*	ACTH	Serum	21/65	3 with 4		1,383		None
1	*B. jararaca*	—	—	55/80					
2	*B. jararaca*	ACTH	—	60/80	1 with 2		0,773		None
3	*B. jararaca*	—	Serum	24/80	1 with 3		24,029		Effective +++
4	*B. jararaca*	ACTH	Serum	25/80	3 with 4		0,029		None
1	*P. fera*	—	—	90/100					
2	*P. fera*	ACTH	—	78/100	1 with 2		5,357		Effective ++
3	*P. fera*	—	Serum	35/100	1 with 3		64,533		Effective +++
4	*P. fera*	ACTH	Serum	61/100	3 with 4		13,542		Negative +++
1	*T. serrulatus*	—	—	122/140					
2	*T. serrulatus*	ACTH	—	110/140	1 with 2		3,621		Effective ±
3	*T. serrulatus*	—	Serum	56/140	1 with 3		67,177		Effective +++
4	*T. serrulatus*	ACTH	Serum	52/140	3 with 4		0,241		None

* ± = possibly significant (?)
\+ = significant
++ = very significant
+++ = highly significant

TABLE 4 — GROUPED DATA OF TABLE 2 WITH MORTALITY FOR EACH VENOM OF DEXAMETHASONE TREATED MICE AND CALCULATIONS OF CHI-SQUARE IN A 2 × 2 TABLE UNDER THE HYPOTHESIS OF INDEPENDENCE

TREATMENT				Cumulative results	COMPARISON BETWEEN GROUPS				Treatment effect *
Group	Venom	Hormone	Specific antivenom	Death/Total	Groups	−1 degree of freedom P=0,001 10,827	P=0,01 6,635	P=0,05 3,841	
1	*C. durissus terrificus*	—	—	78/125					
2	*C. durissus terrificus*	Dexamethasone	—	84/125	1 with 2		0,631		None
3	*C. durissus terrificus*	—	Serum	39/125	1 with 3		24,436		Effective +++
4	*C. durissus terrificus*	Dexamethasone	Serum	65/125	3 with 4		11,301		Negative +++
1	*B. jararaca*	—	—	195/250					
2	*B. jararaca*	Dexamethasone	—	189/250	1 with 2		0,404		None
3	*B. jararaca*	—	Serum	83/250	1 with 3		101,627		Effective +++
4	*B. jararaca*	Dexamethasone	Serum	103/250	3 with 4		3,424		Negative ±
1	*P. fera*	—	—	96/160					
2	*P. fera*	Dexamethasone	—	69/160	1 with 2		9,121		Effective ++
3	*P. fera*	—	Serum	27/160	1 with 3		62,875		Effective +++
4	*P. fera*	Dexamethasone	Serum	52/160	3 with 4		10,505		Negative ++
1	*T. serrulatus*	—	—	121/140					
2	*T. serrulatus*	Dexamethasone	—	95/140	1 with 2		13,692		Effective +++
3	*T. serrulatus*	—	Serum	60/140	1 with 3		58,144		Effective +++
4	*T. serrulatus*	Dexamethasone	Serum	69/140	3 with 4		1,164		None

* ± = possibly significant (?)
\+ = significant
++ = very significant
+++ = highly significant

As for Dexamethasone in doses varying from 0,02 to 0,5 mg per mouse, there was a significant negative action increasing mortality caused by crotalic venom and a slight tendency to this effect with bothropic venom, though there was no activity similar to ACTH when serumtherapy was not done. With spider venom (*P. fera*) and scorpion venom (*T. serrulatus*) Dexamethasone showed a marked protection against these venoms, when serumtherapy was not given, but likewise the ACTH, it had a negative action on the spider envenomation when serumtherapy was associated and no action at all was seen on the scorpion envenomation.

It does not seem that corticoids would aggravate these envenomations by suppressing the mechanism of immunological defense as it has been suggested by Russel and Emery (6), for in none of the venom inoculated groups that have been treated only with hormones the mortality was increased; there was absence of changes or beneficial activity was observed as to spider and scorpion venoms. On the other hand, the negative effect also can not be attributed to a neutralization by corticoids of the antivenom serum effect according to a hypothesis of Knyvett and Molphy (3) since the negative effect was not systematic in the hormone treated groups which have received associated serumtherapy, as can be observed in Table 5.

In cases of spider and scorpion venoms not treated by serumtherapy in which ACTH as well as Dexamethasone diminished mortality, this beneficial effect can be attributed to the decrease of the local pain by the anti-inflammatory action of these hormones. It is known that these venoms have neurotoxins which provoke an intense local pain and this pain stress contributes very much to aggravate the general condition since the mere suppression of pain by other agents withdraws a whole complex of symptoms in man as it was already stated by Rosenfeld et al. (5). The fact that there was no similar action on crotalic and bothropic envenomation can be explained since both venoms do not have pain provoking neurotoxins which act directly on nerves; the one of *Crotalus durissus terrificus* has neurotoxins acting only on the central nervous system without causing any pain and the venom of *Bothrops jararaca* causes local pain by the proteolytic action on tissues at the site of the bite. Summarizing, hormones would not have a direct action on the neurotoxins of spider and scorpion venoms, but they would mitigate the pain provoked by these toxins and would thus remove its consequent stress.

The aggravation of the poisoning by *Phoneutria fera* when the treatment with ACTH or Dexamethasone is associated to serumtherapy could be tentatively explained by assuming that the venom alone would produce a discharge of both hormones and their supplemental administration would come to reenforce this venom action. When serumtherapy is not given, they do not show negative effect since they mitigate the pain stress thus decreasing one of the aggravating components of the poisoning. Together with the antivenom serum which eliminates and diminished pain, hormones would only act through their harmful side synergically with the venom. Envenomation by venom of *Crotalus durissus terrificus* would

TABLE 5 — SCHEMATIC RESULTS OF EFFECTS OF TREATMENT WITH ACTH OR DEXAMETHASONE ASSOCIATED OR NOT WITH SERUMTHERAPY ON THE MORTALITY OF MICE BY THEIR STATISTICAL SIGNIFICANCE AS SHOWN BY THE CHI-SQUARE TEST

SUBSTANCES INJECTED	HORMONE	
	ACTH	Dexamethasone
Crotalus durissus terrificus + hormone	None	None
Crotalus durisus terrificus + antivenom and hormone ..	None	Negative
Bothrops jararaca + hormone	None	None
Bothrops jararaca + antivenom and hormone	None	Possibly favorable
Phoneutria fera + hormone	Favorable	Favorable
Phoneutria fera + antivenom and hormone	Negative	Negative
Tityus serrulatus + hormone	Possibly favorable	Favorable
Tityus serrulatus + antivenom and hormone	None	None

not be aggravated by ACTH administration only by that of Dexamethasone, because this venom would not provoke an ACTH discharge and only of corticoids. These interpretations would lead to assume that venom of *Phoneutria fera* provokes an intensive ACTH and corticoids discharge, while that of *Crotalus durissus terrificus* and *Bothrops jararaca* would only discharge corticoids. The other experimented scorpion venom would not have either one of these actions.

Results show that no generalization is possible as to indication or counter-indication of corticoids in animal venoms poisonings. The table of results is like a mosaic which as the utmost would permit generalization only for similar venoms. Thus ACTH and Dexamethasone are useful and indicated in cases of spider and scorpion envenomations, when the venoms are similar to those of *Phoneutria fera* and *Tityus serrulatus*. They are formally counterindicated in these same cases when specific antivenom serumtherapy is given, Dexamethasone shall be counter-indicated in envenomations by snakes having similar venoms to those of *Crotalus durissus terrificus*, i.e., hemolytic and neurotoxic venoms.

An interpretation of the reasons for these apparently contradictory activities will not only allow a better indication of these hormones, but will also be useful to guide and suggest the physiopathogenic action of these venoms, besides permit-

ting a better understanding of the action and indications of ACTH and corticoids in envenomations.

A secondary observation to the purpose of this paper automatically obtained due to the scheme adopted for experiments is the evidence that serumtherapy with specific antivenom sera, without any auxiliary treatment is really able to diminish mortality provoked by venoms.

Summary

Repeated intramuscular doses of ACTH did not change mortality in mice injected with snake venoms (*Crotalus durissus terrificus* and *Bothrops jararaca*) treated or not with specific antivenom serum. On the other hand, it significantly diminished mortality in animals injected with spider venoms (*Phoneutria fera*) but showing a negative effect on this kind of envenomation when serumtherapy was associated. With scorpion venom (*Tityus serrulatus*) ACTH demonstrated a tendency to protect survival of animals when no serumtherapy was given and absence of any modification when associated to serum.

Repetead intramuscular or intravenous doses of Dexamethasone did not change mortality in mice injected with snake venoms (*Crotalus durissus terrificus* and *Bothrops jararaca*) not treated with serumtherapy. When associated to antivenom serumtherapy, it demonstrated an evident negative effect in the case of crotalic venom and a tendency towards this effect with bothropic venom. With spider venom (*Phoneutria fera*) and scorpion venom (*Tityus serrulatus*) Dexamethasone significantly diminished mortality when serumtherapy was not associated and when it was given, mortality was increased in cases of spider venom and no modifications occur with scorpion venom.

ACTH and corticoid act differently according to the venom also when treatment antivenom serumtherapy is associated.

Complementary, the efficacy of specific antivenom serumtherapy was demonstrated since it significantly diminished mortality in mice injected with venoms of *Crotalus durissus terrificus*, *Bothrops jararaca*, *Phoneutria fera* and *Tityus serrulatus*.

Resumo

O ACTH em doses repetidas injetadas por via intramuscular não modificou a mortalidade de camundongos injetados com venenos de serpentes (*Crotalus durissus terrificus* e *Bothrops jararaca*), tratados ou não com sôro antiveneno específico. Por outro lado, diminuiu significativamente a mortalidade nos animais injetados com venenos de aranha (*Phoneutria fera*), mostrando porém um efeito negativo nêsse envenenamento quando se associou a soroterapia. Com o veneno

de escorpião (*Tityus serrulatus*), demonstrou uma tendência à proteção da sobrevivência dos animais quando não se fêz a soroterapia e ausência de qualquer modificação quando foi dado também o sôro.

A Dexametazona, em doses repetidas injetadas por via intramuscular ou intravenosa, não modificou a mortalidade de camundongos injetados com venenos de serpentes (*Crotalus durissus terrificus* e *Bothrops jararaca*) não tratados pela soroterapia, quando se associou o tratamento pelo sôro antiveneno demonstrou um efeito negativo no caso de veneno crotálico e uma tendência no mesmo sentido com o veneno botrópico. Com os venenos de aranha (*Phoneutria fera*) e de escorpião (*Tityus serrulatus*) a Dexametazona diminuiu significativamente a mortalidade quando não foi feita a soroterapia e quando esta foi aplicada aumentou a mortalidade no caso de veneno de aranha, não tendo produzido modificações com veneno de escorpião.

O ACTH e os corticóides agem diferentemente conforme os tipos de venenos e também quando se associa o tratamento com soros antivenenos. Foi sugerida uma hipótese para explicar essas ações aparentemente contraditórias.

Complementarmente foi demonstrada a eficiência da soroterapia específica que diminuiu significativamente a mortalidade de camundongos injetados com venenos de *Crotalus durissus terrificus*, *Bothrops jararaca*, *Phoneutria fera* e *Tityus serrulatus*.

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