EFFECT OF ROUTE OF ANTITOXIN ADMINISTRATION ON EFFICACY OF TREATMENT OF EXPERIMENTAL TETANUS

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The efficacy of treatment with Diaform-3 antitoxin, given by either intracisternal or intralumbar injection in a dose of 400 i.u./kg, was compared in experiments on 100 rabbits with ascending, hematogenous, and cerebral tetanus caused by injection of 1 c.l.d. of tetanus toxin. Intracisternal injection of the antitoxin was found to be three times more effective than intralumbar (the proportion of animals cured was 31.4 and 10.2% respectively). The latter was effective only in animals with ascending tetanus, evidently because the portal of entry of the toxin into the CNS was along the peripheral nerves of the hind limbs. KEY WORDS: tetanus; antitoxin – routes of administration.

Of all the methods of administration of antitoxin in the case of established tetanus the most effective has been found to be injection into the CSF [3, 7, 11, 13]. Many workers [1, 2, 12] have found that by this method from 85 to 100% of patients with tetanus can be cured. The inefficacy of other routes of administration of antitoxin is attributable to the fact that it does not penetrate in sufficient concentrations to the affected structures of the CNS [14]. At the same time, it has been shown that tetanus toxin, if fixed to protagon or synaptosomes, can be neutralized by high concentrations of antitoxin [6]. The risk of development of complications following injection of antitoxin into the CSF is mainly due to its inadequate purification and imperfections of the manipulative techniques [4, 8-10].

The writer's earlier experiments on rabbits with experimental tetanus showed that intracisternal injection of Diaferm-3 antitoxin led to the survival of up to 40% of animals, whereas intravenous or intracarotid injection was more or less effective only when the antitoxin was injected during the incubation period of the disease.

The object of the present investigation was to compare the efficacy of the intracisternal and intralumbar routes of administration of antitoxin in rabbits with ascending, hematogenous, and cerebral forms of experimental tetanus.

EXPERIMENTAL METHOD

An experimental model of tetanus was produced in rabbits of both sexes weighing 2-3 kg by injection of 1 c.l.d. of tetanus toxin (production batch 21, Leningrad Research Institute of Vaccines and Sera) subcutaneously into the thigh, intravenously, or intracisternally. The dose of toxin given by subcutaneous injection was 60 μg/kg, by intravenous injection 30 μg/kg, and by intracisternal injection of 0.7 μg/kg, i.e., the value of 1 c.l.d. of toxin differed for the different routes of administration. All the control animals died under these circumstances in the course of 3-5 days.

The Diaferm-3 tetanus antitoxin, produced by the I. I. Mechnikov Moscow Research Institute of Vaccines and Sera, was injected in a dose of 400 i.u./kg into animals infected suboccipitally 24 h after injection of the toxin, and into animals infected subcutaneously or intravenously, 48 h after injection, when marked signs of tetanus were present, and observations were maintained thereafter on its development and outcome.

Rabbits which were unable to take food themselves because of trismus were fed parenterally with a nutrient mixture consisting of 20 ml protein hydrolysate, 20 ml medium No. 199, and 1 g glucose, calculated per kilogram body weight, to which streptomycin was added in a dose of 25,000 units/kg to prevent microbial complications. Death of the animals on the first and second day was regarded as the result of complications

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TABLE 1. Dependence of Therapeutic Effect on Routes of Administration of Antitoxin

Route of administration of antitoxin	Method of injection of toxin	No. of animals	Duration of survival, days			
			1–2	3–5	6–17	survived
Intracisternal	Subcutaneously	16	0	4	5	7
	Intravenously	19	0	5	12	2
	Suboccipitally	16	4	2	3	7
Intralumbar	Subcutaneously	16	0	6	7	3
	Intravenously	16	0	7	8	1
	Suboccipitally	17	6	8	2	1

of the manipulations, death on the third to the fifth day as the result of inefficacy of treatment, whereas survival longer than six days, or recovery, was interpreted as the result of antitoxic treatment.

EXPERIMENTAL RESULTS

Experiments were carried out on 100 rabbits. The results are given in Table 1.

The results in Table 1 show that the intracisternal route of injection of antitoxin was at least three times more effective than the intralumbar route (31.4 and 10.2% of animals survived respectively). Better results were obtained in the treatment of ascending and cerebral tetanus (43.6% of animals recovered), evidently on account of the routes of entry of the toxin into the CNS. The relatively high efficacy of the intralumbar route of administration of antitoxin in animals with ascending tetanus is evidence that high concentrations of antitoxin in animals with ascending tetanus is evidence that high concentrations of antitoxin reached the affected parts of the CNS.

It can be concluded from the results of these experiments that experimental tetanus is the result of the action of the toxin not only on spinal neurons, but also on higher levels of the CNS; for that reason the intracisternal route of administration of antitoxin proved to be more effective, in agreement with existing data [5, 7] and modern views on the pathogenesis of tetanus [4, 14].

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