THE DYNAMICS OF THE CHANGE IN COMPLEMENT TITER IN GUINEA PIGS DURING ANAPHYLACTIC SHOCK AND UNDER CONDITIONS OF INHIBITION OF THE SHOCK WITH DIMEDROL

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It is well known that antihistamine preparations such as neoantergan, phenergan, dimedrol, etc., can suppress the toxic effect of histamine on individual organs and on the organism as a whole.

In addition to this, they exhibit considerable activity in allergy and have an inhibitory effect on anaphylactic shock.

However, the mechanism of the protective effect of the indicated preparations in these processes has not yet been sufficiently studied, and requires further investigation.

In particular, the question of whether the desensitizing effect of antihistamine preparations is connected with their influence on the specific immunological reactions occurring in the organism during anaphylactic shock, i.e., those processes which occur with the participation of complement in which an immunological complex is formed between antigen and specific antibodies, has not been studied at all.

The task of the present work was to study the dynamics of the change in complement titer under the usual conditions of the course of anaphylactic shock, as well as under conditions where dimedrol is previously administered to guinea pigs in doses which suppress the development of the shock reactions.

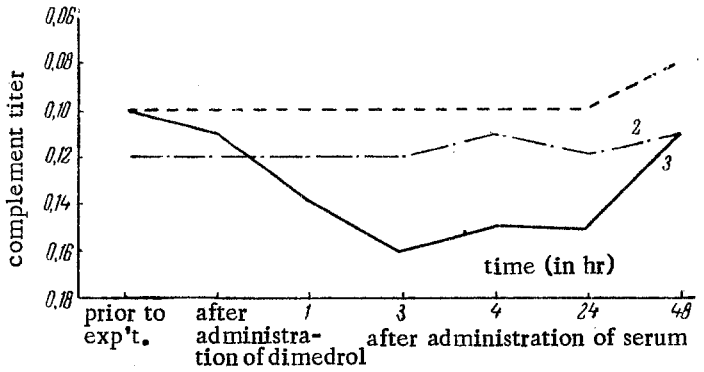
Experimental Methods

The experiments were carried out with guinea pigs weighing 450-550 g. The animals were sensitized with horse serum by a single subcutaneous dose calculated to give 0.01 ml per 100 g of weight of the animal. After 21 days from the time of sensitization, the guinea pigs were divided into three groups: one experimental, and two control. The guinea pigs of the experimental group were first injected subcutaneously with a 1% solution of dimedrol in an amount equal to 40-50 mg/kg of weight, and after 35 min, with an intraperitoneal shock dose of horse serum in the amount of 0.1 ml per 100 g of weight.

The guinea pigs of the second group were injected with serum only, in the same amount as the guinea pigs of the experimental group.

In the third group of animals (technical control), dimedrol and serum were replaced by the administration of corresponding amounts of physiological saline solution.

Blood for determination of complement titer in the serum of the experimental and control animals was taken from the heart in amounts of 1-2 ml. In the experimental group, blood was taken before the experiment, after the administration of dimedrol, and after 1, 3, 4, 24, and 48 hr following the administration of the resolving dose of serum. The same number of blood samples was taken at the same time intervals from the guinea pigs of the control groups.



Change in the complement titer of experimental and control guinea pigs: 1) when dimedrol and serum were administered; 2) when physiological saline solution was administered; 3) when serum was administered.

Serum was obtained from the blood samples collected, and was tested for complement content by the usual method.

A total of 22 experiments was conducted, and 139 complement determinations were made.

Experimental Results

The intraperitoneal administration of serum in a dose of 0.1 ml per 100 g of weight to the guinea pigs of the control group caused severe, although not fatal, shock in all animals. The determination of complement titer in these animals gave the following results. A drop in complement was, as a rule, observed after an hour following the injection of serum.

The maximal drop in complement was noted in 3-4 hr. After 24 hr, the complement level leveled off in some of the pigs, while in others it continued to remain at a low titer. After two days, the complement titer reached the initial level.

A reduction in blood coagulability was observed parallel with the drop in complement titer.

The administration of serum to guinea pigs which had previously received dimedrol injections did not cause the development of anaphylactic shock. Only in two of the eight animals was it possible to observe slight, quickly passing reactions exhibited by ruffling of the fur and scratching of the snout.

The administration of the challenge dose of serum under these experimental conditions did not cause a drop in complement titer either. The initial level of complement was maintained throughout the entire experiment. Moreover, in 48 hr after the administration of serum, complement activity even increased somewhat in nearly all of the guinea pigs in this group.

The administration of physiological saline solution, and the taking of blood from the guinea pigs comprising the third group, did not affect the change in complement titer of the blood (see figure).

The results of the experiments enable us to conclude that, when large challenge doses of serum are administered intraperitoneally to sensitized animals, the development of anaphylactic shock is observed, which is accompanied by a drop in complement titer and reduction in the coagulability of the blood.

The preliminary administration of dimedrol to guinea pigs sensitized with horse serum completely protected the animals from anaphylactic shock and, parallel to this, favored the maintenance of complement at the initial level.

Repeated punctures of the heart, the collection of blood from the heart, as well as the administration of physiological saline solution, had no effect on the complement level in the blood of the guinea pigs.

It is commonly considered that a drop in the complement of the blood of animals is associated with a specific phase of the reaction, brought about by the union of antigen with antibody.

If one adheres to this explanation, it might have been expected that the drop in complement should have coincided in time with the development of anaphylactic shock. However, such parallelism was not observed in our experiments. Shock usually developed in 10-15 min from the time of administration of the serum, while the drop in the complement of the animal's blood came on only after an hour. Furthermore, the maximal drop in complement was noted after 3-4 hr, and sometimes even 24 hr following the shock, i.e., after cessation of the shock.

On the basis of the fact that the drop in complement titer did not coincide in time with the development of the symptoms of anaphylactic shock, it can be assumed that the changes in the complement system are not directly associated with the primary specific reactions. These changes are apparently explained by functional disturbances in the nervous system, the respiratory system, and blood circulation, which arise secondarily under the influence of toxic products produced as the result of the specific immunological reaction. By preventing the disturbances in the indicated organs and systems by the administration of dimedrol to the sensitized animal, we, at the same time, also eliminate the causes for the drop in complement titer during anaphylactic shock.

SUMMARY

In guinea pigs with anaphylactic shock, provoked by injection of specific antigen, the complement titer usually dropped in one hour after its administration, the reduction being maximal in 3-4 hours. In the majority of animals, the complement level was restored in 24 hours after the shock. Preliminary administration of dimedrol prevented the anaphylactic shock and maintained the complement at the initial level in the guinea pigs.