PHYSIOLOGICAL ANALYSIS OF DIMEDROL'S PROPHYLACTIC ACTION IN HEMOHETEROTRANSFUSION SHOCK

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Up to the present, the question of the mechanism behind posttransfusion reactions has not been resolved, but there are much data on the importance of histamine in the development of hemotransfusion shock, and the positive action exerted on its course by the antihistamine preparation, dimedrol [2, 4—7].

It is known that the pharmacodynamics of dimedrol are very complicated. It elevates the excitability of the peripheral cholino- and adrenoreactive systems, blocks the cholinoreactive systems of vegetative ganglia to a moderate degree, and exerts a sedative effect, probably related to its central cholinolytic action.

We attempted to determine the specific value of the enumerated mechanisms in the favorable action of dimedrol on posttransfusion complications.

EXPERIMENTAL METHOD

The investigations were carried out under short term conditions, using local anesthesia, in dogs which were injected subcutaneously with morphine, using a dosage of 0,5 ml of a 1% solution per kg of weight, 35—45 min before initiation of the experiment. Experimental hemoheterotransfusion was caused by the intravenous injection of citrated rabbit blood, using 10 ml per kg of weight. Dimedrol was administered in a dosage of 15 mg per kg of weight, injected intramuscularly 15-20 min before the injection of the citrated rabbit blood.

We investigated the arterial pressure (in the femoral artery), respiration, the general condition of the animal, the state of the pupillary and corneal reflexes, the reaction of respiration and blood circulation to adrenalin and acetylcholine, before, during, and 15, 30, and 45 min after injection of the citrated rabbit blood.

Respiration was recorded via a glass tube inserted in the nostril of the animal and connected with a Marey capsule.

EXPERIMENTAL RESULTS

The control experiments (10) showed that injection of rabbit blood led, in all cases, to development of the typical picture of hemoheterotransfusion shock, characterized by a deep (up to 10—15 mm) and prolonged (in the range of 15—35 min) drop in arterial pressue, which, in certain cases, returned to the original level after 35—45 min. Sometimes the animals did not come out of the shock state, and died (No. 10 and 12).

The injection of dimedrol, in a dosage of 15 mg per kg of weight, preceeding the infusion of the rabbit blood into the dogs, significantly attenuated the shock symptoms: the animals retained their mobility and their reactions to stimuli in the outer environment, and respiratory disturbances were almost never observed, which confirms the data in the literature [2, 5, 6].

In order to elucidate the mechanism behind the prophylactic effect of dimedrol, experiments were set up to determine the excitability of the peripheral adreno- and cholinoreactive systems during hemoheterotransfusion shock, occurring without the administration of dimedrol and in the setting of its application. Prior to injection of the rabbit blood, and 15, 30, and 45 min after it, the dogs were injected with a threshold dose of adrenalin and acetylcholine in a concentration of 1:25,000. We noted the magnitude and character of changes in the arterial pressure, the latent period, and the duration of the hemodynamic reaction.

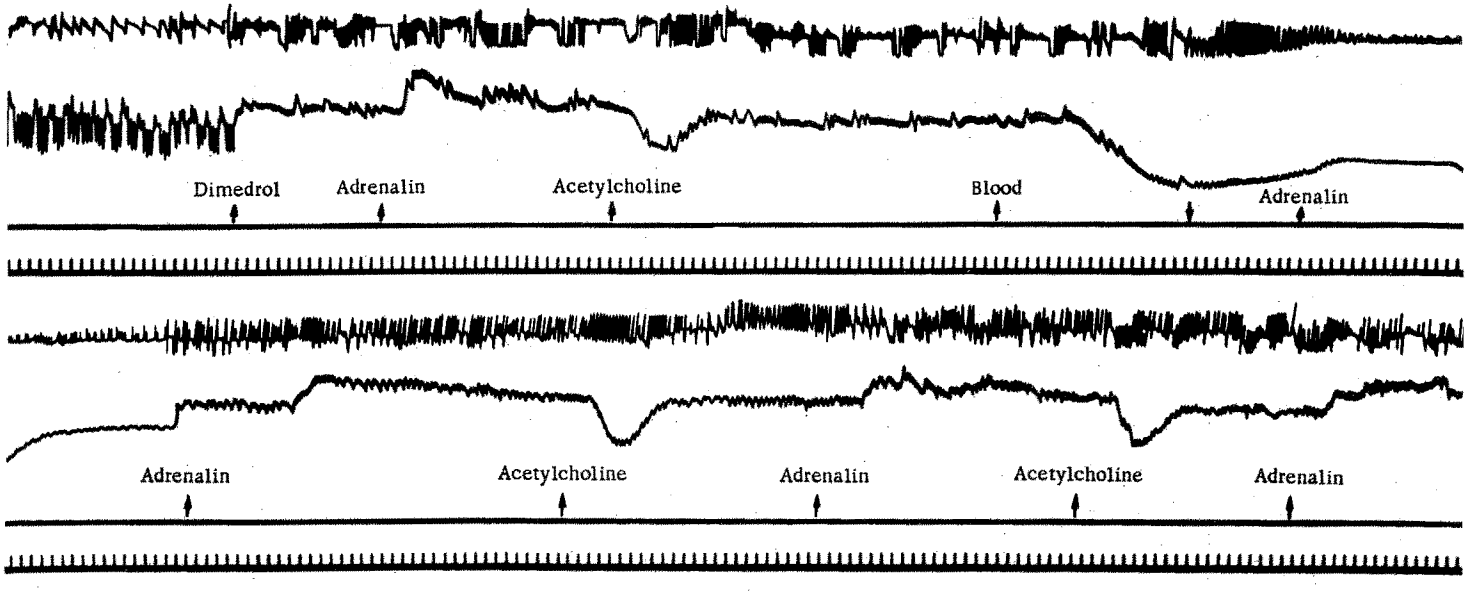
Hemodynamic Reaction to Adrenalin and Acetylcholine During Hemotransfusion Shock

A. Control

Number of experiments	Index	Before the injection of the blood				At the moment of maximal drop in pressure				After injection of the blood											
										by 15 min				by 30 min				by 45 min			
		arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction
		in mm		in seconds		in mm		in seconds		in mm		in seconds		in mm		in seconds		in mm		in seconds	
		To adrenalin																			
10	M	113	+21	7,5	33,1	46,6	No reaction			99	16	15,3	17,2	111,3	15	13	37	115,6	12	14	35
	$m\pm$	4,45	3,8	0,9	6,3	4,47				7,2	6,2	2,1	5,0	4,14	2,7	1,8	10,4	4,18	3,4	2,2	15,7
		To acetylcholine																			
10	M	113	−47	10	45	74	−14	13	36	94,8	−44	11	35	117,5	−53	9	32	123,5	−47	6	65
	$m+$	4,45	3,9	1,5	6,9	7,6	7,7	2,1	1,8	8,3	4,5	1,3	3,1	6,05	3,7	1,8	3,0	6,68	5,9	3,0	53,3

B. In the setting of the action of oxygen

No. of experiments	Amt. of blood injected (in ml/mg)	Index	Original arterial	After injection of dimedrol (before injection of the blood)				At the moment of the drop of arterial pressure				After injection of the blood											
												by 15 min				by 30 min				by 45 min			
				arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction	arterial pressure	magnitude of the changes	latent period of the reaction	duration of the reaction
				in mm		in seconds		in mm		in seconds		in mm		in seconds		in mm		in seconds		in mm		in seconds	
				To adrenalin																			
10	10	M	100	120	+20	10	9	45	29	30	22	101	17	13	20	119	24	12	20	127	15	16	22
		$m\pm$	6,3	8,7	3,03	1,06	3,2	3,2	7,7	7,6	5,5	38,3	2,8	1,9	8,3	7,8	5,3	2,03	5,0	5,4	6,2	2,3	7,5
				To acetylcholine																			
10	10	M	100	119	−51	15	40	49	−25	28	27	108	−45	14	30	127	−51	15	33	126	44	16	31
		$m\pm$	6.3	8.8	4.8	4,8	5.08	8,1	5,9	4,3	1,4	12,2	8,1	2,7	3,5	7,6	5,4	13	2,2	5,8	8,9	2,5	4,6



Hemodynamic reaction to adrenalin and acetylcholine in hemoheterotransfusion shock. Meaning of curves (from above downward): respiration; arterial pressure; zero line; time markings (3 seconds).

As can be seen from the table, the reactions to adrenalin before injection of the blood occurred more rapidly, and were characterized by a longer duration, in control animals than in the animals of the experimental group.

In the period of maximal drop in the arterial pressure, the reaction to adrenalin was absent in the control animals, while in the experimental animals it was clearly manifested, and differed from the reaction of the previous state of investigation only in the longer duration of its latent period and the greater duration of the reaction itself.

At 15 and 30 min after the injection of blood, in the dogs that received dimedrol, the reaction to adrenalin occurred more rapidly than in the control animals, and differed in its shorter duration. At 45 min after the blood injection, these relationships were retained.

The reaction to acetylcholine before injection of the blood was characterized, in the experimental animals, by a more manifest drop in the arterial pressure, by later development and smaller duration, as compared with these indices in the animals of the control group.

In the animals of the experimental group, at the moment of maximal shock hypotension, the injection of acetylcholine caused a slowly developing, but more profound, drop in the arterial pressure in comparison with these indices in the control group. The duration of the reaction was shorter than in the control.

At 15, 30, and 45 min after injection of the blood, the reaction to acetylcholine in the experimental animals occurred later, and was shorter in duration.

To illustrate the typical changes in the hemodynamic reaction to adrenalin and acetylcholine arising in the experimental animals, we present the kymogram of one of the experiments (see figure).

Analysis of the kymogram shows that within 4–6 min after injection of the foreign blood the arterial pressure in the animals already is elevated (mainly through an elevation in the minimal pressure), tachycardia has appeared, the pupils are dilated, and the morphine narcosis has disappeared. This suggests that dimedrol excites the sympathetic nervous system.

Dimedrol markedly intensified the reaction of the arterial pressure to adrenalin, which is in accord with the data of a number of investigators [1, 5, 6, 7]. F. F. Usikov [8] believes that increased formation of acetylcholine in the organism is one of the pathogenetic factors in the development of a posttransfusion reaction, and testifies to an increase in functioning of the cholinergic portion of the nervous system. The investigations of certain authors [2, 3, 6], and the results which we obtained, all indicate that after injection of dimedrol the depressor action of acetylcholine becomes less intense, and return of the arterial pressure to the original level occurs in a shorter period of time.

The presented data clearly show that dimedrol prevents the development of prolonged, shock-type, posttransfusion hypotension in dogs, although it does not completely eliminate the depressor vascular reaction. It causes intensification of the reaction to adrenalin, and weakens the reaction to acetylcholine.

From this, one can conclude that the prophylactic action of dimedrol in hemoheterotransfusion shock is determined, to a large degree, by its ability to increase the excitability of the adrenoreactive systems, and to lower somewhat the excitability of the cholinoreactive systems. However, as was shown by analysis of the data, this mechanism alone cannot explain the prophylactic action of dimedrol in hemoheterotransfusion shock.

SUMMARY

Subject to study was the mechanism of prophylactic effect of dimedrol in hemotransfusion shock. For this purpose excitability of adreno- and cholinoreactive systems was investigated on dogs in hemoheterotransfusion shock without dimedrol (10 experiments) and against the background of dimedrol action. The preparation was injected intramuscularly in a dose of 15 mg/kg of body weight (10 experiments).

As compared to control animals, dimedrol intensified the reaction to adrenaline and weakened the response to acetylcholine. As suggested by the author, the mechanism of prophylactic effect produced by dimedrol in hemotransfusion shock is largely determined by its ability to raise the excitability of adrenoreactive and to reduce the excitability of cholinoreactive systems.

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