INVESTIGATION OF THE ABILITY OF DICOUMARIN TO PREVENT THROMBOSIS CAUSED BY INTRAVENOUS INJECTION OF MASSIVE DOSES OF THROMBOPLASTIN

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Dicoumarin and its derivatives are widely used for the prevention of thrombosis and for therapeutic purposes in the presence of established thrombosis. The object of the present investigation was to determine the level of depression of the prothrombin concentration by means of dicoumarin which could prevent thrombosis from developing in an animal receiving intravenous injection of thromboplastin. The investigation was conducted both in normal animals and in animals in which the anticlotting system was inactivated, i.e., animals in a prethrombotic state.

EXPERIMENTAL METHODS

Experiments were conducted on male albino rats weighing 200-220 g. The prothrombin time was determined by Quick's one-stage method [3]. The prothrombin level was lowered by means of dicoumarin (experimental animals). Control rats were given injections of physiological saline. Thrombosis was caused by intravenous injection of thromboplastin. A prethrombotic state was induced by three methods: 1) keeping the animals on an atherogenic diet [1], 2) administration of chlorpromazine (0.06 ml of a 2.5% solution) [2], and 3) administration of 0.3 ml of a 2% solution of potassium chloride. This dose of potassium chloride was mixed with the thromboplastin solution and the total volume of the mixture was made up to 1 ml before being injected intravenously. Postmortem examination of the dying animals confirmed that the cause of death was thrombosis of the heart cavities and of various veins.

TABLE 1. Comparison of Doses of Thromboplastin Causing Thrombosis in Different States of the Anticlotting System

No. of animals	State of anticlotting system	Dose of thromboplastin causing death of half and shock in most of the animals (in ml)
10	Normal function	2.0-2.5
10	Depression (chloropromazine)	1.0-1.4
10	Depression (potassium chloride)	0.2

EXPERIMENTAL RESULTS

It follows form the results shown in Tables 1 and 2 that 1) the severest prethrombotic state developed as a result of administration of potassium chloride to the animals, and 2) reliable protection against thrombosis was provided only by lowering the prothrombin level below 10%.

TABLE 2. Role of Depression of Blood Prothrombin Level by Dicoumarin in Thrombosis Provoked against the Background of a Normally Functioning Anticlotting System (A) and during Depression of this System Caused by Administration of Chloropromazine (B) or Potassium Chloride (C) and by Keeping Animals on an Atherogenic Diet (D)

Prothrombin concentration (in %)	Number of animals	Number of animals dying	
		absolute	%
	A		
100	55	29	53
25—12	20	11	55
Below 10	28	1	3
	B		
100	42	39	93
25—12	22	20	90
Below 10	29	1	3
	C		
100	26	26	100
25—12	13	9	69
Below 10	26	9	34
	D		
259	13	6	46
9,4	19	5	26

SUMMARY

Dicoumarin was used to reduce the blood prothrombin to the therapeutic level (25-12%) and below 10% in male albino rats; thrombin formation was induced by thromboplastin administration against the background of the normally functioning anticoagulation system and of its depression (caused by keeping the animals on atherogenic diet and by chloropromazine or potassium chloride administration). As established, reliable protection from thrombosis could be attained only by reducing the prothrombin level below the 10% mark. The most prothrombin state developed after intravenous injection of potassium chloride.

LITERATURE CITED

1. G. G. Bazaz'yan, N. P. Sytina, G. V. Andreenko, et al. Byull. éksper. biol., 10, 26 (1961).
2. T. M. Kalishevskaya and B. A. Kudryashov, Fiziol. zh. SSSR, 10, 1234 (1962).
3. B. A. Kudryashov, P. D. Ulitina, and A. A. Pugachev, Byull. éksper. biol., 11, 6, 510 (1941).
