EFFECT OF TRIOFEN ON THE AGGREGATING PROPERTIES OF PLATELETS

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The problem of prevention of the thrombohemorrhagic syndrome is a very acute one in contemporary clinical medicine. Disturbances of the aggregating properties of platelets, expressed primarily as slowing of aggregation and inability of the cells to undergo reversible interaction, are directly related to the formation of this syndrome. Irreversible aggregation is evidence of gross disturbances of platelet function and is a factor predisposing to latent intravascular thrombosis and microcirculatory disorders [3].

Acetylsalicylic acid (aspirin), dipyridamole (Curantyl or Persantin), salicylates, heparin, preparations of the pyrazolone series, xanthins, and nicotinic acid have been used as antiaggregants in clinical practice [1]. Important disadvantages of all known antiaggregants are the low efficacy of most of them (Persantin, pyrazolones), the probability of an undesirable side effect, the impossibility of parenteral administration of most of them (aspirin). Hence the necessity for a search for new and improved antiaggregants. The aim of the present investigation was to study the antiaggregant properties of the drug Triofen (trade mark No. 78660), known as a biological stimulator.

EXPERIMENTAL METHOD

The investigation was based on a study on the effect of Triofen in vitro on aggregation of platelets from 12 normal blood donors and 20 patients with acute suppurative-destructive diseases of the lungs and pleura, in whom hyperaggregation of the erythrocytes was observed [2].

Platelet aggregation was studied by Born's method [4] on a photoelectrometric aggreograph specially designed for the purpose. The measuring part of the aggreograph consisted of an FÉK-56M photoelectric colorimeter, the recording part of an LKD-4 laboratory compensator. Platelet-enriched plasma was mixed in the cuvette with a working edge of 3 mm by means of a fluorine plastic mixer, rotating at a speed of 700 rpm by means of an ÉM-120 electric motor. Platelet-enriched plasma was taken from blood which had been allowed to stand for 1-1.5 h, and platelet-deprived plasma was obtained by centrifugation at 300 rpm for 10 min. Platelet-free plasma was used to adjust the platelet concentration in the enriched plasma to $300\text{-}400\cdot10^9$/liter. The volume of the sample prepared for investigation was 1.5 ml. Adenosine diphosphate, disodium salt (ADP), was used as the aggregating agent, in a final concentration of $3\cdot10^{-7}$ M. The aggregation rate, the disaggregation rate, and the degree of disaggregation of the platelets were used as the most informative parameters. Aggregation of the platelets of each donor and patient was studied in 4 samples: No. 1) before incubation, no. 2) after incubation at 37°C for 1.5 h and with the addition of 20 µl of physiological saline, No. 3) after incubation with dipyridamole in a final concentration of $2.5\cdot10^{-4}$ g/liter (the mean therapeutic dose), and No. 4) after incubation with Triofen in a final concentration of between $1\cdot10^{-5}$ and $1\cdot10^{-6}$ g/liter. There were two series of experiments: with the healthy donors' platelets and with the patients' platelets.

EXPERIMENTAL RESULTS

The investigation showed virtually no difference between parameters of aggregation of healthy blood donors' platelets in all tests in the first series of experiments (Table 1).

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TABLE 1. Effect of Dipyridamole and Triofen on Platelet Aggregation (M ± m)

Serial No.	Experimental conditions	n	Aggregation rate, $\times 10^{-3}$ extinction units/min	Disaggregation rate, $\times 10^{-3}$ extinction	Degree of disaggregation, %
		Donors			
1.	Control before incubation	12	42,7±5,9	14,60±0,16	73,3±2,9
2.	Control after incubation	12	40,9±5,9	15,51±0,14	76,9±3,1
3.	Dipyridamole	12	37,7±4,9	13,42±0,16	75,21±3,9
4.	Triofen, $1 \cdot 10^{-5}$ g/liter	12	38,4±4,6	14,12±0,17	74,22±3,6
5.	Triofen, $1 \cdot 10^{-5}$ g/liter	12	41,8±5,3	14,25±0,19	75,61±3,8
6.	Triofen, $1 \cdot 10^{-5}$ g/liter	12	39,4±4,9	13,96±0,17	75,81±3,4
	$p<0,01$		—	—	—
		Patients			
7.	Control before incubation	20	17,05±2,25	4,02±0,42	47,36±6,25
8.	Control after incubation	20	16,83±2,26	3,92±0,47	44,56±6,15
9.	Dipyridamole	20	23,15±3,07	4,93±1,09	49,69±8,60
10.	Triofen, $1 \cdot 10^{-5}$ g/liter	20	26,13±2,64	5,21±1,28	57,25±7,21
11.	Triofen, $1 \cdot 10^{-5}$ g/liter	20	28,19±2,25	8,82±1,06	77,53±6,08
12.	Triofen, $1 \cdot 10^{-6}$ g/liter	20	24,21±2,31	6,25±0,89	65,34±6,21
	$p<0,01$		11—7, 11—8 12—7, 12—8	11—7, 11—8, 11—9, 12—7, 12—8	11—7, 11—8, 12—7, 12—8, 11—9

The results of addition of Triofen to the platelets from patients with suppurative diseases of the lungs and pleura are given in Table 1. They show that aggregation of platelets from these patients before addition of the test preparations (control) was slowed and was almost irreversible. Incubation itself did not appreciably affect the parameters of aggregation of intact platelets from the patients (control) or from the healthy blood donors, in the first series of experiments.

Treating the platelets with dipyridamole led to a small but not significant improvement of the aggregation properties of these cells, as shown by an increase in the rate of aggregation and in the degree and rate of disaggregation. By contrast with this preparation, incubation of the platelets with Triofen significantly improved the above parameters of ADP-induced aggregation. special experiments showed that the antiaggregative activity of Triofen was most marked in a final concentration of $8.6 \cdot 10^{-5}$ g/liter.

Treatment of platelets with Triofen in vitro thus has a significant and favorable action on the aggregation properties of these cells, if initially disturbed, but has no such effect on platelets from healthy individuals. The results offer basically new opportunities for pharmacologic correction of the platelet stage of hemostasis.

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