# PLATELET AGGREGATION DURING DEPRESSION OF FUNCTION OF THE ANTICLOTTING SYSTEM OF THE BLOOD BY INTRAVENOUS INJECTIONS OF ANTIPLASMIN AND CHLORPROMAZINE

V. E. Pastorova

UDC 612.115.3:(615.273.52+615.214.22:547.869.2

Experiments on albino rats showed that during depression of the function of the anticlotting system produced by intravenous injection of antiplasmin (60 units per animal) or chlorpromazine (0.07 ml of a 2.5% solution), the depression of fibrinolysis, lowering of the heparin level, and features of hypercoagulation are accompanied by a marked increase in platelet aggregation. Elevation of the endogenous thrombin level evidently is a contributory factor. In experiments in vitro antiplasmin had no effect on platelet aggregation but chlorpromazine reduced it.

A previous investigation [6] showed that intravenous injection of the platelet-aggregating agent ADP into healthy rats does not cause death of the animals whereas more than half of the animals receiving a preliminary intravenous injection of antiplasmin or chlorpromazine died from thrombosis under these circumstances. Intravenous injections of antiplasmin and chlorpromazine are known to depress the function of the anticlotting system temporarily [2, 5], and this may modify the level of platelet function and contribute to the formation of thrombi after injection of the platelet-aggregating agent.

In the investigation described below on animals with the function of their anticlotting system depressed by antiplasmin or chlorpromazine, platelet aggregation and the components of the clotting and anticlotting systems of the blood were studied.

## EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 170-180 g. Antiplasmin, obtained from bovine blood [11], was injected intravenously in a dose of 60 units per animal; a blood sample was taken after 5 min. Another blood sample was taken 40 min after intravenous injection of chlorpromazine (0.07 ml of a 2.5% solution). Antiplasmin (12 units/ml) and chlorpromazine (0.015 ml of a 2.5% solution) were added to plasma in vitro also. Aggregation of the platelets in plasma with added platelets on the addition of thrombin solution (0.4 unit/ml) was determined by a turbidimetric method [8] 1, 3, 5, 8, and 10 min after addition of the platelet-aggregating agent. Clotting of the plasma was monitored by means of a thromboelastograph. Free thrombin activity [9], the heparin level [7], the fibrinolytic activity [1], the total lytic activity of the plasma, and nonenzymic fibrinolysis [3] also were determined.

## EXPERIMENTAL RESULTS

The addition of antiplasmin to plasma with added platelets did not disturb platelet aggregation in response to the addition of the platelet-aggregating agent (index of aggregation 1.19 in the control, 2.14 in the experimental series, $P > 0.5$; number of aggregated platelets 27% in the control, 36% in the experiment;

Laboratory of Physiology and Biochemistry of Blood Clotting, Faculty of Biology, M. V. Lomonosov Moscow State University. (Presented by Academician of the Academy of Medical Sciences of the USSR S. E. Severin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 6, pp. 25-27, June, 1974. Original article submitted May 14, 1973.

TABLE 1. Effect of Intravenous Injection of Antiplasmin and Chlorpromazine on Platelet Aggregation and Components of the Clotting and Anticlotting System

| | Statistical index | Aggregation index | No. of aggregated platelets (in %) | Free thrombin (in sec) | Heparin level (in sec) | Fibrinolytic activity (in %) | Total lytic activity (in mm²) | Nonenzymic fibrinolysis (mm²) | Thromboelastogram r | Thromboelastogram k |
|---|---|---|---|---|---|---|---|---|---|---|
| After injection of antiplasmin | | | | | | | | | | |
| Control | $n$ | 7 | 7 | 20 | 22 | 25 | 14 | 12 | 16 | 15 |
| | $M \pm m$ | 1,03±0,02 | 17±13 | 652±15 | 141±15,1 | 16,1±3 | 91±9,3 | 51±13 | 130±8,8 | 140±15 |
| Experiment | $n$ | 7 | 7 | 21 | 22 | 24 | 15 | 14 | 17 | 14 |
| | $M \pm m$ | 2,63±0,47 | 60±7,6 | 320±13 | 95±7 | 4,2±2,5 | 47±9 | 27±7 | 107±7 | 118±13 |
| | $P$ | <0,01 | <0,02 | <0,01 | <0,01 | <0,01 | <0,01 | ≤0,05 | <0,02 | >0,5 |
| After injection of chlorpromazine | | | | | | | | | | |
| Control | $n$ | 10 | 10 | 21 | 19 | 21 | 18 | 17 | 18 | 10 |
| | $M \pm m$ | 1,53±0,15 | 28±6,5 | 722±18,5 | 145±9,5 | 29±4,7 | 42±8 | 22±6 | 112±7,4 | 126±15 |
| Experiment | $n$ | 10 | 10 | 19 | 22 | 20 | 16 | 17 | 17 | 14 |
| | $M \pm m$ | 3,12±0,45 | 60±6 | 592±14 | 105±6,8 | 15±4 | 24±6 | 12±3 | 87±5,1 | 83±9,3 |
| | $P$ | <0,01 | <0,01 | <0,01 | <0,01 | <0,02 | ≤0,05 | >0,5 | <0,02 | <0,02 |

$P > 0.5$). Under similar conditions chlorpromazine considerably reduced both the aggregation index and the number of aggregated platelets ($P < 0.01$), in agreement with results obtained by other workers [4].

The results given in Table 1 show that intravenous injection of antiplasmin led to a marked increase in platelet aggregation. This was combined with evidence of depression of the function of the anticlotting system: inhibition of enzymic and nonenzymic fibrinolysis and lowering of the heparin level – and also with activation of the clotting system – elevation of the free thrombin level and shortening of the blood-clotting time.

In the experimental animals receiving chlorpromazine, besides features reflecting depression of the function of the anticlotting system and hypercoagulation, there was also a marked increase in the index of platelet aggregation and in the precentage of aggregated platelets. In 3 of 12 cases, in which 40 min after injection of chlorpromazine no definite depression of function of the anticlotting system and no hypercoagulation could be observed, platelet aggregation was reduced.

The experiments in vivo thus show that depression of the function of the anticlotting system produced by intravenous injections of antiplasmin and chlorpromazine also leads to a marked increase in platelet aggregation. Increased activity of free endogenous thrombin must be a contributory factor in this effect [10, 12, 13].

## LITERATURE CITED


1. G. V. Andreenko, Lab. Delo, No. 5, 3 (1962).
2. B. A. Kudryashov, G. V. Andreenko, G. G. Bazaz'yan, et al., Vestn. Moskovsk. Univ., No. 2, 3 (1961).
3. B. A. Kudryashov and L. A. Lyapina, Lab. Delo, No. 6, 326 (1971).
4. K. M. Lakin, V. A. Fel'dbaum, and A. A. Lebedeva, in: Problems in Neuro-Humoral Regulation of Blood Clotting under Normal and Pathological Conditions, Proceedings of an All-Union Symposium [in Russian], Chita (1971), p. 83.
5. V. E. Pastorova and B. A. Kudryashov, Vestn. Moskovsk. Univ., No. 1, 3 (1970).
6. V. E. Pastorova and I. P. Titova, Probl. Gematol., No. 7, 32 (1972).
7. F. K. Beller and D. Steichell, Z. ges. exp. Med., 128, 458 (1957).
8. G. V. R. Born, Nature, 194, 927 (1962).
9. H. J. Glueck, J. Appl. Physiol., 6, 650 (1954).
10. K. Grette, Acta Physiol. Scand., 56, 195 (1962).
11. E. C. Loomis, A. Ryder, and G. George, Arch. Biochem., 20, 444 (1949).
12. S. Niewiarowski and D. P. Thomas, Nature, 212, 1544 (1966).
13. B. K. Stuart and D. P. Thomas, Thrombos. Diath. Haemorrh. (Stuttgart), 18, 537 (1967).