DIFFERENCE BETWEEN MECHANISMS OF CHANGES IN PLATELET AND ERYTHROCYTE AGGREGATION IN RENAL FAILURE

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Aggregation reactions of platelets and erythrocytes were studied in chronic renal failure. Differences in the mechanism of aggregation of platelets and erythrocytes are discussed on the basis of data showing opposite changes in the aggregation function of cells of the same subjects under similar conditions.

KEY WORDS: aggregation of platelets; aggregation of erythrocytes.

The physiological role of aggregation of erythrocytes (AE) and platelets (AP) is usually associated with homeostasis, and an increase in the aggregating activity of these cells in pathology is invariably interpreted as a factor adversely affecting the microcirculation; however, the change in the reaction of these cells is often in opposite directions. For example, AP induced by the addition of ADP to platelet-rich plasma is known to be reduced in uremia. At the same time, the present writers showed previously [3] that reversible AE, taking place "spontaneously," is as a rule intensified in uremia. Although the aggregation reactions of these cells are considered to be similar both in their physiological role and in their external picture of conglomeration of the cells, the opposite nature of the changes in these reactions under identical conditions may thus be evidence that AE and AP differ in their mechanism. The object of this investigation was a systematic comparison of changes in the aggregating power of platelets and erythrocytes in patients with the same pathological states.

EXPERIMENTAL METHOD

AP was determined on the BIAN AT-1 analyzer, which records changes in optical density of a suspension of platelets in plasma in the course of aggregation induced by the addition of ADP (Fig. 1). AE was studied by photometric recording of the decrease in the scattering of light by blood in response to the sudden stopping of agitation of blood with a standardized hematocrit index of 40 vols. % [4]. Besides the standard determinations, the blood levels of fibrinogen, creatinine, and urea were determined, together with other indices of marked renal failure: The plasma serotonin concentration was determined by a fluorometric method with o-phthalic aldehyde [2].

Tests were carried out on blood taken from the cubital vein of 31 patients with chronic renal failure (CRF), complicating chronic diffuse glomerulonephritis, chronic pyelonephritis, and amyloidosis and polycystic disease of the kidneys. In 19 cases, AE, blood serotonin activity, the fibrinogen concentration, and hematocrit index were determined simultaneously. In another 12 patients, besides the parameters listed above, AP was determined. Blood from 14 clinically healthy persons and from 10 patients with chronic glomerulonephritis with an isolated urinary syndrome and with intact renal function was tested as the control.

EXPERIMENTAL RESULTS AND DISCUSSION

As Table 1 shows, in blood samples from patients with CRF the hematocrit index showed a marked decrease, the fibrinogen concentration, AE, and the serotonin concentration were increased, but the intensity of AP was reduced with respect to all parameters tested (t_1, ΔD_a,

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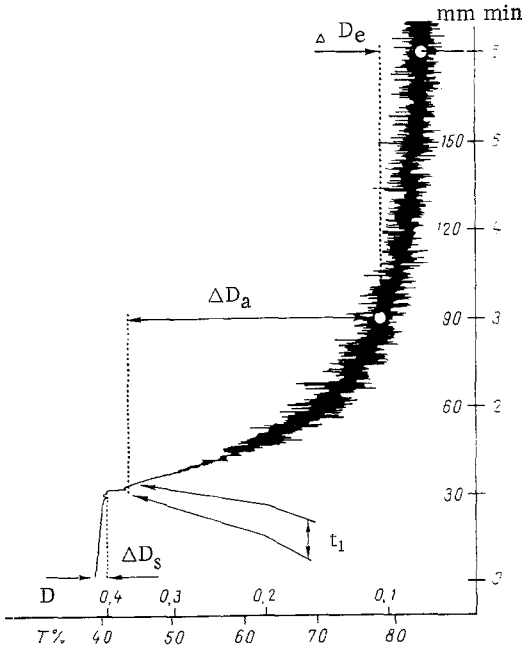

Fig. 1

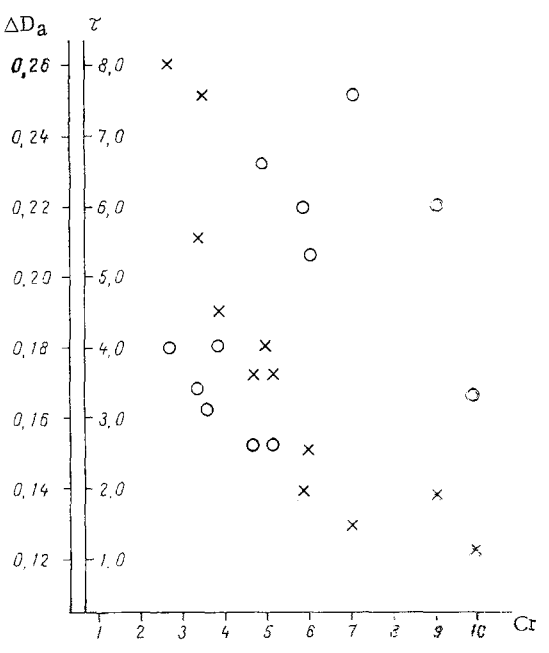

Fig. 2

Fig. 1. Parameters of the AP curve. Abscissa, above: changes in optical density of platelet suspension in plasma during aggregation (in V). ΔD_s) Spontaneous aggregation; t_1) time after addition of aggregating agent to complete fall of optical density; ΔD_a) AP after 2 min; ΔD_e) "exhaustion" of aggregation.

Fig. 2. Dependence of AP (crosses) and AE (circles) on creatinine concentration in blood. Abscissa, creatinine (Cr) concentration (in mg %); ordinate: on left — index of AP (ΔD_a; in scale units); on right — index of AE (τ; in sec).

ΔD_e). The changes in these values observed in the patients differed statistically significantly from those observed in the control group.

Thrombocytopenia was detected in only two patients with CRF (96,000 and 124,000/mm^3), and bleeding was present in both. A decrease in AP was observed, and it was particularly marked in a patient with hemorrhages (t_1 = 6 sec; ΔD_a = 0.128; ΔD_e = 0.011), in agreement with data in the literature [6]. AP also decreased with an increase in the degree of CRF. This was shown by correlation (Fig. 2) between the value of AP and the blood creatinine concentration ($r = -0.8$),* in agreement with data in the literature [7]. Since AP was reduced in patients with CRF regardless of the character of the kidney disease, it must be postulated that the cause of the decrease in AP was a change in the state of the internal milieu connected with uremia and not the character of the kidney lesion.

The blood serotonin concentration of patients with uremia (Table 1) was increased on average by 4-5 times compared with blood of the healthy subjects. In high concentrations serotonin is known to depress AP by changing the properties of the cell membrane [5], but no correlation was found between the serotonin concentration and AP in patients with CRF.

In all blood samples taken during uremia an increased AE was found (Table 1). Spontaneous reversible AE is known to be due primarily to cross-linkages from high-molecular-weight compounds (especially from fibrinogen). Analysis of the data showed no significant correlation between the indices of AE (τ) and the concentrations of serotonin, creatinine, and urea, whereas correlation was found with the ESR and fibrinogen concentration ($r = +0.42$ and $r = +0.36$ respectively).

Hence, in uremia AP is significantly reduced whereas AE is increased. Meanwhile no correlation could be found between the changes in aggregation of these blood cells (Fig. 2).

*All coefficients of correlation given are statistically significant.

TABLE 1. Mean Values of Indices Measured (M ± m)

Index	Healthy subjects	Patients with CRF	Patients with isolated urinary syndrome without CRF
Platelet count in blood, thousands/mm³	264,0±29,6	228,0±27,0	239,0±24,3
P		>0,05	>0,05
Indices of AP:			
— t_1, sec	2,0±0,3	6,5±0,7	2,7±0,4
P		<0,001	>0,05
— ΔD_A	0,245±0,012	0,175±0,013	0,242±0,012
P		<0,01	>0,05
— ΔD	0,020±0,001	0,011±0,002	0,018±0,002
P		<0,001	>0,05
Serotonin level, μg/ml	0,060±0,003	0,254±0,025	0,062±0,003
P		<0,001	>0,05
Index of AE:			
—τ, sec	9,46±1,90	5,05±1,81	8,38±2,36
P		<0,01	>0,05
Fibrinogen concn., g, %	0,180±0,039	0,390±0,214	0,240±0,080
P		<0,01	<0,01
Hematocrit index, vols. %	42,3±3,3	26,8±5,8	42,4±5,2
P		<0,01	>0,05

Legend. P) Probability of absence of differences from blood of clinically healthy subjects; remainder of legend as in Fig. 1.

The reason for this is evidently that the mechanisms of their corresponding aggregation reactions differ. Enhancement of AE in CRF is regularly associated with an increase in the fibrinogen concentration. No clear connection could be found, however, between changes in AP and changes in the blood fibrinogen concentration. In turn, AP is reduced when the creatinine concentration in the blood rises, whereas AE (which is significantly reduced on average) was not so clearly connected with the degree of damage to renal function.

It might be considered that the parameter AP which was studied differed from spontaneous AE in the fact that it was induced artificially by the addition of ADP, whereas AE was entirely due to factors naturally contained in the blood. However, attention is drawn to an investigation [1] in which aggregation of rabbit erythrocytes washed with physiological saline, under the influence of thromboplastin, ADP, and various therapeutic substances was studied and significant differences were found in the mechanisms of induced AE and induced AP as reflected in the effects of these substances.

AE and AP, changing in opposite directions in uremia, thus evidently have a significantly different mechanism, and this fact must be taken into account when modern views on the physiological role of these reactions are analyzed.

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