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Interaction of Bacterial Endotoxin and Liquoid with Blood Platelets: Aggregation and Decrease in the Electrokinetic Charge

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Low platelet counts are common in patients with gram-negative bacteremia (1), and many species of animals develop thrombocytopenia following intravenous injections of Endotoxin (2). The addition of bacterial Endotoxin to rabbit platelet-rich plasma induces massive platelet aggregation. In contrast, bacterial Endotoxin induces only occasional and variable clumping in human platelet-rich plasma (3).

Like Endotoxin, charged polymeric agents induce platelet aggregation, and this is correlated to a decrease in the electrokinetic charge of the blood platelets (4). Liquoid, a heparinlike synthetic anticoagulant, is an acid polymer which aggregates platelets in vitro (5) and also provokes the generalized Shwartzman reaction in rabbits (6).

Endotoxin, Liquoid and many other agents can induce platelet aggregation both in vitro and in vivo, but the detailed mechanism of this platelet aggregation is still unknown. In this paper, platelet aggregation induced by both Endotoxin and Liquoid is shown to correlate with a decrease in the electrokinetic charge of the platelets. This effect on the platelet surface charge may explain some types of platelet aggregation. In addition, it is possible that such surface changes may reflect a release of procoagulant material. We have only studied platelets and red cells, but it is possible that these agents affect other cells in similar ways.

Materials

Animals. Albino rabbits of both sexes weighing 2,100–2,800 g were used. They were fed rabbit pellet food (Statens Institutt for Folkehelse, Oslo).

Liquoid, a synthetic acid polymer, (sodium polyanethol sulfonate), was kindly supplied by Hoffman-La Roche, Basle, Switzerland. Solutions of Liquoid (Batch A 183627) were made up in saline immediately before use.

Endotoxin (lipopolysaccharide type W, E. coli 0111: B 4, Difco Labs., Detroit, U.S.A.) was suspended in saline in concentrations of 0.2 and 2.0 mg/ml for the in vivo and the in vitro experiments, respectively.

Citrate anticoagulant was prepared in two ways. For human blood we used trisodium citrate 12.0 g, citric acid 4.58 g, and dextrose 25 g, made up to 1 l with distilled water, and for rabbit blood 6 parts of 0.1 M sodium citrate and 4 parts of 0.1 M citric acid.

Heparin was obtained from Nyegaard & Co., Oslo (5,000 I.U./ml).

Apyrase (Sigma Chemical Co., St. Louis, Missouri, U.S.A., lot 77 B-5000) was dissolved in saline in a concentration of 10 mg/ml immediately before use.

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Methods

Preparation of test samples: Human blood was obtained from healthy blood donors by collecting 9 parts of blood from an antecubital vein into 1 part of anticoagulant in plastic tubes. Blood samples from rabbits were obtained in two ways:

1. During Nembutal anesthesia blood was collected from the aorta using a 20 gauge needle attached to plastic tubing, allowing 9 parts of blood to flow into a plastic tube containing 1 part of citrate anticoagulant or heparin.

2. By heart puncture of Nembutal-anesthesized rabbits, 9 parts of blood were collected into a plastic syringe containing 1 part of citrate anticoagulant.

Platelet-rich plasma (PRP) was obtained by centrifuging blood at 250 g for 10 min at room temperature. *Platelet-poor plasma* (PPP) was obtained by centrifuging blood at 1,000 g for 20 min. PPP for coagulation studies was stored at $-28°$ C.

For in vivo experiments, Liquoid was injected i. v. in Nembutal-anesthesized rabbits in doses of 13 mg/kg body weight. Endotoxin was injected i. v. in two consecutive doses: The first was 150 μg/kg body weight, and 24 hrs later the second dose (100 μg/kg) was given.

Platelet and erythrocyte electrophoresis was performed with a technique described previously (8). Human PRP was diluted with PPP to contain about 1×10^8 platelets and about 1×10^7 erythrocytes per mm^3. The electrophoretic mobility of 10–20 platelets and 10 erythrocytes was measured in each sample. The measurements were made at 25° C, and the electrophoretic mobility of platelets and erythrocytes in plasma was corrected by multiplying with the relative viscosity to water at 25° C. The electrophoretic mobilities are expressed as μ/sec/V/cm; these values are negative since the cells travel towards the anode. For simplicity, the negative sign is omitted. For determination of the experimental error, double determinations of 25 samples have been done with blind technique. Standard error in % of the mean was 2.2% for platelets and 2.3% for erythrocytes.

Platelet aggregation was assessed microscopically in the cell electrophoresis apparatus (the optical equipment with 800 times magnification and phase contrast made it possible to differentiate between platelets, small platelet aggregates and erythrocytes).

Platelets were counted by a slight modification of the method of Brecher et al. (9).

Fibrinogen was measured with Godal's modification (10) of the method of Blombäck and Blombäck (11).

Factor V was measured according to Stormorken (12).

Factor VIII was measured by an activated partial thromboplastin time assay with a cephalin-kaolin reagent and human hereditary factor VIII-deficiency substrate plasma (13).

Results

A. Experiments with Liquoid

Rabbit platelets in vitro: Rabbit and human platelets had almost the same electrophoretic mobility in citrated plasma. Rabbit erythrocytes, however, had less than half of the electrophoretic mobility of human erythrocytes (Fig. 1). In concentrations above 10 μg/ml, Liquoid progressively reduced the electrophoretic mobility of platelets in plasma, while the mobility of erythrocytes was unchanged (Fig. 1). The concentrations of Liquoid which reduced the electrophoretic mobility of platelets also induced platelet aggregation. With increasing concentrations of Liquoid, the aggregates became larger and more tightly packed. This occurred in both citrated and heparinized (0.1 mg/ml final concentration) plasma. The effect, both on platelet electrophoretic mobility and on platelet aggregation, appeared quickly and was present when measuring was started about 3 min after the addition of Liquoid. The effects were irreversible and increased only a little when followed for 3 hrs. The electrophoretic mobility of almost all platelets was reduced, and small aggregates of 2–5 platelets had the same mobility as single platelets.

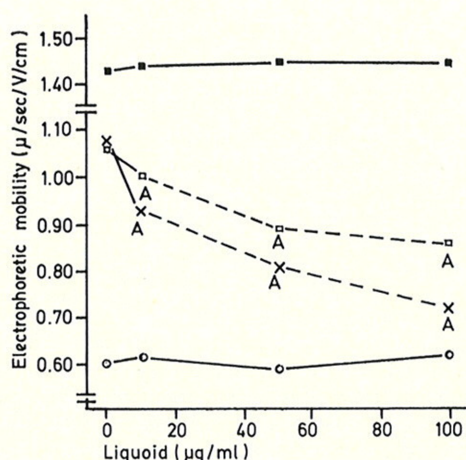

Fig. 1. *Electrophoretic mobility of rabbit and human platelets and erythrocytes in PRP with addition of Liquoid in different concentrations.* A broken line and the letter A denote platelet aggregation. The values given are the mean of 5 experiments. ×——× = rabbit platelets, ○——○ = rabbit erythrocytes, □——□ = human platelets, ■——■ = human erythrocytes.

EDTA inhibited the effect of Liquoid. Thus, in citrated plasma Liquoid in a concentration of 100 μg/ml reduced the electrophoretic mobility of rabbit platelets from 1.07 to 0.71 μ/sec/V/cm, but in the presence of EDTA (0.25% final concentration) only to 0.97 μ/sec/V/cm (Table 1). Platelet aggregation was also inhibited by EDTA.

Apyrase, which contains ADP-ase, did not influence either the reduction in platelet electrophoretic mobility nor the platelet aggregation (Table 1). Thus, aggregation of platelets by Liquoid is apparently not mediated by ADP.

Table 1. *The Effect of Liquoid on Rabbit Platelet Electrophoretic Mobility (P, μ/sec/V/cm) and Aggregation (Agg) in Plasma, and the Influence of EDTA and Apyrase on this Effect.* The platelet aggregation was assessed in the cell electrophoresis apparatus. The electrophoretic mobility of erythrocytes (E) was measured in the same samples.

Sample	Saline 0.1 ml			Liquoid 100 μg/ml			Liquoid 100 μg/ml + Apyrase 0.1 ml			Liquoid 100 μg/ml + EDTA 0.25%		
	P	Agg	E	P	Agg	E	P	Agg	E	P	Agg	E
1	1.02	—	0.63	0.72	+++	0.65	0.69	+++	0.57	0.93	—	
2	1.06	(+)	0.60	0.69	+++	0.58	0.65	++	0.60	0.96	+	0.70
3	0.99	—	0.58	0.73	+++	0.52	0.61	+++		1.02	—	0.52
	1.03	—	0.60	0.71	+++	0.58	0.65	+++	0.59	0.97	—	0.61

Rabbit platelets in vivo: Liquoid had an immediate effect on platelets in vivo. The electrophoretic mobility of platelets in samples taken 5 min after the injection was reduced to a mean of 87% of normal, and the platelet count was less than half of the original value (Fig. 2). Two hours later the platelet counts were still very low, and the platelet electrophoretic mobility was only 59% of normal. Even though there were few

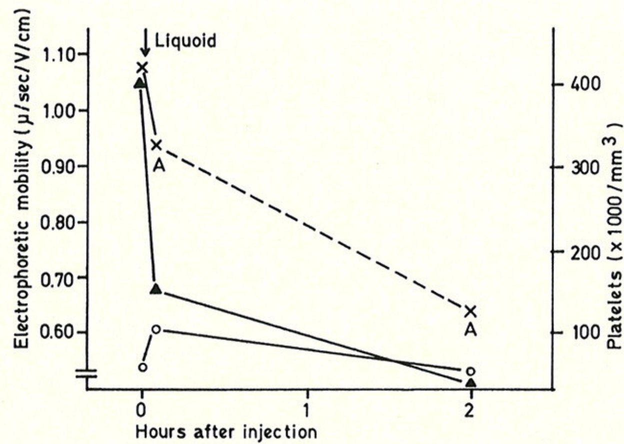

Fig. 2. *Platelet counts and electrophoretic mobility of rabbit platelets and erythrocytes in citrated PRP after intravenous injection of Liquoid 13 mg/kg body weight.* A broken line and the letter A denote platelet aggregation. The values given are the mean of samples from 3 animals. ×———× = electrophoretic mobility of platelets, ○———○ = electrophoretic mobility of erythrocytes, ▲———▲ = platelet counts.

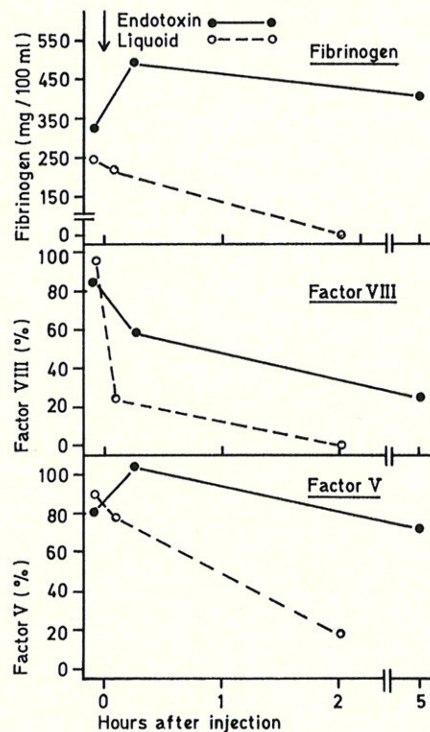

Fig. 3. *Plasma fibrinogen and factors V and VIII after a single injection of Liquoid (13 mg/kg body weight) or after two injections of Endotoxin (150 and 100 μg/kg body weight).* The values are the mean of samples from 6 rabbits injected with Endotoxin and of 3 rabbits injected with Liquoid.

platelets, many of them were in small aggregates. All platelets were similarly affected. Plasma fibrinogen and factors V and VIII were progressively reduced (Fig. 3).

Human platelets in vitro: Addition of Liquoid in vitro had similar effects on human platelets as on rabbit platelets. However, when higher concentrations of Liquoid were tested, a biphasic effect was obtained (Fig. 4). In a concentration of only 5 μg/ml, Liquoid reduced the electrophoretic mobility of platelets, but the effect was small, and platelet aggregation was not induced. A concentration of 10 μg/ml produced inconstant and transient platelet aggregation, and 50 μg/ml induced massive aggregation. The effect both on the electrophoretic mobility and on platelet aggregation was immediate and irreversible for at least 3 hrs. All platelets were similarly affected. In concentrations of 50–200 μg/ml, Liquoid also changed the morphology of platelets with swelling and fused aggregates, resembling thrombin-induced aggregates. Liquoid in concentrations of 1.25–2.5 mg/ml macroscopically precipitated fibrinogen in the plasma and induced platelet aggregation. With 10 mg/ml of Liquoid fibrinogen precipitation was not visible, the electrophoretic mobility of platelets was increased, and platelet aggregation was *not* induced (Fig. 4).

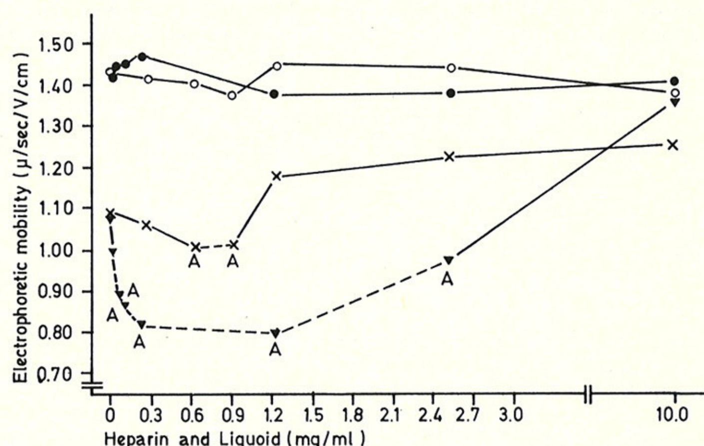

Fig. 4. *Electrophoretic mobility of human platelets and erythrocytes in citrated PRP with additions of Liquoid or heparin in different concentrations.* A broken line and the letter A denote platelet aggregation. The values given are the mean of 5 experiments. ×——× = platelets with addition of heparin, ▲——▲ = platelets with addition of Liquoid, ○——○ = erythrocytes with addition of heparin, ●——● = erythrocytes with addition of Liquoid.

EDTA in a final concentration of 0.25% almost completely blocked the reduction of electrophoretic mobility and platelet aggregation (Table 2).

Apyrase inhibited the ADP-effect on platelets, both the aggregation and the reduction in electrophoretic mobility (Table 3). However, it did not inhibit the reduction of electrophoretic mobility of platelets or the platelet aggregation induced by Liquoid (Table 2). For unknown reasons, Apyrase and Liquoid together reduced the electrophoretic mobility of erythrocytes (Table 2), and platelets could be observed adhering to the erythrocytes.

Liquoid is a heparin-like agent. In Fig. 4 the effects of heparin and Liquoid on platelets are compared. In principle, the effects on electrophoretic mobility and platelet

Table 2. *The Effect of Liquoid on Human Platelet Electrophoretic Mobility (P, μ/sec/V/cm) and Aggregation (Agg) in Plasma.* Platelet aggregation was assessed in the cell electrophoresis apparatus. The electrophoretic mobility of erythrocytes (E) was measured in the same samples.

Sample	Saline 0.1 ml			Liquoid 100 μg/ml			Liquoid 100 μg/ml + Apyrase 0.1 ml			Liquoid 100 μg/ml + EDTA 0.25%		
	P	Agg	E	P	Agg	E	P	Agg	E	P	Agg	E
1	1.08	–	1.44	0.86	+++	1.42				1.07	–	1.38
2	1.16	–	1.47	0.88	+++	1.53				1.14	(+)	1.42
3	1.05	–	1.45	0.87	++	1.42				0.98	–	1.31
4	1.06	–	1.43	0.88	+++	1.50	0.87	+++	1.04			
5	1.04	–	1.36	0.74	+++	1.41	0.77	+++	1.07			
	1.08	–	1.43	0.85	+++	1.46	0.82	+++	1.06	1.06	–	1.37

Table 3. *The Effect of ADP (0.5 μg/ml) on Rabbit Platelet Electrophoretic Mobility (P, μ/sec/V/cm) and Aggregation (Agg) in Plasma.* The results obtained when Apyrase (0.1 ml) was added to 3.9 ml PRP prior to addition of ADP (0.5 μg/ml) are given in the last column. Platelet aggregation was assessed in the cell electrophoresis apparatus.

Sample	Saline 0.1 ml		ADP 0.5 μg/ml		ADP 0.5 μg/ml + Apyrase 0.1 ml	
	P	Agg	P	Agg	P	Agg
1	0.99	–	0.86	+++	0.99	(+)
2	1.06	–	0.95	+++	1.07	+
3	1.09	–	0.91	+++	1.03	+
	1.05	–	0.91	+++	1.03	+

aggregation of the two agents are the same, but Liquoid is much more potent. Heparin in concentrations of 0.62 and 0.87 mg/ml produced a small reduction in platelet electrophoretic mobility and slight platelet aggregation; higher concentrations increased the electrophoretic mobility and did not induce platelet aggregation.

B. *Experiments with Endotoxin*

Rabbit platelets in vitro: Endotoxin added to PRP in concentrations of 50 and 100 μg/ml reduced the electrophoretic mobility of platelets to 83% of normal and aggregated the platelets (Fig. 5). The effect both on the electrophoretic mobility and on platelet aggregation was much smaller than the effect of Liquoid. Liquoid affected all platelets in the same way, but with Endotoxin some of the platelets remained unchanged with a normal electrophoretic mobility. The effect was present 10 min after addition of Endotoxin and did not change during the following 3 hrs. It was the same with citrate and heparin as anticoagulants, but EDTA blocked it (Table 4). Apyrase added prior to addition of Endotoxin did not prevent either the reduction in electrophoretic mobility nor the platelet aggregation (Table 4).

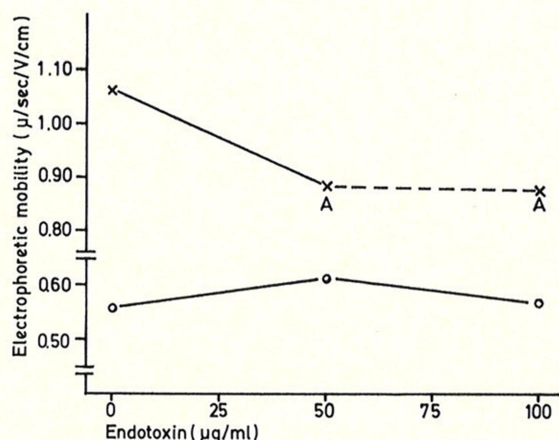

Fig. 5. *Electrophoretic mobility of rabbit platelets and erythrocytes in PRP after addition of Endotoxin in different concentrations.* A broken line and the letter A denote platelet aggregation. The values given are the mean of 3 experiments with heparin PRP and 5 with citrated PRP. ×——× = electrophoretic mobility of platelets, ○——○ = electrophoretic mobility of erythrocytes.

Table 4. *The Effect of Endotoxin on Rabbit Platelet Electrophoretic Mobility (P, μ/sec/V/cm) and Platelet Aggregation (Agg) in Plasma.* Platelet aggregation was assessed in the cell electrophoresis apparatus. The electrophoretic mobility of erythrocytes (E) was measured in the same samples.

Samples	Saline 0.1 ml			Endotoxin 100 μg/ml			Endotoxin 100 μg/ml + Apyrase 0.1 ml			Endotoxin 100 μg/ ml + EDTA 0.25%		
	P	Agg	E	P	Agg	E	P	Agg	E	P	Agg	E
1	1.07	–	0.59	0.88	++	0.59	0.94	++	0.62	1.05	–	0.56
2	1.11	–	0.59	0.90	++	0.56	0.97	++	0.63	1.09	–	0.63
3	1.11	–	0.66	0.94	++	0.63	0.93	+	0.62	1.09	–	0.66
	1.10	–	0.61	0.91	++	0.59	0.94	++	0.62	1.08	–	0.61

Rabbit platelets in vivo: Endotoxin injections in rabbits reduced the platelet counts (Fig. 6), but there were great variations. The electrophoretic mobility of platelets was reduced to a mean of 91% of normal 15 min after the second injection and to a mean of 82% after 5 hrs. There were great variations in the electrophoretic mobility of the platelets, and some platelets remained normal. Slight platelet aggregation was observed in these samples, and small aggregates of 2–5 platelets always had reduced electrophoretic mobility. The mobility of the erythrocytes was almost unchanged (Fig. 6).

Plasma fibrinogen was increased in the samples taken 15 min after the second injection. After 5 hrs, there was a small reduction but still higher values than in the samples taken before the Endotoxin injections (Fig. 3). Factor V showed the same pattern, while factor VIII was reduced both at 15 min and 5 hrs after the second Endotoxin injection.

Human platelets in vitro: There was no significant aggregation of human platelets after addition of Endotoxin to citrated PRP. When heparin was used, slight platelet aggregation was observed both in the samples with Endotoxin and in the controls. Thus, the aggregating effect of Endotoxin could not be evaluated, but, at most, it was

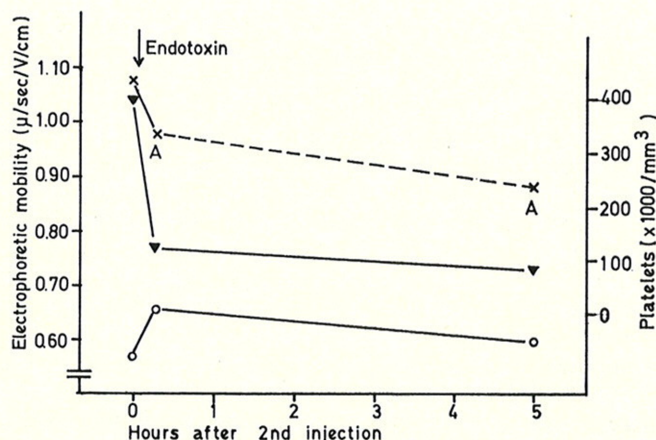

Fig. 6. *Platelet counts and electrophoretic mobility of rabbit platelets and erythrocytes in citrated PRP after 2 injections of Endotoxin (150 and 1000 μg/kg body weight) 24 hrs apart.* A broken line and the letter A denote platelet aggregation. The values given are the mean of samples from 6 animals. ×——× = electrophoretic mobility of platelets, ○——○ = electrophoretic mobility of erythrocytes, ▲——▲ = platelet counts.

small. In citrated PRP there was no change in the electrophoretic mobility of platelets or erythrocytes after addition of Endotoxin 100 μg/ml. In heparinized PRP the electrophoretic mobility of platelets was reduced from 1.07 to 0.96 μ/sec/V/cm, while the mobility of erythrocytes was unchanged.

It should be noted that the addition to plasma of these agents had no significant effect on pH and the relative viscosity of the plasmas.

Discussion

Both Endotoxin and Liquoid reduced the electrophoretic mobility of platelets but did not influence the mobility of erythrocytes, pH or the relative viscosity of the plasmas. It is reasonable to conclude, therefore, that the reduced electrophoretic mobility of platelets resulted from an effect on the negative electrokinetic charge of the platelets themselves and not from changes in the suspending medium. The decreased surface charge reduces the electrostatic repulsive forces between the platelets and could thereby facilitate platelet aggregation. The changes in the electrokinetic slip plane of the platelets could also be an expression of other effects on the platelet membranes resulting in platelet aggregation.

Heparin and the acid polymeric agents Liquoid and dextran sulphate all have the same pattern of effects on the platelet electrokinetic charge and aggregation (4). These agents are chemically different, but they share negatively charged sulphate groups. The reduction in the platelet electrokinetic charge by small concentrations of these agents may be explained by a specific adsorbtion to the platelet surface of a complex of the charged polymeric agent and divalent ions, calcium or magnesium. When the complex has a net positive charge, it reduces the platelet electrophoretic mobility, resulting in platelet aggregation. When no more divalent ions are present in the plasma, adsorbtion of the polymeric agent alone will increase the number of negatively charged groups on the platelet surface, resulting in increased electrophoretic

mobility of the platelets and prevention of the platelet aggregation. This hypothesis explains the biphasic curve in Fig. 4 and the preventiv effect of EDTA.

Acid polymeric agents and Endotoxin have strikingly similar effects on platelet electrophoretic mobility and aggregation. We have previously shown that ADPase prevents platelet aggregation by ADP but not by anionic and cationic polymeric agents (4). In the present investigation both Endotoxin and Liquoid induced irreversible platelet aggregation in the presence of ADPase. It is known that both Endotoxin and Liquoid provoke the release reaction from blood platelets (5, 14). However, Davis & Palmer (15) found that low-molecular dextran did not prevent thrombocytopenia by Endotoxin, but it completely prevented the release of serotonin and histamin. Our results indicate that the effect on platelet electrophoretic mobility and aggregation is not mediated through release of ADP.

The effect of polymeric agents and Endotoxin is also similar in their dependence of divalent ions, as EDTA blocked the reactions with all these agents.

However, there are also some differences in the effects. Liquoid reduced the electrophoretic mobility of rabbit platelets in vitro to a mean of 59% of normal and to a mean of 68% in vivo, and the mobility of human platelets was reduced to 74% of normal. The effect was fast, irreversible and dosedependent. All platelets were more or less affected. Endotoxin reduced the electrophoretic mobility of rabbit platelets only to 83% of normal both in vitro and in vivo, and had no effect on human platelets. The effect of Endotoxin is thus species dependent, suggesting that immunological factors may be involved. The dose dependence was less obvious with Endotoxin. Some platelets did not react to Endotoxin, retaining a normal electrophoretic mobility. This is in accordance with the effect on platelet electrophoretic mobility by particulate matters, like polystyrene latex particles (16), suggesting an active response of some platelets to Endotoxin.

Endotoxin affected platelet electrokinetic charge and platelet count, and the coagulation factor studies showed reduction of Factor VIII but not of Factor V and fibrinogen. Liquoid had much more potent effect on the platelets and reduced plasma fibrinogen and coagulation factors, indicating intravascular coagulation.

Liquoid provokes the generalized Shartzman reaction, while heparin prevents it. Both agents appear to have two effects: an effect on cell membrane and an anticoagulant effect. With Lquoid, the former effect predominates, resulting in intravascular coagulation and the Shwartzman reaction. With heparin, the latter effect predominates, preventing intravascular coagulation and the Shwartzman reaction. The mechanism which triggers the intravascular coagulation after injections of Endotoxin or Liquoid is unknown. Evensen & Jeremic (7) have suggested that Liquoid releases clot-promoting activity from the tissues, since thrombocytopenic animals are not protected against the reaction. Liquoid and Endotoxin could well affect the membranes of other cells in addition to the platelets.

Platelet aggregation is important in arterial thrombosis, transplant rejection processes and during certain infectious diseases. There is a need, therefore, for agents which may prevent platelet aggregation. Polymeric agents in certain doses increase the electrokinetic charge of platelets and prevent platelet aggregation in vitro. They could possibly be of clinical value.

Summary

The effects of Endotoxin and Liquoid on the electrophoretic mobility of human platelets and erythrocytes in vitro and on rabbit platelets and erythrocytes in vivo and in vitro have been investigated.

Liquoid reduced the electrophoretic mobility of human platelets to 74% of normal and rabbit platelets to 59% in vitro and to 68% of normal in vivo, while the erythrocytes were unchanged. Liquoid induced massive aggregation of both human and rabbit platelets. In very high concentrations, Liquoid increased the electrophoretic mobility of human platelets and did not induce aggregation.

Endotoxin reduced the electrophoretic mobility of rabbit platelets to 83% of normal and aggregated the platelets, but had none of these effects on human platelets.

The effects of Endotoxin and Liquoid were inhibited by EDTA, but not by ADPase, suggesting that aggregation was not mediated through ADP.

We conclude that Liquoid has the same pattern of effects on the electrokinetic charge of platelets and platelet aggregation as the acid polymeric agents dextran sulphate and heparin. There was good correlation between reduction in the electrokinetic charge of the platelets and platelet aggregation. There were striking similarities between the effects of these agents and Endotoxin.

Résumé

On a étudié les effet d'une endotoxine et du Liquoid sur la mobilité électrophorétique des plaquettes et érythrocytes humains in vitro et de celle des plaquettes et érythrocytes de lapin in vivo et in vitro.

Le Liquoid réduit la mobilité électrophorétique des plaquettes humaines à 74% de la valeur normale et des plaquettes de lapin à 59% in vitro et 68% in vivo; les érythrocytes ne sont pas touchés. Le Liquoid provoque une agrégation massive des plaquettes humaines et de lapin. Aux concentrations très élevées le Liquoid augmente la mobilité électrophorétique des plaquettes humaines et ne provoque pas l'agrégation.

L'endotoxine réduit la mobilité électrophorétique des plaquettes de lapin à 83% de la valeur normale et agrège les plaquettes, par contre elle n'a aucune influence sur les plaquettes humaines.

Les effets de l'endotoxine et du Liquoid sont inhibés par l'EDTA mais pas par l'ADPase; ce résultat suggère que dans ce cas l'agrégation n'est pas produite par l'ADP.

Nous concluons que le Liquoid a les mêmes effets sur la charge électrocinétique des plaquettes et leur agrégation que les polymères acides: sulfate de dextran et héparine. Il y a une bonne corrélation entre la réduction de la charge électrocinétique et l'agrégation des plaquettes. Il y a une ressemblance nette entre l'effet de ces agents et ceux de l'endotoxine.

Zusammenfassung

Es wurde die Wirkung von Endotoxin und Liquoid auf die elektrophoretische Wanderungsgeschwindigkeit menschlicher Thrombozyten und Erythrozyten in vitro und auf Kaninchenplättchen und Erythrozyten in vivo und in vitro untersucht.

Liquoid reduziert die elektrophoretische Mobilität menschlicher Plättchen auf 74% der Norm und jene der Kaninchenplättchen auf 59% der Norm in vitro und auf 68% der Norm in vivo, während die Mobilität der Erythrozyten nicht verändert wird. Liquoid verursacht eine massive Aggregation der Plättchen von Menschen und Kaninchen. In sehr hohen Konzentrationen steigert Liquoid die elektrophoretische Mobilität menschlicher Plättchen und verursacht keine Aggregation.

Endotoxin vermindert die elektrophoretische Mobilität der Kaninchenplättchen auf 83% der Norm und aggregiert die Plättchen, hat aber keine Wirkung auf menschliche Plättchen.

Die Wirkungen von Endotoxin und Liquoid wurden durch EDTA, nicht aber durch ADPase gehemmt, was darauf hindeutet, daß diese Aggregation nicht durch ADP vermittelt wird.

Wir kommen zu dem Schluß, daß Liquoid dieselbe Art der Wirkungen auf die elektrokinetische Ladung der Plättchen und die Plättchenaggregation ausübt wie die sauren polymeren Agentien Dextransulfat und Heparin. Es fand sich eine gute Korrelation zwischen der Verminderung der elektrokinetischen Ladung der Plättchen und der Plättchenaggregation. Es fanden sich erstaunliche Ähnlichkeiten zwischen den Wirkungen dieser Agentien und jenen von Endotoxin.

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