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COAGULATION AND FIBRINOLYSIS IN A PATIENT WITH EXTRACORPOREAL LIVER PERFUSION

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Marked coagulation and fibrinolysis disturbances were observed in a patient during extracorporeal heterologous liver perfusion. The most significant changes were: thrombocytopenia, high and rapid heparin disappearence from the systemic circulation, low fibrinogen concentration, and high fibrinolytic activity in the euglobulin fraction.

Extracorporeal liver perfusion for treatment of patients with hepatic coma is technically feasible if there is no clot formation in the perfusion system, as well as in the isolated heterologous liver. To prevent coagulation heparin should be administered intravenously throughout the whole procedure. The appropriate dosage and time of administration of heparin should be carefully checked. It should also be remembered that patients with acute liver insufficiency display major coagulation and fibrinolysis disorders due to hepatocyte damage. In order to control patients, hemostasis during the perfusion procedure serial studies of the coagulation and fibrinolysis system should be carried out. The introductory experimental studies of this type were performed on pigs (Łukasiewicz, 1970).

In the following paper the results of studies on the coagulation and fibrinolysis system in patient J. R. will be presented. Two consecutive perfusions took place on April 8 and 10, 1969.

METHODS

The coagulation and fibrinolysis system was studied in the patient: 1) before perfusion, 2) during the first perfusion lasting for 3 hr, and two days later during a 6 hr perfusion, 3) daily for five days following the last perfusion procedure. The following parameters were measured in the

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peripheral blood of the patient: blood clotting time with bovine thrombin, blood platelet count, plasma fibrinogen concentration, and euglobulin lysis time. Because of total heparinization of the patient, measurement of plasma coagulation factors was impossible. Blood clotting time was measured using a standard amount of bovine thrombin. Thirty to forty units of thrombin were added to the blood sample. Clotting time above 5 minutes was considered to be the minimum necessary to avoid clotting within the perfusion system. The test was repeated every 10 minutes. If the clotting time decreased below 5 min, additional doses of heparin were administered.

Clotting time estimation with a high standard dose of thrombin proved to be extremely useful in our studies. Usually there is a high and rapid consumption of heparin within the heterologous liver, which affects the heparin concentration in the peripheral blood directly. Heparin disappeares rapidly from the peripheral circulation, thus the Lee-White method proves to be too slow to detect the rapidly occurring changes.

Heparin was administered intravenously in an initial dose of 4 mg/kg, immediately before the revascularization of the porcine liver, and thereafter every time when thrombin clotting time decreased below 5 min. Increased fibrinolytic activity of the blood was controlled with intravenous EACA in a dose of 0·1 g/kg and AMCHA 20 mg/kg, usually 2—3 times during one perfusion procedure.

RESULTS

Blood coagulation and fibrinolysis studies performed before perfusion failed to detect any signficant abnormalities. There was medium degree thrombocytopenia (120,000 per cu mm), and a latent form of fibrinolysis with the euglobulin lysis time 115 minutes (normal 180—220 min).

During the perfusion high anti-heparin activity of the plasma was observed with rapid disappearence of heparin from the circulation, and

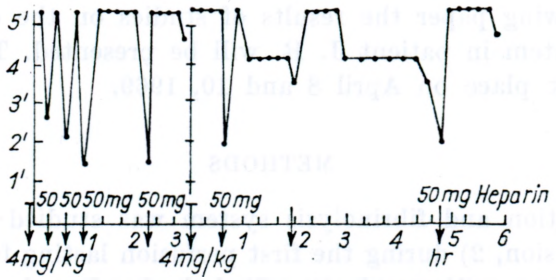

Fig. 1. Changes in the thrombin clotting time indicating rapid disappearence of heparin from the systemic circulation.

low thrombin clotting time. The heparin dosage during the 3 and 6 hr perfusion is shown in Fig. 1.

The platelet count decreased during the 3 hr perfusion on the average to 90,000/cu mm, and fibrinogen to 180 mg%. This occurred already in the first hour of the perfusion. Euglobulin lysis time decreased steadily

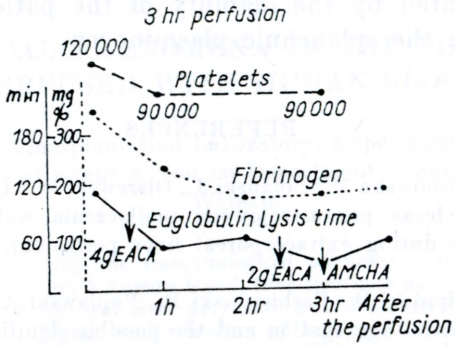

Fig. 2. Platelet count and fibrinolysis parameters in the peripheral blood during a 3 hr perfusion.

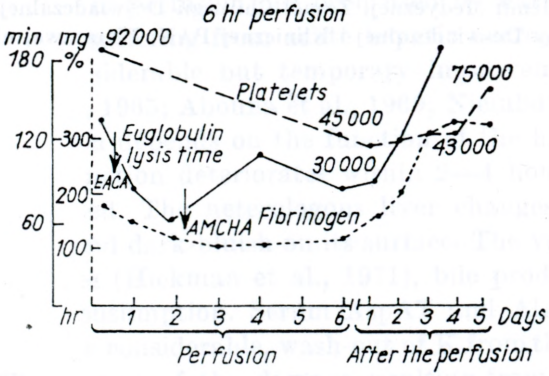

Fig. 3. Changes in platelet count and fibrinolysis during a 6 hr perfusion and the post-perfusion recovery.

despite administration of fibrinolysis inhibitors (Fig. 2). During the 6 hr perfusion the platelet count decreased to 45,000/cu mm and fibrinogen to 110 mg%. It took 4—5 days after the perfusion for the values of platelet, fibrinogen and euglobulin lysis time to return to the normal levels (Fig. 3).

DISCUSSION

Data obtained from our studies indicate that a constant decrease in peripheral blood platelet count and a high antiheparin activity of plasma develop during porcine liver perfusion with blood of a human with liver

insufficiency. Ths high anti-heparin activity may be the result of platelets trapping in the heterologous liver, their disintegration and release of platelet factor 4 into the circulation. Circulating factor 4 may initiate the process of paracoagulation (Niewiarowski et al., 1969). High doses of heparin afford only partial protection against platelet trapping and aggregation. Activation of the fibrinolytic system is probably a secondary phenomenon, initiated by the inability of the patient's own destroyeid liver to deactivate the splanchnic plasminogen.

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