Thursday, July 16, 1981

Poster Presentations

Endotoxin – I

11:00–12:30 h

Grand Ballroom Lobby Boards 228–231

0732

ENDOTOXINS AND PROCOAGULANT ACTIVITIES OF ASCITIC FLUID. H. Murr, P. Schüssler, G.E. Rindfleisch, J. Eisenburg, E. Hiller. Klinikum Großhadern, 8000 München 70, F.R.G.

Procoagulant activities in ascitic fluid of patients with cirrhosis of the liver have been reported repeatedly. It has been suggested that they cause DIC after reinfusion of ascitic fluid, however, the nature of these factors is unknown. Since endotoxins have been found in ascitic fluid and it is known that they can greatly augment the procoagulant activities of monocytes and macrophages, we assayed for the presence of endotoxin and compared the procoagulant activities in each of 15 specimens of ascitic fluid caused either by cirrhosis of the liver or by metastasizing tumors.

Endotoxins were assayed by the limulus test. Procoagulant activities were determined by thrombelastography, thrombin generation test, the presence of soluble fibrin monomer complexes (SFMC) and the ability to activate prothrombin complex and factor X.

Endotoxins were detected in 12 of 15 specimens of ascitic fluid caused by cirrhosis of the liver. In 11 of the endotoxin positive and in 2 of the 3 endotoxin negative samples procoagulant activity was present (i.e. shortened reaction time, increased thrombin generation, activation of prothrombin complex). In contrast, in only one out of the 15 samples of tumerous ascitic fluid the limulus test was positive. Nevertheless, in 9 of these 15 specimens procoagulant activity was present. In all specimens increased amounts of SFMC were found.

The precise mechanism for the activation of the coagulation system following ascitic fluid reinfusion remains to be established. In addition to stimulation of macrophages by endotoxin other factors like tissue thromboplastin release from tumor cells or injured tissues may account for the procoagulant activity of ascitic fluid.

0733

PROSTANOIDS AND ENDOTOXAEMIA IN THE MINI-PIG. J. Westwick, S. Krishnamurthi, M. Scully, Y. Newman, P. Webb, V.V. Kakkar. Thrombosis Research Unit, King's College Hospital Medical School, London, England.

Infusion (iv) of endotoxin (E coli 0111 B4) at a conc. of 1, 10, 100 or 1000ng/kg/min into mini-pigs with sampling every 20 mins produced a dose related fall in WBC, platelets, blood pressure (BP) and early large increases in plasma thromboxane (Tx) B_2 with only minor changes in plasma 6-oxo-$PGF_{1\alpha}$ conc. In 5 pigs endotoxin infusion at 100 ng/kg/min for 40 min produced elevated plasma levels of TxB_2 from pre-infusion value of 40±5 to 750±50pg/ml, while WBC, platelets and BP expressed as % of pre-infusion value were 40±8, 81±6 and 105±5% respectively. At the end of the endotoxin infusion (100 min) plasma TxB_2 had decreased to 120±10pg/ml; WBC, platelets and BP were 22±4, 62±4, 63±5% of pre-infusion value. In 5 other pigs receiving saline only, no significant changes in any of the above parameters were observed.

Thus there is an excess of thromboxane production compared to PGI_2 in endotoxaemia. We attempted to determine the contribution of this prostanoid imbalance to endotoxaemia, by treating groups of 5 to 9 mini-pigs with either PGI_2 (125 ng/kg/min, continuously), or a potent and selective Tx synthesis inhibitor, UK, 37, 248 (7.5mg/kg as a bolus 10 min before) or lignocaine (20mg/kg as bolus 10 mins before followed by an infusion of 2mg/min) prior to endotoxin infusion. Both PGI_2 and lignocaine maintained the BP at pre-endotoxin values, but did not have a significant effect on the leucopenia and thrombocytopaenia or on the elevation of plasma TxB_2. While the Tx synthesis inhibitor produced a significant ($p<0.05$) but not a maximum inhibition of the drop in BP, a marked inhibition of plasma TxB_2 formation, but with no effect on the leucopenia or thrombocytopaenia induced by the endotoxin infusion.

Although Tx formation is a sensitive indicator of endotoxaemia and precedes the development of hypotension, it is not contributory to the thrombocytopaenia or the leucopenia. However both PGI_2 and the Tx synthesis inhibitor by correcting the prostanoid balance appear to be therapeutically useful in endotoxaemia.