Title: CHANGES IN LIPOPOLYSACCHARIDE CONCENTRATIONS IN HEPATIC PORTAL AND SYSTEMIC ARTERIAL PLASMA DURING INTESTINAL ISCHEMIA IN MONKEYS

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Introduction. Lipopolysaccharides (LPS), also known as endotoxins or pyrogens, are highly toxic components of the outer cell membrane of gram-negative bacteria which are always found in mammalian intestines. The permeability properties of the gut wall normally prevent the leakage of this toxic LPS into the circulation. The barrier to endotoxin can be broken down by a wide variety of causes such as ischemia[1], hyperthermia[2], ionizing radiation[3], hypoxia[4] and hemorrhagic enteritis[5]. In man, the mortality as a result of endotoxemia is still at an unacceptably high rate 30-80%[6]. Intestinal ischemia produced by the occlusion of the superior mesenteric artery (SMA) is a useful model for studying the pathophysiological changes which are associated with endotoxin shock. Related studies, using feline[7] and primate[8] superior mesenteric artery occlusion (SMAO) shock models, have shown the time course of changes in LPS concentration in the systemic arterial plasma. The elevated plasma LPS levels seen in these studies is thought to originate from the gut. However, the quantitative relationships in time between intestinal insult and hepatic portal and systemic plasma LPS concentrations have not yet been reported.

Method. Four adolescent monkeys were anesthetized with ketamine. Catheters were inserted into a femoral vein (for fluid and drug infusion), and both femoral arteries (for removal of blood samples and for recording of blood pressure respectively.) Rectal temperature was monitored continuously using a telethermometer. The abdominal cavity was opened and the SMA identified and a "Medican" 16G catheter was inserted into the hepatic portal vein for removal of blood samples. 30 min were allowed for recovery before baseline blood samples were taken from the femoral artery and the portal vein. The SMA was then clamped for 1 hr and blood samples were taken simultaneously as above at 20 min intervals during this hour. Blood samples were taken at 5-20 min during the 2 hr reperfusion period. Blood samples were collected into heparinized, pyrogen-free tubes at 0^{o}C.

The plasma samples were analysed using the chromogenic substrate modification of the LAL test[9]. Statistical analysis was done using paired and unpaired student's t-tests.

Results. The LPS concentration before occlusion of the SMA in the hepatic portal and systemic arterial circulation were 0.071 $\pm$ 0.005 and 0.077 $\pm$ 0.009 ng/ml respectively. At the end of the occlusion period there was no significant increase in either of the two abovementioned parameters. The LPS concentration in the portal plasma increased immediately on removal of the occlusion to peak at 0.445 $\pm$ 0.178 ng/ml ($p < 0.01$) within about 15 min, whereas in the systemic arterial circulation the LPS concentration began to rise after a delay of approximately 10 min to peak at 0.308 $\pm$ 0.176 ng/ml within about 25 min of reperfusion. The mean arterial pressure was found to decline significantly ($p < 0.01$) after the peak LPS concentration was reached in the systemic arterial plasma whilst the heart rate showed a small but insignificant increase.

Conclusion. These data show that portal endotoxemia occurs within 5 min of reperfusion following SMAO while systemic endotoxemia lags by 10 min and therefore the origin of the increased plasma LPS is from the gut. This has great therapeutic implications in possible prevention of endotoxemia and septic shock[8].

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