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Protective effect of pancreatitis-associated protein

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Keywords

Acute phase response, acute respiratory distress syndrome, neutrophils

Comments

This paper provides another piece in the jigsaw puzzle of inflammatory and anti-inflammatory mediators. What remains to be seen is whether these effects occur in more complex models.

Introduction

Severe pancreatitis is associated with lung injury. This lung injury is due to the release of inflammatory mediators resulting in capillary leak and pulmonary oedema. During acute pancreatitis, a secretory protein known as pancreatitis-associated protein (PAP) is secreted and the concentration of PAP correlates with the severity of the disease. High levels of PAP have also been shown to be associated with improvements in outcome, at least in rats.

Aims

To evaluate the effect of PAP in leucocyte induced lung injury. The effects of PAP on pulmonary vascular resistance, oedema formation and the synthesis of thromboxane A_2 (TxA_2) were investigated.

Methods

Isolated perfused rabbit lungs were mounted on a weight transducer. Because of the constant flow of perfusate, changes in perfusion pressure directly reflect changes in pulmonary vascular resistance. Rat PAP was prepared from animals in which pancreatitis had been induced, and was extracted by affinity chromatography. Thirty lung preparations were then randomly assigned to receive either PAP only, be submitted to an inflammatory response with *N* formyl-Met-Leu-Phe (fMLP) only, or two different doses

of PAP followed by activation of leucocytes with fMLP. TxA_2 activation was then measured via the accumulation of the metabolite thromboxane B_2 (TxB_2). Weight gain of the organ preparation and mean pulmonary artery pressure (mpap) were recorded.

Results

The lung preparations exposed to PAP only did not exhibit any gain in weight, TxB_2 release, or change in mpap. Leucocyte activation led to increases in mpap of 26 ± 13 mm Hg in the controls. This was attenuated to 15 ± 7 mm Hg with the lower dose of PAP and 9 ± 4 mm Hg with the higher dose. Weight gain was reduced from 9 g to either 2 g or 1 g at the different doses of PAP. TxB_2levels showed similar diminution following leucocyte activation after administration of PAP.

Discussion

PAP is synthesised during acute pancreatitis and the level of PAP correlates with both the severity of disease and increased survival in rats. This experiment demonstrated that clinically relevant amounts of PAP show protective effects in preventing the leak in pulmonary vasculature and attenuating the rise in mpap. The reduction in mpap may be secondary to the fact that release of TxA_2, a potent pulmonary vasopressor, is attenuated by PAP. Potential problems with the study are the applicabilty of an isolated organ study to the situation *in vivo*, and the fact that rat PAP was used in rabbits (rabbit PAP has yet to be sequenced).

References

1. Heller A, Fiedler F, Schmeck J, Luck V, Iovanna JL, Koch T: Pancreatitis-associated protein protects the lung from leukocyte-induced injury. Anesthesiology. 1999, 91: 1408-1414.