Fresh frozen plasma therapy in acute pancreatitis: an experimental study

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Summary

Fresh frozen plasma therapy was assessed in a rat model of acute haemorrhagic pancreatitis incorporating the facility for continuous intravenous infusion in the unrestrained animal. Infusions including fresh frozen plasma were shown to significantly improve 72 h survival in the model compared to crystalloid (P < 0.001) and colloid (P < 0.05) control groups. The mechanism of this improved survival has yet to be elucidated, but this work supports the establishment of a controlled clinical trial of fresh frozen plasma therapy in this disease.

Introduction

Despite improvements in general supportative measures, the mortality from acute pancreatitis in the United Kingdom still approaches 10%. Although many specific therapies have been proposed for this disease, none has consistently been shown to improve outcome in controlled clinical trials.

In 1983 an uncontrolled clinical study from Cuschieri et al. [1] reported a low mortality from acute pancreatitis (3.7%) in a consecutive series of 239 patients treated with intravenous fresh frozen plasma (FFP) therapy during the first five days of the
illness. The total volume of FFP administered ranged from 6–11 units (1500–2500 ml). When looking for a mechanism to explain this apparent benefit, the colloid value of FFP was not thought to be significant as it represented only 20–30% of colloid administered to severe cases. A possible explanation was that FFP replenished the levels of naturally occurring antiproteases, particularly alpha₂ macroglobulin, thus improving the binding and elimination of the toxic broth of pancreatic enzymes from the tissues and bloodstream.

Before embarking on a clinical trial of FFP therapy in acute pancreatitis, more evidence was sought for a beneficial effect in an animal model of the disease.

Materials and Methods

An animal model of acute pancreatitis

Acute pancreatitis was induced in male albino AS rats weighing 250–300 g using a well-established technique based on that reported by Lankisch et al. [2]. Under general anaesthesia a 24 G Quick-Cath intravenous cannula (Travenol Laboratories Ltd., Castlebar, County Mayo, Ireland) was introduced from the antimesenteric border into the lumen of the duodenum and the teflon cannula was advanced into the oblique opening of the common duct on the mesenteric border of the duodenum. A microvascular clamp was placed on the bile duct at the liver hilum to prevent passage of retrograde infusate into the liver, creating a closed pancreatic ductal system. Two ml/kg rat body weight of a freshly prepared mixture of 0.2% partly purified porcine enterokinase (Sigma Chemical Company Ltd., Poole, Dorset, U.K.) and 3.5% sodium taurocholate (BDH Chemicals Ltd., Poole, Dorset, U.K.) in 150 mmol NaCl was infused into the pancreatic duct system at 3 ml/h from a syringe pump.

At the termination of the infusion, the microvascular clamp and cannula were removed restoring biliary and pancreatic drainage, and the puncture hole in the antimesenteric border of the duodenum was closed with a single 5/0 silk suture. The duodenal loop was returned to the abdominal cavity and the abdominal wall closed.

A system for continuous intravenous infusion in the unrestrained rat

In order to compare the effect of various intravenous fluid regimens on survival of the model, a system for continuous intravenous infusion of fluids was developed. Modifications were made to a system originally described by Lemmel and Good [3] in 1971.

Intravenous infusions were placed in 60 ml sterile syringes mounted on syringe-pumps. Fluid was conducted to the animal along a 90 cm length of fine polyethylene tubing (Portex, internal diameter 0.28 mm, external diameter 0.61 mm, Fisons Medical Equipment, Loughborough, Leicestershire, U.K.) protected by a 40 cm length of flexible coiled stainless steel spring (8 mm external diameter made of 0.5 mm diameter wire with 10 turns per centimetre, Coil Springs, Bevans Holdings, South Wigston,