Intragastric ethanol depresses pancreatic vascular perfusion (PVP) partly via an endothelin-mediated mechanism

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Reduced PVP is known to contribute to the development of necrosis in acute pancreatitis. Acute ethanol consumption can result in acute pancreatitis, however its effects on PVP have not been well characterized. The ethanol-induced change in PVP may involve endothelins. Aim: To investigate the effects of ethanol on PVP *in-vivo* and a possible role for endothelins. Methods: Possums (n=31) were anaesthetised (intravenous thiopentone infusion; 5-10mg/kg/h) for the duration of the experiment. Ethanol was administered via IV infusion (1g/kg in saline over 1 hour) or via intragastric (IG) bolus injection (2g/kg in water). In separate experiments the endothelin antagonist tezosentan (Actelion; 1mg/kg/min at 3ml/hr; n=7) was administered an hour before the IG ethanol and continued for the duration of the experiment. Blood ethanol, blood pressure (BP) and PVP (Laser Doppler fluxmetry) in the head, body and tail of the pancreas were monitored over 4 hours. Results: IV and IG ethanol increased blood ethanol levels peaking at 253 ± 76 mg/100mL (n=7) and 275 ± 45 mg/100mL; (n=9) respectively. IV ethanol did not significantly change BP or PVP. In contrast, IG ethanol decreased PVP in the head, body and tail after 1h to 61 ± 7, 58 ± 5 and 47 ± 9% of baseline respectively. Generally PVP began to recover towards baseline from about 2.5 hours post-ethanol administration, however there was no significant effect on BP. IV saline (n=7) and IG water (n=8) did not alter BP or PVP. Treatment with tezosentan appears to block the ethanol-induced fall in PVP. Conclusion: These data suggest that IG ethanol depresses PVP, which could facilitate pancreatic damage. The tezosentan data suggest that at least part of the ethanol-induced PVP response is mediated by endothelins.

Supported in part by the NH&MRC of Australia (229901).