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Clinical hepatology

P01 THE EFFECT OF INTRAOPERATIVE N-ACETYLCYSTEINE ON HEPATOCELLULAR INJURY DURING LAPAROSCOPIC BARIATRIC SURGERY: A RANDOMISED CONTROLLED TRIAL

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Introduction The combination of pneumoperitoneum and intra-operative retraction of the left lobe of the liver leads to hepatocellular injury during laparoscopic oesophago-gastric surgery, with often more than a sixfold rise in serum transaminases. Fatty livers are more susceptible to ischaemic insults and increased oxidative stress.

Aim The aim of the study was to investigate whether the antioxidant N-acetylcysteine (NAC) could reduce liver injury during laparoscopic sleeve gastrectomy.

Method Patients undergoing laparoscopic sleeve gastrectomy were allocated to receive intraoperative NAC infusion or standard anaesthetic treatment in a single blind randomised controlled trial. Blood samples were taken before and at the end of surgery and on post-operative days 1–4. Primary endpoints included serum aminotransferases and clinical outcomes. Secondary measures were markers of oxidative stress (superoxide dismutase, lipid peroxidation (TBARS) and liver injury (cytokeratin-18 M30 and M65) and plasma TRAIL and FasL for apoptosis.

Results 20 patients (14 females, median age 44 (27–64) years, median BMI 62 (39–83) kg/m²) were recruited; NAC n=10, control n=10. Demographic parameters and baseline liver function were similar [pre-op ALT NAC median 25 U/ml (IQR 24–42) vs control 30.5 (29–44)]. The peak rise in liver enzymes was on day 1, but the levels were not significantly different between the groups. ALT: NAC median 126 (IQR 73–627) vs control 136 (107–239); AST: NAC 130 IU/l (68–504) vs Control 124 (72–237). There were no significant differences in day 1 superoxide dismutase (NAC 0.48 pg/ml vs Control 0.66), TBARS (NAC 8.84 nmol/ml vs Control 12.47), CK18-M30 (NAC 340 U/l vs 471) and CK18-M65 (NAC 803.5 U/l vs 878). There was a significant reduction in TRAIL and FasL after POD1 (TRAIL pre-op 100.6 pg/ml day 138.8, p<0.01; FasL pre-op 94.6 pg/ml vs POD1 67.5, p<0.01), but there were no significant differences between the treatment groups. Rates of complications and length of stay were not significantly different.

Conclusion NAC was not shown reduce intraoperative liver injury in this small number of patients. The heterogenous nature of the bariatric patient population, with differences in comorbidities, body mass index and intra-abdominal anatomy, makes this difficult. Significant hepatocyte injury does occur through both necrosis and apoptosis, which does not appear to be mediated by TRAIL or FasL.

P02 APOPTOSIS IN PARACETAMOL-INDUCED ACUTE LIVER FAILURE: IMPORTANCE OF EXTRA-HEPATIC ORGAN DYSFUNCTION

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Introduction Both necrotic and apoptotic hepatocyte death pathways have been implicated in paracetamol induced ALF (PALF). Elevated circulating levels of M30, a marker of caspase-3 activation,

Abstract P02 Figure 1 Regional levels of M30 (marker of cleaved cytokeratin-18) in four cases of Paracetamol-induced acute liver failure.

have been demonstrated in this condition and are postulated to reflect hepatocellular apoptosis. This novel marker has also been reported to have clinical utility as a prognostic indicator in ALF. However, published results are conflicting and it remains unclear whether significant hepatocyte apoptosis is clinically relevant in PALF.

Aim To investigate the role of hepatocyte apoptosis in PALF.

Method Serum M30 levels were quantified by ELISA (Peviva, Bromma, Sweden) in 62 patients with PALF (34 spontaneous survivors (S) and 28 OLT or died (D)). Control groups of 10 healthy volunteers and 20 chronic HCV patients were used for comparison. Clinical outcome measures in PALF were correlated with M30 levels. In four patients undergoing transplantation for PALF, blood was sampled from the hepatic vein (HV), portal vein (PV) and a systemic artery and serum levels of M30 quantified as above. A focused proteome apoptosis array was performed on liver homogenates from 4 PALF cases and 4 controls. Protein was quantified using a modified Lowry assay and concentrations normalised. Array films were scanned and analysed in ImageJ. H&E stained liver sections from AALF patients were examined for histological evidence of apoptosis.

Results Serum M30 levels were significantly elevated in PALF (3970 IU/l) compared with both healthy volunteers (144 IU/l) and HCV patients (170 IU/l) (p<0.001). Serum levels of M30 were significantly elevated in PALF-D compared to PALF-S (5199 vs 2357 IU/l; p<0.0005). There was a transportal gradient of M30 in all patients tested, with highest levels in the PV and lowest in the HV

Abstract P02 Figure 2 Downregulation of apoptosis-associated proteins in AALF patients (n=4) compared with controls (n=4).