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TITLE: THE EFFECTS OF GRADED HEMORRHAGE ON LIVER OXYGENATION AND ETHANOL CLEARANCE

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Hemorrhagic shock results in a redistribution of cardiac output from peripheral tissues (skeletal muscle, the splanchnic bed, skin) to vital organs (heart, lungs, brain). Severe blood loss will cause vasoconstriction in the splanchnic bed. The effects are usually measured as changes in mean arterial blood pressure (MAP), heart rate and blood gases (all centrally obtained data). However, centrally measured data may not reflect changes in individual organs.

The present study was undertaken in an attempt to relate ethanol clearance (Cl_{EtOH}), as a marker of liver function during graded hemorrhage, to liver oxygenation (p_tO_2) and MAP.

Sprague-Dawley rats, anesthetized with pentobarbital, were bled in a stepwise fashion, and liver pO_2 MAP and Cl_{EtOH} were recorded at MAP = control, 100, 80, 70, 60, 50 and 40mmHg, respectively. Liver tissue oxygenation was measured with the 8-channel MDO oxygen electrode placed directly on the exposed liver surface[1]. In the first group of 6 rats liver pO_2 was measured every 10 sec. The second group (also 6 rats) was used to measure Cl_{EtOH} using the same graded hemorrhage protocol, but in steps lasting 30 min. A plasma ethanol concentration of 22mM was maintained using a constant rate infusion. Cl_{EtOH} at each blood pressure level was calculated from the difference between the infusion rate and EtOH accumulation rate.

Results

MAP (mmHg)	Cl_{EtOH} (umol/kg/min)	p_tO_2 (mmHg)
120	217	20.5±2.7
100	218	15.8±2.5
80	85	9.9±3.8
70	--	5.6±2.0
60	11	2.1±1.1
50	--	2.3±0.9
40	0	1.3±0.9

The results indicate that liver pO_2 decreases in a fairly linear fashion from control to approx. 10% of control as MAP decreases from control to 60mmHg. Interestingly, tissue pO_2 was 50% of control at MAP 80mmHg, and 25% of control at MAP 70mmHg. These data suggest a strong relationship between MAP and liver surface pO_2, therefore, liver pO_2 may be mostly blood flow dependent at MAPs greater than 60mmHg.

Clearance of EtOH began to decline at MAPs below 100mmHg, and ceased at liver pO_2s less than 2mmHg and at MAPs lower than 60mmHg. These data indicate a good correlation between liver oxygenation and clearance of ethanol, and show that even small blood pressure reductions affect liver metabolism of EtOH.

Reference

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TITLE: GLUCOSE/INSULIN DECREASES POTASSIUM LEVEL IN ANHEPATIC PATIENTS.

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Significant hyperkalemia is frequently seen in patients undergoing orthotopic liver transplantation (OLT), especially during massive transfusion and immediately after reperfusion of the grafted liver (1). In healthy human volunteers and in patients with renal failure, insulin and glucose effectively lowers serum potassium levels (K^+) (2,3). However, the effectiveness of the treatment is unknown in patients undergoing OLT who are resistant to insulin (4) and have marginal or no hepatic function.

After institutional approval and informed consent, 34 adult patients presenting for OLT with serum K^+ levels greater than 4.0 mEq/L at the onset of the anhepatic stage were studied. Patients with diabetes mellitus and for retransplantation were excluded. Anesthetic and monitoring techniques have been described previously (5). The patients were randomized to one of two groups. Group 1 patients received only Plasmalyte (500 mL), and served as controls. Group 2 patients received a bolus of regular insulin (20 u, IV) and a glucose infusion (500 mL of D_5W) over 5 min during the early anhepatic stage. Serum levels of K^+ and glucose levels were determined at the following intervals: 5 min before (GI-5') and 5, 10, 15, 30, 45, and 60 min after the administration of glucose/insulin (GI+5', GI+10', GI+15', GI+30', GI+45', and GI+60') and 30 sec and 5 and 30 min after graft reperfusion (III+30", III+5', and III+30'). Statistical analysis was performed using one factor ANOVA and ANOVA for repeated measures, with statistical significance at $p < 0.05$. Values are presented as mean ± SD.

In group 1, K^+ did not change during the anhepatic stage (Fig 1). K^+ increased 30 sec after reperfusion, but returned to baseline at 5 and 30 min after reperfusion. In group 2, K^+ decreased during the anhepatic stage, and were lower than in group 1 within 15 min and lower than its baseline value within 30 min of the glucose/insulin administration. Although the K^+ increased 30 sec after reperfusion in all patients, its level was lower in group 2 (5.94 vs 7.28 mEq/L, respectively). No treatment related adnormality blood glucose or serum potassium level abnormality were seen.

The results of this study show that glucose/insulin administration can significantly lower the serum potassium levels even in anhepatic patients. This regimen can be used to treat hyperkalemia in patients undergoing OLT to mitigate the ill effects of hyperkalemia on the cardiovascular system. The mechanisms of action of glucose/insulin in decreasing potassium levels in the absence of the liver remains to be studied.

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