The Liver Response to Hemorrhagic Shock and Subsequent Resuscitation –fMRI analysis

[3]Matot .I and ,[1]Barash .H ,[2]Pappo .O ,[1]Abramovitch .R
,.Pathology Dept[2] ,Israel ,Jerusalem ,Hadassah Hebrew University Medical Center ,Goldyne Savad Institute for Gene Therapy[1]
ssah Hebrew University Hada ,Critical Care &Anesthesiology [3] ,Israel ,Jerusalem ,Hadassah Hebrew University Medical Center
lIsrae ,Jerusalem ,Medical Center

Background/ Aims:
The liver is a target for injury in low flow states associated with trauma and hemorrhage. Even after initial successful resuscitation, liver damage may persist for a prolonged period. Currently, there is an ongoing discussion regarding resuscitation strategies. Markers of liver injury are either invasive or not rapidly responding. MRI may offer an innovative, noninvasive and clinically relevant alternative to evaluate liver injury. We recently demonstrated the feasibility of fMRI utilizing hypercapnia and hyperoxia for monitoring changes in liver perfusion and the distribution of arterial vs. portal blood[1] without contrast agent administration. In the present study, we aimed to characterize the liver response to hemorrhagic shock and subsequent resuscitation as assessed by fMRI.

Methods:
Animal: Experiments were performed on male Sabra rats (390±50g). Catheters were inserted into both femoral veins and arteries for measurements of blood pressure, for bleeding (1 ml/min) and for administration of resuscitation. *Experimental groups (n= 5-8/group): Control group (CG):* Rats underwent sham operation. *Hemorrhagic shock group (HSG):* blood volume withdrawal was performed to mean arterial pressure (MAP) of 25±3mmHg (35% of the rat's blood volume). *Resuscitation groups:* 10 min following controlled hemorrhage, rats were resuscitated with Ringer Lactate (RL; 60 ml/h) or Adrenalin (Ad; 1.2 ml/h) to MAP of 50mmHg or to pre-hemorrhage (baseline BL) MAP. Rats were sacrificed 6h later. Blood was withdrawn for liver enzymes assessment (ALT, AST and ALP) and livers were excised for histology and TUNEL analysis. ***MRI:*** Experiments were preformed on a 4.7T Bruker Biospec spectrometer using a bird cage coil. Changes in hepatic hemodynamics were evaluated from T_2* weighted GE images (TR/TE=147/10ms) acquired during breathing of air, air-CO_2 (5% CO_2), and carbogen as described previously[1]. MRI was acquired: at baseline, after controlled hemorrhage and after resuscitation.

Results and Discussion:
ΔSo_2 and ΔSco_2 values of the livers (% change in signal-intensity due to hyperoxia and hypercapnia, respectively) in the CG were 22±9% and -20±10%, respectively (Fig 1A). Hemorrhagic shock caused significant decrease in ΔSo_2 values (4±1%), while the mean value of ΔSco_2 (-4±1%) was significantly higher (Fig 1A; HSG), suggesting a decrease in red blood cell volume and vascular reactivity resulting from the physiological response of the body to hypovolemia. fMRI performed immediately after resuscitation revealed that adrenalin infusion (to 50MAP or to BL pressures) improved liver perfusion as reflected by the significant increase in ΔS values, while RL did not improve perfusion significantly (Fig 1A). Within each resuscitative intervention, no significant differences in liver perfusion were noted when comparing resuscitation to low (50) vs high (BL) MAP. Rat's liver enzymes levels did not increase immediately after induction of hemorrhagic shock, and significant elevations were observed only 6 hours later (Fig 1B). Only adrenalin resuscitation lowered the elevated levels of ALT and AST significantly compared to those measured 6 hours following RL resuscitation or hemorrhagic shock (Fig 1B).

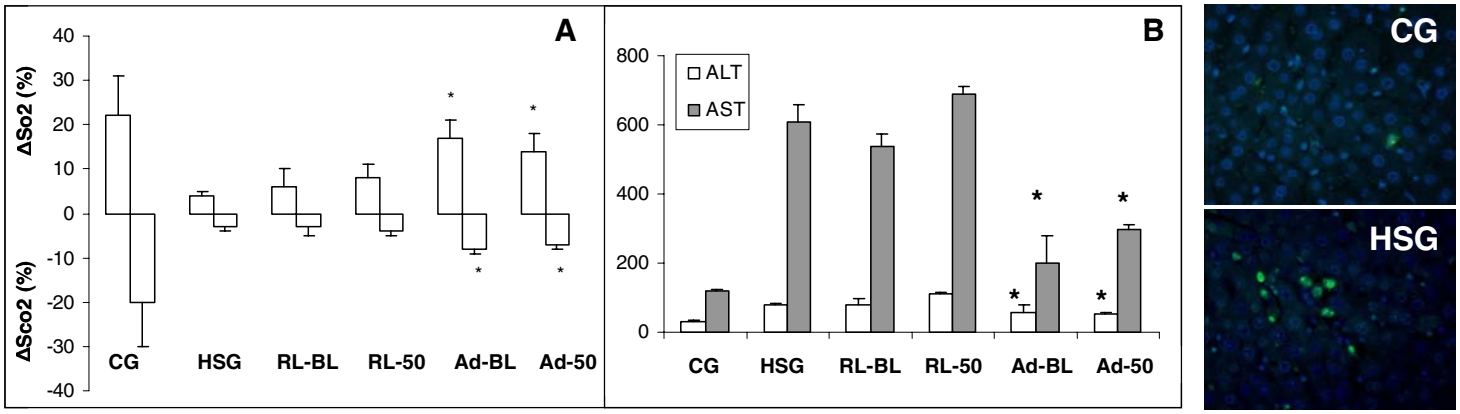

Figure 1: Effect of hemorrhagic shock and resuscitation with RL or adrenalin on mean ΔSo_2 and mean ΔSco_2 values (A) as obtained immediately and on liver enzymes levels (B) as measured 6hr later. (ALT-Alanine aminotransferase; AST-aspartate aminotransferase). Right- Representative TUNEL assay of liver sections from CG and HSG.

Evidence of apoptosis and cell injury could only be found 6 hours following hemorrhagic shock. In the HSG liver damage manifested by fatty changes, and diffuse acidophilic bodies was observed. Adrenalin treatment, but not RL, attenuated liver injury and apoptosis.

In summary, only fMRI proved to be sensitive to *early* changes in liver perfusion that contribute to liver damage and therefore, it may be considered as a noninvasive, rapidly-responding tool to monitor liver outcome subsequent to hemorrhage and resuscitation. Using fMRI we demonstrated that during hemorrhagic shock, adrenalin may be preferable to RL as an initial measure to attenuate liver injury.

References: 1. Barash H, Gross E, Matot I, Edrei Y, Tsarfaty G, Spira G, Vlodavsky I, Galun E, Abramovitch R.; [2006] Radiology in press.