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SHOCK 2025 Annual Conference

Saturday, May 31, 2025

01:05 PM-02:30 PM

Grand Ballroom (Mezz.)

Plenary Session 1: Prehospital Trauma Resuscitation and Results of Recent Clinical Trials

Moderator(s): Rosemary Kozar, Manabu Kinoshita

Capillary Perfusing Targeting Oxygen Transfer in Prehospital Shock Resuscitation

Martin Mangino

Virginia Commonwealth University, Richmond, Virginia, United States

Role of Coagulation Factor Concentrates for Trauma Resuscitation

Martin Schreiber

Oregon Health & Science University, Portland, Oregon, United States

Recent Clinical Trials of Blood Products for Prehospital Acute Trauma Resuscitation

Jason L. Sperry

University of Pittsburgh, Pittsburgh, Pennsylvania, United States

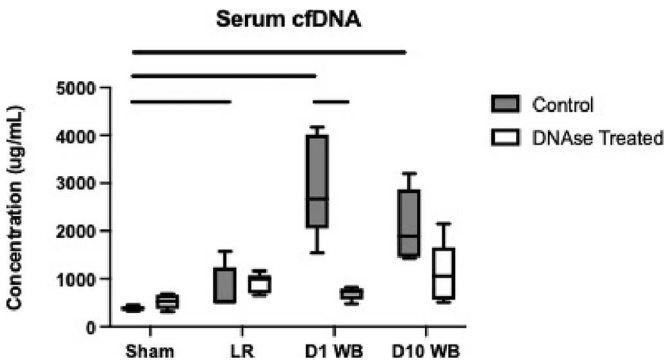
DNASE TREATMENT ATTENUATES SERUM CELL FREE DNA AFTER POLYTRAUMA AND RESUSCITATION

Lindsey Wattley, Ellen Becker, Gregory C. Wetmore, Rebecca M. Schuster, Lisa England, Charles C. Caldwell, Michael Goodman, and Timothy A. Pritts. University of Cincinnati, Cincinnati, Ohio, United States

Introduction: Prior studies have shown that cell free DNA (cfDNA) is increased in serum after trauma, likely due to formation of neutrophil extracellular traps (NETs) in response to stress and inflammation. NETosis after trauma is associated with increased inflammation and immune-related thrombosis. The effect of different resuscitation strategies on NETosis has not been evaluated. We hypothesized (1) that the serum cfDNA after polytrauma, shock and resuscitation would vary amongst resuscitation strategies and (2) that treatment with DNAse would decrease the cfDNA response to trauma.

Methods: 10- to 12-week-old C57BL/6 male mice underwent polytrauma (laparotomy, rectus crush, splenic laceration, splenectomy) and pressure-controlled hemorrhagic shock followed by resuscitation with lactated Ringers (LR), or murine whole blood stored for 1 or 10 days. Immediately following resuscitation mice were treated with or without DNAse via intraperitoneal injection. Mice were euthanized after one hour and serum was collected. Serum cfDNA was assessed using Quant-It PicoGreen dsDNA assay kit.

Results: Polytrauma mice resuscitated with any strategy demonstrated higher levels of cfDNA compared to sham mice. Resuscitation with whole blood led to increased cfDNA compared to resuscitation with LR. DNAse treatment alone did not change cfDNA levels in sham mice. However, DNAse treatment decreased the cfDNA response in mice to day 1 WB but not day 10 WB. (Figure)



Conclusions: Whole blood resuscitation leads to increased cfDNA after polytrauma, but this effect may be attenuated with DNAse treatment after resuscitation. cfDNA in whole blood increases over time during storage, however, the cfDNA response in mice is more pronounced after resuscitation with day one whole blood versus day 10 whole blood. This response could be attributed to more viable leukocytes in day one whole blood leading to increased NETosis and a stronger cfDNA response.

PREHOSPITAL ADMINISTRATION OF 25% ALBUMIN OR PLASMA MAINTAINS MITOCHONDRIAL RESPIRATORY CAPACITY IN RATS WITH DECOMPENSATED HEMORRHAGIC SHOCK

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Introduction: Plasma (PL) and 25% albumin (AB) are frequently used for prehospital resuscitation in traumatic hemorrhagic shock (THS). Both improve survival prior to whole blood resuscitation, yet their effects on mitochondrial function, essential for cellular metabolism and organ viability, remain underexplored. Mitochondrial dysfunction plays a critical role in multi-organ failure following trauma. This study evaluates the impact of PL and AB on mitochondrial respiratory capacity and oxidative phosphorylation (OXPHOS) in liver, kidney, and skeletal muscle tissues in a rat model of hemorrhagic shock.

Methods: Isoflurane-anesthetized male Sprague-Dawley rats were subjected to hemorrhage (65% of estimated blood volume [EBV]) following a fixed-volume protocol: 40% in 2 minutes (min), 40% in 8 min, and 20% over 10 min. At 20 min post-hemorrhage, rats were randomized into one of four groups to receive PL (20% EBV), AB (4% EBV), or PL or AB followed by fresh whole blood (FWB, 20% EBV) after 1 hour (hr). Blood samples were collected for lactate and creatinine measurements. At 4 hr, liver, kidney, and tibialis anterior muscle tissues were harvested, and mitochondrial function was assessed using high-resolution respirometry (Oroboros Oxygraph 2 K). Mitochondrial respiration was measured after tissue permeabilization with digitonin. Substrates were added to stimulate OXPHOS, and oxygen consumption recorded after adding ADP to activate complex I and succinate for complex II. Maximal respiratory capacity (MAX state) assessed after adding oligomycin and titrating FCCP. Samples normalized based on tissue wet weight (mg). Data analyzed using a two-sample t-test, significance set at $P < 0.05$.

Results: At 4 hr, mean arterial pressure (MAP) was 35 ± 3 mmHg. PL or AB administration significantly improved MAP (PL: 80 ± 7 and AB: 77 ± 12 mmHg). Fresh whole blood resuscitation (FWB) at 1 hr further increased MAP (PL-FWB: 106 ± 22 and AB-FWB: 112 ± 15 mmHg). Additionally, lactate and creatinine levels were lower in the PL/AB-FWB groups. Mitochondrial respiratory function assessed in liver and kidney displayed no significant differences in functionality between PL and AB groups, with or without FWB. In skeletal muscle, PL significantly improved OXPHOS compared to AB (PL: 73 ± 27 vs. AB: 27 ± 7 pmol O2/second/mg, $p = 0.008$). FWB fully attenuated this difference.

Conclusions: In trauma settings where whole blood may not be immediately available, shelf-stable products such as freeze-dried plasma (FDP) and hyperoncotic 25% albumin may offer important resuscitation alternatives. These products improve survival and support mitochondrial function in critical tissues, potentially reducing morbidity. Our findings suggest that FDP and 25% albumin can enhance mitochondrial function in multiple tissues, with or without FWB resuscitation.

PREHOSPITAL LYOPHILIZED CRYOPRECIPITATE IMPROVES COAGULATION FUNCTION AND BLOOD PRESSURE COMPARED TO CRYSTALLOID IN A NONHUMAN PRIMATE POLYTRAUMA HEMORRHAGE MODEL

Clifford G. Morgan[1], Erica M. Molina[1], Leslie E. Neidert[1], Ha N. Choe[2], Jeffrey D. Biberston1, Brendan S. O'Brien[1], Philip C. Spinella[3], Emily Mihalko[3], and Susan Shea[3]. [1]Expeditionary & Trauma Medicine, Naval Medical Research Unit San Antonio, Fort Sam

Introduction: 40-60% of mechanically ventilated (MV) patients develop long-term cognitive impairment. Preclinical studies reveal that infection elicits the production of beta amyloid within the lung, which disseminates to peripheral organs, including the brain. These beta amyloid variants can have either antimicrobial properties or be cytotoxic to the host. We hypothesized that higher beta amyloid in the plasma of septic patients would be associated with greater severity of cognitive impairment.

Methods: The MENDS2 multi-site RCT enrolled MV patients with sepsis to sedation with dexmedetomidine or propofol. We measured beta amyloid 38, 40, and 42 using a Meso Scale Discovery ELISA plate (4D8 antibody) on ICU Day 3. Patients underwent a validated telephone interview for cognitive status (TICS-T) exam at 6 months that assessed memory and executive function. Normal TICS-T scores are 50 ± 10. TICS-T scores of approximately 35 denote mild cognitive impairment and scores of less than 25 are consistent with severe cognitive impairment. We studied the associations of beta amyloid concentrations with TICS-T scores using linear regression adjusted for age, APACHE score, and mental status.

Results: In the 88 patients enrolled at Vanderbilt, the mean ± SEM values for beta amyloid 38 (Ab_{x-38}), 40 (Ab_{x-40}), and 42 (Ab_{x-42}) among all patients were 680.8 ± 1215 pg/mL, 280 ± 158.9 pg/mL, and 46 ± 47.2 pg/mL, respectively, which are approximately three times higher than those in healthy controls (data not shown). The average TICS-T score for the cohort at 6 months was 39 ± 13.8. Forty-one percent of patients scored below 35 and 11% of the patients scored below 25. Beta amyloid concentrations differed among patients depending on their TICS scores (see Table 1). In our multivariable analysis of beta amyloid we were unable to demonstrate a statistically significant association between Ab_{x-38} ($p = 0.13$), Ab_{x-40} ($p = 0.06$), and Ab_{x-42} ($p = 0.07$) and TICS scores.

Conclusions: While beta amyloid concentrations in our cohort of septic patients were higher than levels in healthy controls, we found no association between higher levels and more severe neurocognitive impairment. Contrary to our hypothesis, those with lower levels of beta amyloid showed trends towards more severe cognitive impairment. Future studies should elucidate the trajectories of beta amyloid in sepsis and its role in cognition.

Beta Amyloid In Relation to TICS-T Score

AUTOREGULATION OF BLOOD FLOW IN A RAT MODEL OF SEPTIC SHOCK

Alexandre A. Steiner[1], Eduardo Moretti[1], Deymisson Feitosa[1], Grover Guzman[2], Abner Rodrigues[2], Luiz Baccala[3], and Andre Fujita[2]. [1]Universidade de Sao Paulo Instituto de Ciencias Biomedicas, São Paulo, SP, Brazil, [2]Universidade de Sao Paulo Instituto de Matematica e Estatistica, São Paulo, SP, Brazil, [3]Universidade de Sao Paulo Escola Politecnica, Universidade de Sao Paulo Escola Politecnica, São Paulo, SP, BR, academic/eng, São Paulo, SP, Brazil

Introduction: A recent study has called attention to the possibility that the tissue autoregulation of blood flow may play a role in the development of hypotension in a rat model of endotoxic shock. The hypothesis is that prioritization of the local mechanisms of blood flow regulation over the brain-driven mechanisms of pressure regulation (baroreflex) underscore the early development of hypotension in this model. The next logical step is to test this hypothesis in animal models of systemic inflammation induced by live bacteria.

Methods: In the present study, we evaluated hemodynamics with the highest possible temporal resolution as well as proxies of dynamic autoregulation in rats subjected to cecal ligation and perforation (CLP).

Results: Four sequential hemodynamic profiles were uncovered by this approach: in PROFILE 1, flow (Q) and pressure (P) fell while total peripheral resistance (R) remained stable; in PROFILE 2, there was an increase in R, which resulted in a partial recovery in P, but worsened the drop in Q; in PROFILE 3, there was a drop in R associated with a recovery in Q, while P remained relatively stable at a level below baseline (stable hypotension); and in PROFILE 4, a rapid fall in Q initiated a terminal phase in which R gradually increased in an uncompensated fashion (no recovery in P and terminal fall in Q). Of these, PROFILE 3 resembles the alterations that were associated with heightened autoregulation in the model of endotoxic shock. Dynamic autoregulation was then evaluated in PROFILE 3 using frequency-domain analyses of squared coherence and partial dependent coherence. Contrary to our expectation, though, coherence was unaffected at the time corresponding to this hemodynamic profile, and partial dependent coherence was even weakened.

Conclusions: These findings indicate that there are fundamental differences in autoregulatory control during the hypotensive responses induced by endotoxin (LPS) and cecal ligation and perforation (CLP).

	Sham	HS+ Vehicle	HS+ Enoblock
ALT (IU/L)	8.2 ± 1.2	90.9 ± 14.4*	58.1 ± 3.8#
AST (IU/L)	53.0 ± 4.8	330.5 ± 11.4*	275.7 ± 11.9#
IL-6 (pg/ml)	1.0 ± 0.0	1180 ± 456*	154.4 ± 79.5#
IL-6 mRNA (fold change)	1.1 ± 0.2	12.2 ± 3.6*	3.9 ± 1.3#
TNF-α mRNA (fold change)	1.1 ± 0.1	12.1 ± 2.9*	2.1 ± 0.5#
IL-1β mRNA (fold change)	1.1 ± 0.2	21.0 ± 6.1*	8.3 ± 4.4
KC mRNA (fold change)	1.0 ± 0.1	179.5 ± 25.5*	91.9 ± 31.9#
MIP-2 mRNA (fold change)	1.0 ± 0.1	5.3 ± 1.6*	1.2 ± 0.4#

The data are analyzed by one-way-ANOVA and represented as mean ± SE. *p

COMPARATIVE ANALYSIS OF EXTRACTION METHODS OF EXTRACELLULAR VESICLES IN SERUM AND PLASMA OF CHILDREN WITH SEPSIS

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Introduction: Sepsis is a systemic response to an infection and causes significant mortality in pediatric intensive care units. Small extracellular vesicles (EVs) are nanoparticles (30-150 nm) that play a pivotal role for cell-to-cell communication through transferring of their cargo content, thus affecting both physiological cellular functions and inflammatory processes. In the context of liquid biopsy, EVs offer a minimally invasive method for disease diagnosis and monitoring. To investigate cargo and function of EVs, many methods have been developed to enrich EVs from biological fluids based on their physical, biochemical, and affinity properties. However, these methods have yet to be standardized for efficiency and purity of extraction. In a clinical observational study, we investigated whether EV levels are elevated in plasma and serum from children with sepsis and whether they are associated with severity of organ failure. We also compared the efficiency of EV isolation by ultracentrifugation or phosphatidylserine(PS)-affinity enrichment strategy.

Methods: De-identified frozen plasma and serum samples of 48 children were obtained from the Cincinnati Children's Hospital Medical Center Discover Together Biobank (control non-septic patients) and the Critical Care Medicine Biorepository (patients with sepsis). All samples were collected (on day 1 of enrollement and day 3) under Institutional Review Board approved protocols. Plasma and serum EV were isolated by ultracentrifugation and PS-affinity method. Efficiency, size distribution and concentration of EVs were determined by nanoparticle tracking analysis.

Results: Independently of the extraction method, higher concentrations of EVs (at least 2.5-fold) were counted in serum samples compared to plasma samples, which aligns with the observation that retrieved vesicles are consistently more abundant in serum than in plasma. The concentration of serum-derived EVs was significantly higher in patients with sepsis both