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The Effects of Class IV Hemorrhagic Hypotensive Shock and Its Resuscitation with Fluids and Adjuvant Vasopressors or Cellular Energy Replenishment on the Splanchnic Microcirculation

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Background

Traumatic exsanguination leading to class IV hemorrhagic shock as defined by the Committee on Trauma of the American College of Surgeons requires aggressive resuscitation with crystalloids and packed cells together with the temporary administration of either norepinephrine or vasopressin to manage a persistent hypotension that is not corrected by aggressive fluid resuscitation. However, the use of vasopressors in the resuscitation from hemorrhagic hypovolemic shock is controversial as these drugs may worsen the pre-existing splanchnic hypoperfusion by virtue of their vascular action. In previous intravital microscopy studies of the terminal ileum in rats, we demonstrated that adequate resuscitation which restores and maintains central hemodynamics, as clinical end-points of resuscitation, does not restore or maintain splanchnic tissue perfusion, which instead exhibits a persistent and progressive intestinal microvascular vasoconstriction and end-organ tissue hypoperfusion. In other intravital microscopy studies we have shown that resuscitation from hemorrhagic shock with small volumes of hypertonic saline does not restore or maintain the pre-hemorrhage blood pressure, but selectively prevent the post-resuscitation vasoconstriction of the pre-mucosal pre-capillary arterioles of the terminal ileum. In contrast, the replenishment of the hemorrhage-induced depletion of endothelial energy stores with vitasol, restored the pre-hemorrhage arterial pressure and selectively prevented the post-resuscitation vasoconstriction of the pre-mucosal pre-capillary arterioles suggesting a positive inotropic effect of vitasol. Therefore, such inotropic action merits the administration of vitasol during

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fluid resuscitation from severe hemorrhagic shock. It is well established that hemorrhagic shock profoundly depletes cellular adenosine nucleotides. This depletion occurs as the hemorrhage-induced splanchnic hypoperfusion decreases the supply of oxygen to end-organ tissue and cells, resulting in failure of ATP generation by oxidative phosphorylation and the activation of the alternative cellular ATP generation from the low yield anaerobic glycolysis pathway. Studies designed to directly assess the status of the splanchnic microcirculation during severe hemorrhage shock and its resuscitation is scant. As the ischemic hypoperfused gut is central in the pathophysiology of shock and largely determine resuscitation outcome, we were prompted to use our intravital microscopy technology to directly examine the intestinal microvasculature response to traumatic exsanguinations and during their resuscitations with either norepinephrine or vasopressin as opposed to direct cytosolic energy replenishment.

Methods

Anesthetized male Sprague-Dawley rats underwent initial venous withdrawal of 30% of the calculated animal's blood volume over 15 min (shed blood preserved in heparin-rinsed syringe for later resuscitation). This was followed by phase-2 of uncontrolled hemorrhage as induced by transection of the splenic parenchyma at the two ends of the organ and severing one of the branches of the splenic artery. The transected organ was returned to the abdominal cavity for free arterial and venous bleeding until class IV hemorrhage is achieved [defined by persistent mean arterial pressure, MAP < 40 mmHg, and a shock index (ratio of heart rate and systolic arterial pressure), SI ≥ 5 for successive 10 minutes during the period of active uncontrolled bleeding]. Following this, homeostasis was established by rapid ligation of the splenic pedicle and the animals were assigned to 4 resuscitation groups: 1) Conventional resuscitation (shed blood returned + double the shed blood volume as lactated Ringers, CR); or adjuvant resuscitations with: 2) CR + norepinephrine; 3) CR + vasopressin; and 4) CR + vitasol. Four-level, A1 through A4 arterioles in the terminal ileum were examined with Intravital Microscopy and their diameters timely measured at baseline, during shock, and during 2h post-resuscitation.

Results

There were no differences between the four groups in pre-hemorrhage baseline metabolic parameters, blood gases and acid base status. In all four groups, class IV hemorrhagic shock remarkably decreased hemoglobin, hematocrit and produced a metabolic acidosis characterized by low pH, PCO2, HCO3, TCO2 and an increase in the base deficit as compared with the baseline pre-hemorrhage levels. None of the four resuscitation methods restored parameters of the metabolic panel or blood gases and acidosis to pre-hemorrhage baseline levels. Class IV hemorrhagic shock caused differential arteriole responses with vasoconstriction from baseline of A1 and A2 ($-22.1 \pm 1.9\%$), and vasodilation of the A3 and A4 arterioles ($+22.2 \pm 2.8\%$). Resuscitation initially restored A1 and A2 diameters to near baseline. This was followed by post-resuscitation A1 and A2 vasoconstriction in all groups except in the vitasol group ($-8.1 \pm 3.4\%$). The hemorrhage-induced vasodilation of the A3 and A4 arterioles was maintained during the post-resuscitation observation period in the CR ($+55.3 \pm 6.4\%$) and the vitasol groups ($+39.5 \pm 5.2\%$), but remarkably attenuated in the norepinephrine ($+9.6 \pm 5.8\%$) and vasopressin ($+9.4 \pm 8.8$) groups.

Conclusions

The temporary administration of norepinephrine or vasopressin as adjuvants to fluid resuscitation from severe hemorrhagic shock has deleterious effects on the splanchnic microcirculation. Endothelial cell resuscitation by cytosolic energy replenishment produces better metabolic and microvascular profiles as compared with adjuvant vasopressor resuscitation.