Systemic and Microcirculatory Effects of Severe Hemorrhage and Resuscitation Using a Hemoglobin-Based Oxygen Carrier (HBOC)

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This study investigated the systemic (heart rate, mean arterial pressure) and microcirculatory (vasoactivity, interstitial fluid oxygenation - ISF PO\(_2\)) impact of two resuscitation fluids: a novel third generation HBOC (Sanguinate\textsuperscript{TM}; Prolong Pharmaceuticals\textsuperscript{TM}, South Plainfield, NJ), and a non-oxygen carrying colloid volume control (Hextend\textsuperscript{TM}; Hospira, Inc, Lake Forest, IL). Male Sprague-Dawley rats underwent a controlled 45% blood volume hemorrhage at 3.5 ml x min\(^{-1}\) x kg\(^{-1}\) through a cannulated carotid artery and were maintained in this hypovolemic, hemorrhagic shock phase for 30 minutes. Resuscitation fluids were infused at a rate of 3.5 ml x min\(^{-1}\) x kg\(^{-1}\) to a volume equal to 20% of the total estimated blood volume through a cannulated jugular vein. Systemic measurements were recorded via a cannulated femoral artery that was connected to a pressure transducer (MP150; Biopac Systems, Inc, Goleta, CA) while microcirculatory parameters were collected through phosphorescence quenching and intravital microscopic examination of the exteriorized spinotrapezius muscle. Compared to baseline, the 45% hemorrhage produced a significant reduction in heart rate, blood pressure, arterial diameter and ISF PO\(_2\) in all animals. Resuscitation with either HBOC or Hextend\textsuperscript{TM} animals improved the systemic parameters towards baseline, but only HBOC-treated animals showed an improvement in ISF PO\(_2\). The impact of improved systemic variables was evident in mortality with untreated animals (sham) expiring an hour after hemorrhage, while Hextend resuscitated animals expired after 4 hours. HBOC animals survived for the entire 8 hour observation period. In addition to extended survival times, HBOC animals showed steady systemic and microcirculatory parameters. Hextend\textsuperscript{TM} resuscitated animals, however, developed rigor mortis in their limbs at approximately 3 hours post-hemorrhage, which was concurrent with a rapid decline in systemic variables. These results demonstrate that while reestablishing blood pressure is acutely important
for post-hemorrhage survival, restoring oxygen delivery to peripheral tissues is critical for improving long-term outcomes.

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