The Pathophysiology of Compartment Syndrome: The Contribution of Inflammation to Muscle Injury in a Leukocyte Deplete Rodent Model

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Introduction: Increased intracompartmental pressure results in tissue ischemia and cell death. The pathophysiologic mechanism by which compartment syndrome (CS) cell damage is not well understood. This study was designed to measure the effects of increased intracompartmental pressure on skeletal muscle microcirculation, inflammation, and cell viability using intravital videomicroscopy in a neutropenic rodent model.

Materials and Methods: Forty male Wistar rats (175–250 g) were randomized into two groups, control vs neutropenia. Twenty rats were injected with high dose cyclophosphamide (250mg/kg) and rendered neutropenic. Blood chemistry was drawn to ensure neutropenia at 72 hours post injection. The animals were anesthetized with isoflurane. Carotid artery was cannulated to monitor mean arterial pressure. Compartment syndrome was induced by saline infusion into the anterior compartment of the hind limb. Compartment pressure was controlled between 30–40mmHg and maintained for either 0, 15, 45 or 90 minute intervals. Following reperfusion via fasciotomy, the extensor digitorum longus muscle was exposed and visualized using Intravital Videomicroscopy (IVVM) to quantify the number of perfused capillaries as a measure of microvascular dysfunction. White cell recruitment including adherent and rolling leukocytes were quantified to measure the inflammatory response. Irreversible muscle cellular injury was measured using a fluorescent vital dye labeling the nuclei of severely injured cells.

Results: There was a reduction in the capillary perfusion in the muscle exposed to increased intercompartmental pressure. The number of continuously perfused capillaries decreased as the duration of compartment syndrome increased compared to controls (p < 0.05). The number of capillaries not perfusing following fasciotomy increased with increased duration of CS between experimental groups. The proportion of injured cells decreased in neutropenic animals as compared to non-leukocyte deplete animals in the 0, 15-, 45-, and 90-min compartment syndrome groups respectively (p<0.05).

Discussion: Increasing the duration of compartment syndrome results in a marked decrease in capillary perfusion from continuously perfused muscle in the control group to an intermittent or to a non-perfused profile in the experimental groups. Muscle ischemia is evidenced by irreversible cell damage. A severe acute inflammatory component was detected in compartment syndrome; the role of inflammation in muscle damage in compartment syndrome is unknown but is believed to be a driving force in the generation of cell injury and reduced capillary perfusion. Neutropenia was protective against cell injury in all experimental groups.
