The Effects of C1 Esterase Inhibitor and Hydrogen Sulfide on Ischemia/Reperfusion Injury in a Microvascular Porcine Model of Vascularized Composite Tissue Transplantation

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Abstract
Background: Devastating extremity injuries are prevalent but most often survivable on the modern battlefield. The complexity of these injuries requires advanced methods of reconstruction. This study validated the feasibility of gracilis myocutaneous flap transplantation via microvascular free tissue transfer in a porcine model. The physiologic insult, however, from ischemia and reperfusion injury pose as challenges to tissue/flap viability. This model will facilitate study of vascularized composite auto-transplant physiology and the roles of solutions with properties shown to mitigate the effects of ischemia and reperfusion injury. Ultimately, this model will provide a platform for evolving methods for reconstructing previously non-reconstructable injuries.

Material and Methods: A donor gracilis myocutaneous flap is procured from Yorkshire swine. The right external carotid artery and internal jugular vein are prepared as the recipient axis for microvascular anastomoses. Group 1 undergoes immediate microvascular anastamosis with resultant 1 hour ischemic period. Group 2 undergoes delayed anastamosis with 3 hour ischemic period. Group 3 undergoes a 3 hour ischemic period during which time the flap receives an interim perfusion of c1 esterase inhibitor solution. Similarly, Group 4 undergoes the same ischemic time as Group 3 with an interim perfusion of hydrogen sulfide. Markers of ischemia-reperfusion injury (CK, LDH, AST) are evaluated following anastamosis and on post-operative days 1, 2, 7 and 14.

Results: A novel porcine model for microvascular composite tissue transplantation is demonstrated. Ischemia-period dependent elevations in circulating biomarkers (LDH, CK, and AST) demonstrate the effects of prolonged ischemia. Control groups (1& 2) showed marked LDH elevation without significant statistical intergroup difference (p=0.250). Treatment groups (3 & 4) showed a significant decrease in LDH levels compared to the controls. Similarly, there was a notable difference in the levels of CK and AST levels when comparing control and treatment groups.

Conclusions: A novel method of vascularized gracilis myocutaneous flap transplantation was validated in the Yorkshire swine. Assays for skeletal muscle tissue injury (LDH, CK, and AST) showed ischemia-period dependent response providing assessment of ischemia-reperfusion injury at the cellular level in the control groups. Interim perfusion with c1 esterase inhibitor and hydrogen sulfide demonstrated an improvement in markers of ischemia-reperfusion injury. Subsequent studies will transition these findings to potentiate vascularized composite allo-transplantation.