Systemic Glucose-Insulin-Potassium Reduces Skeletal Muscle Injury, Kidney Injury, and Pain in a Murine Ischemia-Reperfusion Model

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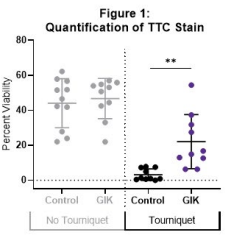
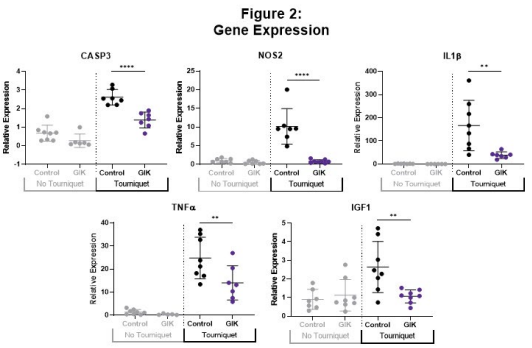
Purpose: Glucose-insulin-potassium (GIK) protects cardiac muscle from ischemia reperfusion (IR) injury; however, GIK's ability to protect skeletal muscle from IR injury is unknown. Given the similarities between cardiac and skeletal muscle, we hypothesized that GIK would reduce skeletal muscle damage and thus kidney injury following extremity IR injury.

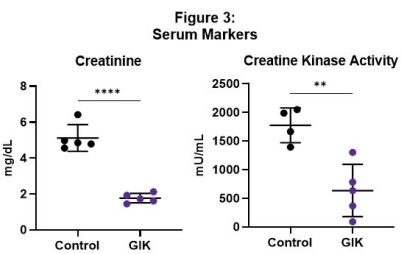
Methods: 20 C57BL/6 mice (10 control, 10 GIK) sustained IR injury (2.5-hour ischemia, 24-hour reperfusion) using a hindlimb rubber band tourniquet. From tourniquet placement until euthanasia, continuous subcutaneous osmotic pumps infused either saline control (0.9% sodium chloride) or GIK (40% glucose, 50 U/L insulin, 80 mEq/L KCl, pH 4.5) at 16 μL/hr. At sacrifice, skeletal muscle viability (triphenyltetrazolium chloride [TTC]) and gene expression were analyzed, serum creatinine and creatine kinase activity were measured, and a validated murine ethogram was used to quantify pain before euthanasia.

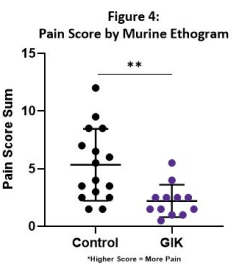
Results: GIK treatment resulted in a significant protection of skeletal muscle with increased viability (GIK 22.1%) compared to saline control (control 3.1%) ($P = 0.006$) (Fig. 1), a significant reduction in gene expression markers of cell death (caspase 3 [CASP3], $P<0.001$) and inflammation (nitric oxide synthase 2 [NOS2], $P<0.001$; interleukin [IL]1β, $P = 0.002$; tumor necrosis factor [TNF]α, $P = 0.012$; insulin-like growth factor [IGF]1, $p=0.007$) (Fig. 2), and a significant reduction in serum creatinine ($P<0.0001$) and serum creatine kinase activity ($P = 0.0037$) (Fig. 3). Lastly, GIK led to a significant reduction in IR-related pain ($P = 0.003$) (Fig. 4).

Conclusion: Systemic GIK infusion protects murine skeletal muscle from cell death, kidneys from reperfusion metabolites, and reduces pain following IR injury through reducing post-ischemic inflammation. Future human studies are required to evaluate GIK's role in elective and traumatic orthopaedic settings.









See the meeting app for complete listing of authors' disclosure information. Schedule and presenters subject to change.