Functional and morphological recovery of skeletal muscles from mast cell depleted mice after ischaemia reperfusion injury

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Ischaemia Reperfusion (IR) injury of skeletal muscle is a significant cause of morbidity following traumatic injury and a major complication after replantation of severed limbs. Mast cells are a pivotal upstream effector in the pathogenesis of IR injury to murine skeletal muscles [1]. Following 70 min ischaemia and 24 h reperfusion, muscles from mast cell-depleted mice (MCD) were more resistant to IR injury than normal congenic littermates (65.2% vs 18.5% viability by NBT assay). We examined muscle functional properties and morphology during recovery from IR injury and tested the hypothesis that muscles from MCD mice would exhibit better recovery than muscles from littermate controls. The mice were anaesthetised (i.p. injection of 4% chloral hydrate, 10mg/kg) and the hind limbs underwent tourniquet ischaemia at 36^{o}C for 70 min, after which the mice were allowed to recover during reperfusion. At the relevant reperfusion times, mice were re-anaesthetised, tissue removed and the mice then sacrificed. Morphology of the extensor digitorum longus muscle was assessed at time points between 2 and 21 d and function was assessed *in vitro* at 21 d post-injury using established methods. Muscle morphology was qualitatively similar between MCD and littermate controls. At 2 d post-injury, the muscle parenchyma was composed of both healthy and necrotic fibres and infiltrated by inflammatory cells. Necrotic fibres were surrounded by desmin-positive myoblasts and myotubes with central nuclei. The proportion of healthy fibres decreased progressively between 14-21 d and the proportion of centrally nucleated fibres increased. Although force per cross-sectional area of injured muscles was 61.3% of uninjured values for MCD mice compared with 46.0% for normal littermates, no other differences in contractile parameters were evident. The unexpected similarity in structural and functional recovery between MCD and normal littermates suggests that muscle viability does not predict long term morphologic and functional recovery after IR injury.

(1) Bortolotto SK, Morrison WA, Han X, Messina A. Lab. Invest 2004: 84(9), 1103-1111.