Intramuscular injection of the β-agonist formoterol enhances muscle regeneration in rats after myotoxic injury

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Developing therapies to enhance muscle regeneration is critical for improving the physical outcome of patients suffering muscle injuries. Systemic administration of β-adrenoceptor agonists to rats exerts an anabolic action on skeletal muscle and hastens recovery of function after injury, but clinical application has so far been limited by side effects, such as cardiac hypertrophy. We tested the hypothesis that intramuscular (i.m.) injection of the β-agonist, formoterol, could improve functional muscle repair after bupivacaine-induced injury in rats without causing deleterious effects on the heart. Adult rats were anaesthetised (ketamine 100 mg/kg and xylazine 10 mg/kg, i.p.) and the right EDL muscle was surgically exposed and injected with bupivacaine to destroy all fibres. The left EDL muscle served as the uninjured control. At 5 days post-injury, rats received either an i.m. injection of formoterol (100 μg) into the regenerating muscle, or allowed to recover without treatment. After myotoxic injury, functional recovery was assessed *in vitro* at 7, 10, 14, and 21 days post-injury. Rats were anaesthetised (as described above) for excision of muscles and then killed by cardiac excision. At 7 days post-injury, formoterol treated muscles had 19% greater mass, 50% greater maximum force, and 51% greater average fibre cross-sectional area, than untreated muscles. There were no differences in these parameters at later times. A single i.m. injection of formoterol enhanced early regeneration and the absence of cardiac hypertrophy suggested that this was a safe mode of administration with potential therapeutic application. Treatment efficacy will likely depend on multiple injections during recovery.

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