Comparison of injury and repair in mouse skeletal muscle after treatment with the myotoxic agents, bupivacaine or notexin

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The anaesthetic bupivacaine hydrochloride and the toxic component of tiger snake venom, notexin, are myotoxins regularly employed in experimental muscle research for studying muscle regeneration. Muscle degeneration and regeneration after myotoxic injury (bupivacaine and notexin) are well characterised in rats but not mice. Our aim was to compare functional and morphological properties of regenerating mouse skeletal muscle after notexin or bupivacaine injection. Mice were anaesthetised with an intraperitoneal (i.p.) injection of sodium pentobarbital (60 mg/kg) and the extensor digitorum longus muscle of the right hindlimb of male C57BL/10 mice was injected to maximal holding capacity with either bupivacaine or notexin. The left EDL muscle was not injected and served as the uninjured control. Muscle degeneration/regeneration was examined at 3, 7 or 10 days post-injury from assessments of morphology using standard histological and immunohistochemical techniques, and function (maximum force, P_o). Mice were anaesthetised with sodium pentobarbital (60 mg/kg, i.p) and the muscles excised for examination. The mice were killed by cardiac excision whilst still anaesthetised deeply. At 3 days post-injury, bupivacaine caused degeneration of only ~45% of muscle fibres and reduced P_o to ~42% of uninjured muscles. In contrast, notexin caused complete fibre breakdown and obliterated all functional capacity. At 7 days post-injury, P_o of bupivacaine-injured muscles was ~65% that of control, whereas notexin-injured muscles only produced ~10% P_o of control. By 10 days, P_o of bupivacaine-injured muscles was ~71% of control, and P_o of notexin-injured muscles was ~39% of control. At 7 and 10 days post bupivacaine injury, ~30% of muscle cross-sections contained centrally nucleated fibres, characteristic of successful muscle regeneration. In contrast, 7 and 10 days following notexin injury, 100% of the total muscle cross-section contained centrally nucleated fibres. Our results demonstrate that in mice notexin causes more severe muscle injury than bupivacaine, and is therefore a more suitable model of experimental injury for studying muscle regeneration.

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