LONG TERM MODEL OF BOTULINUM TOXIN-INDUCED MUSCLE WEAKNESS IN THE RABBIT

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Introduction

Muscle weakness is one of the earliest and most common symptoms of patients with osteoarthritis (OA) (1). Although many experimental models of OA include muscular weakness, no model has studied this factor satisfactorily for long periods of time. The purpose of this study was to assess muscle weakness over a period of six months in order to validate an experimental model of muscle weakness for future use in the study of OA.

Methods

Muscle weakness was produced by monthly injections of the neurotoxin clostridium botulinum type A (BTX-A) in the quadriceps muscle of six New Zealand white rabbits. Muscle weakness was assessed by calculating the difference in knee extensor torque between experimental and contralateral hind limb (which was injected with a saline solution). Knee extensor torques were obtained at three different knee angles with a custom-built force sensor bar placed distally on the tibia. Knee extensor torque was produced with supramaximal stimulation (100 Hz, 500 ms) of the quadriceps muscles through the femoral nerve. Maximum isometric knee extensor torque was recorded at multiple knee angles in order to investigate if muscle weakness between hind limbs persists over a physiological range of motion. Muscle mass of the rectus femoris, vastus lateralis, vastus intermedius and vastus medialis muscles was evaluated post mortem using a commercial scale with an accuracy of 0.001g. All outcome measures are reported as relative percent deficits, comparing the BTX-A injected hind limb to the contralateral (sham) hind limb.

Results and Discussion

Muscle weakness across all three tested knee angles was approximately 60%, suggesting that BTX-A had a similar effect across the physiological range of motion and produced weakness over the six months testing protocol (Figure 1).

Atrophy, measured as the deficit in muscle mass between experimental and control limbs, was greatest for the vastus lateralis and smallest for the vastus medialis (Figure 2). This difference in atrophy may represent a difference in fiber type composition between the quadriceps muscles. BTX-A has been reported to have a greater effect on fast-twitch (type II) muscle fibers (2).

Conclusions

Monthly injections of BTX-A, a potent neuromuscular blocking agent, over a six months period, created a chronic functional muscle weakness model in the New Zealand white rabbit. This model may be used to systematically study the possible effects of muscle weakness on joint degeneration, either as an isolated intervention, or in combination with other interventions known to create knee joint degeneration.

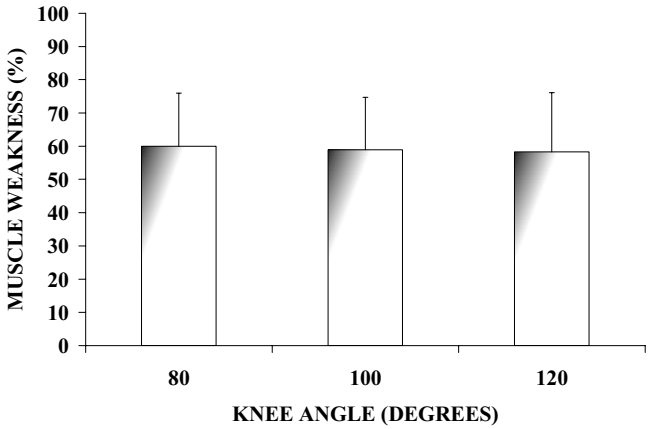

Figure 1. Muscle weakness (mean and standard deviation) of the knee extensor muscles obtained at three different joint angles.

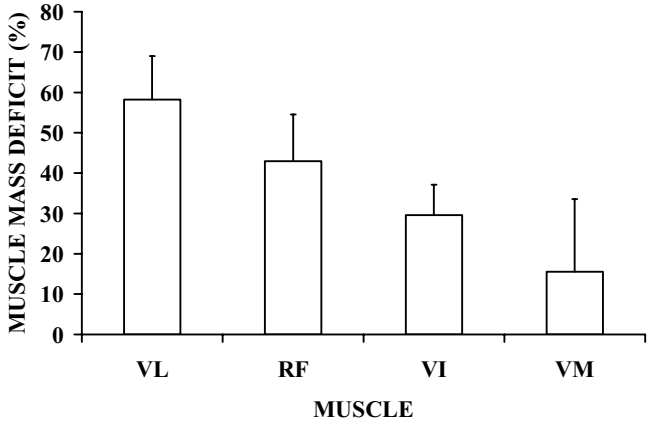

Figure 2. Muscle mass deficit (mean and standard deviation) of the knee extensor muscles (VL = vastus lateralis; RF = rectus femoris; VI = vastus intermedius; VM = vastus medialis).

References

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Acknowledgements

The Canadian Institutes of Health Research (CIHR), The Canada Research Chair Programme, CAPES-Brazil, UFRGS-Brazil.