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PASSIVE SKELETAL MUSCLE MECHANICS AND STRUCTURE CHANGES FOLLOWING BOTOX INJECTIONS

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INTRODUCTION

Spasticity is a symptom often found in neuromuscular diseases such as Cerebral Palsy (CP). Spasticity is characterised by involuntary muscular contractions caused by lesions in the brain developed at or just after birth [1]. Spasticity, over time, causes increased passive stiffness and hypoextensibility [2]. A current treatment to provide temporary relief from spasticity is the application of botulinum toxin type-A (BTXA) injections. BTXA is a neurotoxin that prevents the release of acetylcholine at neuromuscular junctions, therefore relaxing the muscle [3]. Recent literature suggests that BTXA decreases passive stiffness by changing skeletal muscle structural components [3]. These include changes to connective tissue such as collagen structure, contractile proteins such as myosin, as well as structural proteins such as titin [3]. Unfortunately, there is limited information regarding these changes to skeletal muscle structural components caused by BTXA despite being used clinically [3]. There is limited literature of the effects of short term BTXA on passive mechanics in skeletal muscle [3]. Therefore, the purpose of this experiment was to obtain a deeper understanding of the effects of BTXA injections on skeletal muscle properties first in passive mechanic changes and secondly through structural changes during an acute 5 day protocol.

METHODS

A New Zealand white rabbit animal model (n=4) was used. One hind limb acted as the experimental leg and the contralateral leg acted as the control. A pre- and post-test for passive force was performed using a minimally traumatic pin and motor system, once before a BTXA injection (3.5u/kg) and once 5 days after injection. Each test consisted of 5 trials, each with 3 movements (25°/sec). The BTXA was divided into 4 doses and injected intramuscularly into 4 quadrants of the lower limb plantar flexors (proximal medial, proximal lateral, distal medial and distal lateral) of the experimental limb. When the post-test was completed the rabbits were euthanized and the hind limbs extracted for future tissue work.

RESULTS

Two rabbits showed a trend of decreasing passive force after BTXA, like the example showed in Figure 1, and two rabbits showed a trend of increasing passive force after BTXA. No changes from the pre- to post- test results were statistically significant. There was also no statistical difference in passive forces when all four were considered.

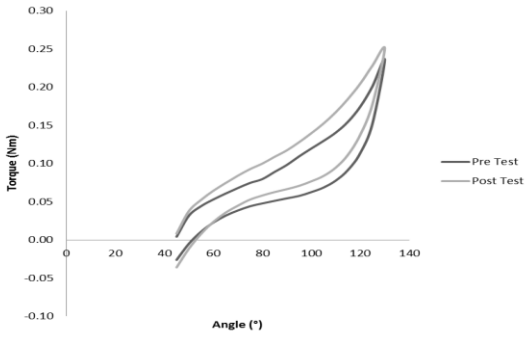

Figure 1. Passive torque vs. ankle joint graph for one rabbit showing a decrease in passive force from pre-test to post-test recording. A paired sample t-test determined that there was no difference in passive force between pre- and post-test measurements across all animals.

DISCUSSION AND CONCLUSIONS

Our results show that BTXA does not change passive force. If these results are accurate, despite being an effective tool in preventing spasticity, BTXA would need to be supplemented with other treatments to improve on stiffness and hypoextensibility in CP patients. However previous literature suggests that passive force decreases with the injection of BTXA [3], therefore possibilities why this did not occur may be due to: the amount of BTXA injected, the number of rabbits, and the sensitivity of our equipment. In the future we will continue to test changes in passive force using two additional rabbits to increase the sample size, as well as use the extracted tissue from each rabbit to run titin isoform tests, collagen content tests, and sarcomere count tests to observe if BTXA caused changes in the skeletal muscle structure itself.

REFERENCES

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