The Effects of Electrical Stimulation on Muscle Injected with Botulinum Toxin A (Botox)

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INTRODUCTION

Botulinum toxin type A (BTX-A) is a frequently used treatment in neuromuscular disorders characterized by increased neuromuscular activity such as in cerebral palsy (CP) and following stroke [1]. BTX-A acts by preventing the release of acetylcholine at the neuromuscular junction, creating a chemical denervation and muscle paralysis [1,2,3]. The beneficial effects of BTX-A injections are well recognized [1]. However, recent works have shown that BTX-A treatment has specific adverse effects causing muscle atrophy, strength loss, fat invasion, and loss of contractile material in target and non-target muscles [2,3]. We speculated that these adverse effects might be prevented if BTX-A injected muscles could be strengthened through regular exercise. However, because of the denervation induced by BTX-A, voluntary exercise is precluded, but direct muscle electrical stimulation (ES) is possible and may offer an opportunity to limit or prevent many of the adverse effects created by BTX-A treatment.

Therefore, the purpose of this study was to determine the effects of direct muscle ES on strength, mass, and contractile material of the quadriceps femoris muscles of New Zealand White (NZW) rabbits.

METHODS

Seventeen, one year old, female NZW rabbits were divided into three groups as follows: Control (n=5), BTX-A (n=5), and BTX-A+ES groups (n=7). Control group rabbits received saline injections. Rabbits in both BTX-A groups received monthly BTX-A injections (3.5U/Kg) into the left quadriceps femoris for six months. In addition, the BTX-A+ES group was exposed to three weekly ES training sessions for the BTX-A injected muscles (15min of cyclic activation, 0.5s on and 1.5s off at 20% of maximal muscle activation).

Outcome measures included knee extensor strength, muscle mass and the percentage of contractile material. Mass and strength were assessed by weighing the muscles and measuring the maximal isometric strength across the physiological knee joint range of motion. The percentage of contractile material was determined histologically by quantifying the area fraction of the contractile material compared to the total muscle cross-sectional area.

A 3 way-ANOVA with the main factors leg (injected and non-injected contralateral control) groups (Control, Experimental BTX-A without ES, and Experiment BTX-A with ES Groups) and muscles (vastus lateralis, rectus femoris, and vastus medialis) was performed using a level of significance of 0.05.

RESULTS AND DISCUSSION

Electrical stimulation partially preserved muscle strength in target and non-target muscles of BTX-A+ES compared to BTX-A group rabbits (p<0.05; Fig 1).

Muscle mass in target muscles was significantly greater for the BTX-A+ES compared to BTX-A group rabbits (p<0.05). Furthermore, muscle mass for the non-target muscles of the BTX-A+ES group reached control group values (p>0.05; Fig 2). Muscle mass preservation was muscle specific, being greater for the vastus lateralis than the remaining muscles (results not shown).

Contractile material was found to be around 96% for Control group rabbits. Contractile material was
significantly decreased \( p<0.05 \) for the target (43\% ±9.7) and non-target vastus lateralis (74\% ±6.5\%) in BTX-A group rabbits. For BTX-A+ES group, loss of contractile material was significantly greater \( (p<0.05) \) in the injected limb (28\% loss) compared to the contralateral limb (4\% loss) (Figure 3; \( p<0.05 \)), showing that ES partially and fully preserved the contractile material in target and non-target muscles, respectively.

**CONCLUSIONS**

Direct electrical stimulation of BTX-A injected muscles partially preserves strength, mass and contractile material in target muscles and completely preserves muscle mass and contractile material in non-target muscles far removed from the injection site. These results suggest that low level direct electrical stimulation might be a valuable treatment companion to BTX-A treatments, allowing for the beneficial effects of the treatment while simultaneously limiting adverse effects in target muscles and eliminating adverse effects in non-target muscles.

**REFERENCES**