INTRODUCTION

Botulinum toxin type-A (BTX-A) is a frequently used treatment modality to relax spastic muscles by preventing acetylcholine release at the motor endplate [1]. Although considered safe, previous studies have suggested that BTX-A injections cause severe atrophy and muscle degeneration in target and non-target muscles [2]. BTX-A treatments often comprise multiple injections separated by 3-4 months due to the time limited action of the toxin. Depending on the injection/recovery protocol, muscle function may be compromised following a period of BTX-A treatments. However, muscle recovery following repeat BTX-A injections is anecdotal with no systematic research backing of clinical claims. Therefore, the purpose of this study was to investigate if muscle properties and structure fully recover within six months following a six months BTX-A treatment protocol.

METHODS

Twenty-seven skeletally mature NZW rabbits were divided into 5 groups: Control (n=5), BTX-A+0M (n=5), BTX-A+1M (n=5), BTX-A+3M (n=5), BTX-A+6M (n=7). Control group animals received equal volume saline injections. Experimental group animals received monthly BTX-A injections (3.5U/kg) unilaterally for six months, and were evaluated after 0, 1, 3, and 6 months of recovery (BTX-A+0M/+1M/+3M/+6M). Outcome measures included isometric knee extensor strength, muscle mass, and area fraction of contractile material in injected and non-injected muscles. Muscle mass and strength were assessed by weighing the muscles and measuring the maximal isometric strength via femoral nerve stimulation. The percentage of contractile material was determined histologically by the area fraction of contractile material to total muscle cross-sectional area. A 2 way-ANOVA with main factors leg (injected and non-injected contralateral) and groups (Control, BTX-A+0M/+1M/+3M/+6M) was performed (α=0.05).

RESULTS

Muscle strength was partially and completely recovered in the injected and non-injected hind limbs for BTX-A+6M group animals, respectively. Peak strength was reached after 1 month of recovery (BTX-A+1M), with no further recovery at 3 and 6 months (Fig 1). Muscle mass recovered in a similar manner to strength (results not shown). The area fraction of contractile material in control group animals was 96%. The area fraction of contractile material in injected hind limbs for the 6 month recovery animals but not for the 1 and 3 months recovery animals. The percent area fraction of contractile material showed no recovery in the 1, 3, and 6 months recovery group animals compared to the 0 months recovery animals (Fig 2).

DISCUSSION AND CONCLUSIONS

Muscle strength, mass and percent contractile material following a six months BTX-A treatment protocol did not fully recover in injected and contralateral non-injected quadriceps muscles of rabbits. While strength and mass recovered to a certain degree, there was no apparent improvement of the percentage of contractile material, suggesting that strength/mass recovery occur at a different rate than recovery of structure. Since structure is typically not evaluated in patients receiving BTX-A treatments, measurements of strength, volume and mass may not appropriately reflect the long-term structural damage in muscles following BTX-A treatment.

REFERENCES


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