**Botulinum toxin for hereditary spastic paraplegia: effects on motor and non-motor manifestations**

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**Introduction:** Motor and non-motor manifestations are common, disabling and bothersome features of Hereditary spastic paraplegia (HSP), a heterogeneous group of neurodegenerative disorders characterized by progressive spasticity and weakness of the lower limbs. Botulinum toxin type A (Btx-A) is considered an effective and first-line treatment for spasticity. Therefore we intent to assess the efficacy of Btx-A in patients with HSP.

**Materials and Methods:** Thirty-three Brazilian patients with pure and complicated HSP were evaluated before and after the administration of Btx-A by the Spastic Paraplegia Rating Scale, Modified Fatigue Impact Scale, Epworth Sleepiness Scale, Brief Pain Inventory, Beck Depression Inventory, Modified Ashworth Scale, Medical Research Council scale and walking speed for 10 meters.

**Results:** Mean age of patients was 41.7 ±13.6 years and there were 18 women.Most patients had a pure phenotype and *SPG4* was the most frequent genotype (45.4%). Btx-A applications resulted in decrease of spasticity at the adductor muscles, but no other significant motor change. In contrast, patients noticed improved fatigue after the treatment. This study occurred between February/2013 and December/2014.

**Discussion:** In terms of motor manifestations, our study identified hip adductor spasticity improvement as the main result but no significant functional gain, since gait velocity remained stable between applications. This is in contrast to Rousseaux and De Niet who found positive results with Btx-A in comfortable gait velocity, but not in maximum gait speed. We believe that such differences might be due to the different application protocols and also the distinct profile of the patients in each study. The major contribution of this study was the assessment of Btx-A on HSP-related non-motor manifestations. We found a significant improvement of fatigue after treatment, especially its physical domain. So, we hypothesize that Btx-A relieves spasticity, improves the biomechanics of gait and therefore, improves fatigue in these subjects. Pain is another important and frequent non-motor feature of HSP, affecting 73.3% of patients and surprisingly, we were not able to demonstrate significant pain improvement after Btx-A injections. One possible explanation is that this cohort was largely pain-free (mean BPI intensity score <2), so that identification of further improvement was difficult (floor effect). Additionally, injection protocols were different for each patient in terms of doses and application sites. So, we believe that some patients might have improved, whereas others did not. Then, lumping all patients together, we might have lost statistical significance on these effects.

**Conclusion:** In this uncontrolled study, Btx-A resulted in no significant functional motor improvement for HSP, but fatigue improved after treatment. Further controlled studies are needed to determine whether Btx-A is useful for subjects with HSP.

**References:** [1] Rousseaux M et al., Eur J Neurol. 14:206-212, 2007; [2] de Niet M et al., J Rehabil Med. 47:147-153, 2015; [3] Servelhere KR et al., Eur J Neurol. 23:408-411, 2016.