Botulinum toxin A injections improved wrist and finger spasticity after stroke

Brashear A, Gordon MF, Elovic E, et al. **Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke.** N Engl J Med. 2002;347:395-400.

QUESTION

In patients who have had a stroke, is a set of botulinum toxin A (BTA) injections more effective than placebo in improving wrist and finger spasticity?

DESIGN

Randomized (unclear allocation concealment*), blinded (clinicians, patients, and outcome assessors),* placebo-controlled trial with 12-week follow-up (Botox Post-Stroke Spasticity Study Group).

SETTING

19 centers in the United States.

PATIENTS

126 patients who were ≥ 21 years of age (mean age 61 y, 50% men) and had a stroke in the past 6 months; focal spasticity of the wrist and fingers; and evidence of difficulty with hygiene and dressing, pain, or wrist or finger malposition confirmed by a score of 2 or 3 on the Disability Assessment Scale (DAS) (0 = no disability and 3 = severe disability). Exclusion criteria were fixed contracture or muscle atrophy in the spastic limb; treatment of the limb with any botulinum toxin serotype, phenol, alcohol, or surgery; change in oral medication for spasticity in the past 3 months; treatment with intrathecal baclofen or agents affecting neuromuscular transmission; or pregnancy. 122 patients (97%) completed the study.

INTERVENTION

Patients were allocated to 200 to 240 units of BTA (Botox, commercial lot 2024, Allergan, San Diego, CA, USA) (n = 64) or placebo (n = 62). BTA and placebo were administered as 1 set of injections of 50 units into each of 4 wrist and finger muscles with optional injections into 1 or 2 thumb muscles.

MAIN OUTCOME MEASURES

Functional disability at 6 weeks assessed by the DAS. Patients selected 1 of the 4 areas of disability (hygiene, dressing, pain, or limb position) as the principal target of treatment and reported improvement as ≥ 1 point decrease in the DAS.

MAIN RESULTS

At 6 weeks, more patients who received BTA reported improvement in the principal target of treatment than did patients who received placebo (Table). The difference was maintained at 12 weeks (P = 0.02). More patients who received BTA had greater improvement in all areas of disability than did patients who received placebo (Table). The groups did not differ for any adverse effects.

CONCLUSION

In patients who have had a stroke and have wrist and finger spasticity, botulinum toxin A injections improved functional disability.

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*See Glossary.

Botulinum toxin A vs placebo for wrist and finger spasticity at 6 weeks†

Outcomes	Botulinum toxin A	Placebo	RBI (95% CI)	NNT (CI)
Improvement in the principal target of treatment	62%	27%	128% (49 to 262)	3 (2 to 6)
Improvement in all areas of disability	83%	53%	56% (22 to 106)	4 (3 to 8)

†Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

COMMENTARY

The trial by Brashear and colleagues reinforces the results of another randomized trial (1), showing that intramuscular injections of BTA effectively reduce disabling symptoms of focal spasticity of the wrist and finger flexors, such as local pain, poor palm hygiene (e.g., palm maceration, ulceration, and infection), and difficulty positioning the limb for dressing and other activities of daily living.

The benefits of focal BTA injections over oral and intrathecal antispasticity drugs such as baclofen are that they are safe when used in recommended doses by trained personnel, they avoid the systemic and central adverse effects (e.g., sedation) that limit the use of higher doses of medical therapies, and nonrandomized studies suggest that they are more effective in reducing focal muscle spasticity. Furthermore, the antispasticity effects are not permanent in the event of an adverse outcome, unlike phenol injections and surgical resection of dorsal nerve roots (rhizotomy).

The caveats are that effective and tolerable BTA administration is operator-dependent and arguably technique-dependent (e.g., electromyography-guided injections), the capacity to treat large groups of spastic muscles is restricted by dose limitations, the procedure needs to be repeated about every 3 months to maintain effectiveness, the toxin and specialist's time are expensive, and the treatment is not a panacea—it is merely an adjunct to regular physical therapy.

Further research is required to determine whether the effectiveness of BTA for focal spasticity in the upper limb can be generalized to the lower limb in stroke patients whose gait is affected; to more precisely characterize which patients are likely to benefit; to see whether treating focal spasticity translates into long-term functional improvement; to ascertain the relevance of neutralizing antibodies to long-term efficacy and outcome; and to evaluate the cost-effectiveness of regular, long-term injections of BTA, which are consuming increasing quantities of neurologists' time.

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Reference

1. **Bhakta BB, Cozens JA, Chamberlain MA, Bamford JM.** Impact of botulinum toxin type A on disability and carer burden due to arm spasticity after stroke: a randomised double blind placebo controlled trial. J Neurol Neurosurg Psychiatry. 2000;69:217-21.