Geste antagoniste: Infiltration of its trigger point with Botulinum neurotoxin type A in cervical dystonia

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ABSTRACT

**Introduction.** Sensory components, as pain and the geste antagoniste (GA), are present in dystonia; GA temporarily diminishes the abnormal movement. Intramuscular botulinum neurotoxin (IM BoNT) is an efficacious treatment for cervical dystonia (CD) and also for some sensory conditions, such as postherpetic neuralgia and diabetic neuropathy.

**Hypothesis.** This work tried to assess whether subcutaneous BoNT (SCBoNT), applied at the trigger point of GA, could increase the efficacy of IMBoNT in CD.

**Evaluation of Hypothesis.** Nine patients with CD and an identified a GA were recruited. While receiving IMBoNT, five of them had no dystonia while sitting, and four had improved dystonia; seven experienced pain. In addition to the dose of IMBoNT, every patient received SCBoNT at the trigger point of GA, during eight to twenty-four months.

During this period, among the five patients without dystonia at rest, one reported disappearance of torticollis during gait, and three saw the interval between IMBoNT prolonged by four or six weeks. Among four with persistent dystonia, one attained a normal neck position, and two experienced amelioration of dystonia. Pain was diminished in five patients.

**Conclusion.** SCBoNT infiltration of the trigger point resulted in additional benefit in seven out of nine patients treated with IMBoNT. SC BoNT at the trigger point of GA might constitute a means of improving CD by itself, or of increasing the benefit provided by IM BoNT or other therapies. Further studies are needed to confirm this hypothesis.

Key Words: Cervical Dystonia; Botulinum Toxin; Geste Antagoniste; Trigger Point; Sensory Stimulation.
INTRODUCTION
Dystonia is a hyperkinetic motor syndrome, considered to induce motor manifestations in an exclusive manner [1,2]. However, pain is a common symptom in cervical dystonia (CD), and abnormal processing of sensory inputs from voluntary muscle has been demonstrated in focal forms of the disease [1,3-6]. A distinct feature of dystonic movements, especially in CD, is that they can be transiently diminished or abolished by sensory stimuli applied at the affected body part, or someplace near it (geste antagoniste or sensory trick) [7]. A mean reduction of head deviation of 60%, suppression of abnormal muscle activity on electromyographic recordings, and modification of the activity of the motor cortex on positron emission tomography have all been demonstrated during application of the geste antagoniste (GA) [7-10]. Its mechanism of action is still undetermined.

Intramuscular (IM) infiltration of botulinum neurotoxin (BoNT) is an efficacious therapeutic modality for CD [11]. In addition, recent reports have uncovered a beneficial effect of subcutaneous (SC) infiltration of BoNT in some sensory conditions, such as postherpetic neuralgia, diabetic neuropathy and trigeminal neuralgia [12-14].

HYPOTHESIS
The idea behind this work has been whether, taking into account the sensory component present in dystonia (represented by GA), and the efficacy of SC BoNT in sensory disorders, SC BoNT applied at the spot that triggers GA, might constitute a useful adjunctive therapy to IM BoNT in CD.

EVALUATION OF HYPOTHESIS
Nine patients with CD (7 females and 2 males), aged 35 to 80 years, identified a GA. Informed consent was obtained for subcutaneous administration of BoNT, this study being conducted in accordance with the Declaration of Helsinki and the local ethics committee.

Eight patients had idiopathic CD, and one, tardive dystonia secondary to neuroleptic treatment. Five patients exhibited predominant torticollis; three, retrocollis, and one, anterocollis. Neck pain was an additional complaint in seven cases.
Every patient had identified a trigger point, at which slight touch reduced or suppressed the involuntary movement. Four patients located that point at the chin; three, at the back of the neck; one, at the occiput; and another one, at the right shoulder.

IM infiltration of BoNT type A at twelve-week intervals had been their main treatment for CD, for four to nine years: six patients received Botox (Allergan Inc, Irvine, United States), 150-400 units, and three, 300-900 units of Dysport (Ipsen Biopharm Limited, Wrexham, United Kingdom). When IM administration of BoNT attained a stable benefit (table 1), five patients recovered a normal neck position when sitting, of whom two experienced torticollis during gait. The remaining four patients persisted with abnormal, though improved, neck postures while seated, which became worse walking.

Six patients received 20 SC units of Botox, and three, 40 SC units of Dysport, at the referred to trigger point, along with the usual IM dose of BoNT; this was kept unchanged, and no drugs were added, or their doses modified, during the follow-up period, which varied between eight and twenty-four months.

During follow-up (table 1), among five patients with a normal neck posture at rest with IM BoNT, one reported disappearance of torticollis during gait; in two, the interval between IM BoNT infiltrations could be delayed to sixteen weeks, and in another, to eighteen. One patient, among four with an abnormal posture during IM BoNT, attained a normal neck position sitting, and two others experienced amelioration in neck posture. Pain was decreased in five out of seven instances.

The described improvements were apparent from the first SC infiltration of BoNT. No worsening of dystonia was noted during follow-up, and every patient chose to continue with SC BoNT at the end of the study.

DISCUSSION
Taking advantage of GA to ameliorate CD has been proposed previously [3,15], although this idea has not been taken to clinical practice in a controlled setting.

This work shows that SC BoNT infiltration of the point that triggers GA resulted in additional symptomatic relief in seven out of nine patients treated with IM BoNT: improvement or normalization of anomalous neck postures while seated, suppression of dystonia when walking, diminished neck pain and prolongation of the interval between IM BoNT infiltrations, were all noted.
Nevertheless, two patients did not obtain an added benefit from SC BoNT. Patient 9, who had tardive dystonia, obtained no additional benefit from SC BoNT, possibly due to an increased resistance of tardive CD to BoNT [16]. On the other hand, patient 5 had no torticollis at rest or walking, leaving little room for improvement with SC BoNT.

Pain associated with cervical dystonia has been reduced by BoNT [17], and in this series, neck pain was decreased by SC BoNT, in five among seven patients.

No worsening in dystonia or pain, nor adverse effects of any kind were noted during SC infiltration of BoNT, attesting to the safety of this procedure.

The present results, though favourable, must be regarded as preliminary, considering the observational nature of this work. Nevertheless, they support the idea that modification of peripheral sensory feedback might bring about a significant reduction of abnormal movements and pain in CD.

BoNT acts by blocking exocytosis of acetylcholine at the neuromuscular junction, although this effect alone appears inadequate to explain the neurotoxin’s sensory activity. In fact, BoNT also inhibits liberation of the pain chemical mediators glutamate, substance P and calcitonin gene-related peptide at axonal endings, and is able to reach the spinal cord after migrating along sensory axons [18,19]. The interaction of BoNT with sensory structures could account for its efficacy in the treatment of neuropathic pain, and for the additional clinical improvement of pain and dystonia in this series.

CONCLUSION

SC administration of BoNT at the GA trigger point in CD might prove a useful, safe and simple method to ameliorate abnormal movements in CD, either by itself, or by increasing the benefit provided by IM BoNT or other therapies. Controlled clinical trials with SC BoNT in CD, alone or in combination with other treatments, would be desirable in order to test the feasibility of this hypothesis.
REFERENCES


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*Table 1. - Dystonia and neck pain during treatment with botulinum toxin*
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Abbreviations: BoT, botulinum toxin; IM, intramuscular; Interval: time between intramuscular infiltrations of botulinum toxin; SC, subcutaneous.