

Two Doses of Botulinum Toxin Type A for the Treatment of Trigeminal Neuralgia: Observation of Therapeutic Effect from A Randomized, Placebo-Controlled Trial

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Received date: June 06, 2017; Accepted date: June 19, 2017; Published date: June 22, 2017

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Commentary

Trigeminal neuralgia (TN) is severe and recurring pain distributed unilaterally along a branch of the trigeminal nerve [1,2]. The application of BTX-A to relieve TN was first reported in 2002, and its safety and effectiveness was later confirmed by series studies [3-13]. In 2012, our team conducted the first RCT study in this field, and obtained the prima facie evidence of BTX-A for TN. Subsequently, we took a different dose of BTX-A to carry out a larger RCT study, so far it is the only attempt [6]. The aim of this study was to explore an effective and safe dose of BTX-A for the treatment.

For this purpose, we conducted the RCT study since November 2012, and adopted local multi-point injection in 84 cases of classical TN with different doses of BTX-A. Eighty four patients were randomized into following groups: placebo (n=28); BTX-A 25U (n=27); BTX-A 75U (n=29). Follow-up visits were conducted every week after the injection to observe the pain severity, efficacy and adverse reactions at endpoint. The result showed BTX-A injection in TN is efficient and no significant difference between 25U and 75U groups. All adverse reactions were graded as mild or moderate.

This trial did not mean that the efficacy of BTX-A lasted only 8 weeks, and another study we showed that BTX-A for TN treatment has considerable therapeutic effects lasting several months [8]. Of course, the work of clinical research is huge and full of uncertainties, so our research is not perfect. At present, we continue to improve our treatment methods and carry out related studies (such as the comparison between single and repeated administration, not yet published). Cooperative prospective studies that involve multiple centers are planned to elucidate the optimal treatment for TN in the coming years.

Botulinum toxin type A (BTX-A) relieving trigeminal neuralgia (TN) was first mentioned in 1998 [14], and the first case about BTX-A in the treatment of TN was reported in 2002 [3]. Many studies have gradually confirmed the effectiveness of BTX-A for next ten years [5,15-20]. But until 2012, it still has doubts about the effect of BTX-A in treatment of TN [21]. Several RCT studies [4,6,9,22] including us, seem to prove the role of BTX-A in the treatment of TN, but it doesn't seem to be universally accepted. Because the sample of the studies which was mentioned before is small and the design has many limitations, so it is difficult to be widely accepted. But in my opinion, BTX-A as an effective therapy should be highly considered, and I hope it will be spread around the world like the treatment of hemifacial spasm and torticollis. Since 2010 we carried out the treatment and have injected for hundreds of cases, including the elderly, critically ill patients, patients with surgical sequelae (such as Radiofrequency ablation), and other forms of refractory TN. BTX-A still has its

problem, nevertheless, shows greater potential for immediate clinical application.

First of all, BTX-A treatment of TN, compared with the traditional oral therapy, has mild and reversible side effects, especially in intractable trigeminal neuralgia with poor efficacy of oral medication. Since 1999, we have applied botulinum toxin to treat hemifacial spasm, torticollis and other diseases. So far, no sequelae or obvious adverse reactions have been observed. In China, the doctor-patient relationship is poor, and the treatment with less adverse often become the first choice, otherwise complications and sequelae can become the direct cause of violence in medical treatment.

Second, BTX-A therapy is cheaper than surgical treatment, especially for patients in underdeveloped countries. For example, in our country, the patients receiving BTX therapy only pay about 1000 RMB each time, while surgery requires 30000-40000 RMB, even if radiofrequency ablation also needs 10000 RMB. In addition neurosurgery carries its own risks, and we have encountered cases with permanent sequelae these years. In general, BTX-A as a non-operative approach may be simpler, less expensive, easier to administer with fewer complications, and may be better tolerated than surgery by many patients (especially rural patients).

Third, this treatment is suitable for all types of people, except in some special cases (such as myasthenia gravis). For example, elderly or patients with cardiovascular and cerebrovascular diseases who are unable to tolerate oral or surgical treatment can be well tolerated with BTX-A injections.

Fourth, the method is simple and easy to operate and generalize. Especially in the remote areas, where the medical conditions are poor, they cannot carry out other treatments but oral analgesics. The surgery, for example microvascular decompression, is relatively complex and expensive, which restricts its application in rural and remote areas. In contrast, the therapy of BTX-A injection can be learned with a little practice in a short period of time.

Because of the different site and type for each case, there was no same treatment strategy, but an individualized therapy. And full use of this treatment needs accumulation of experience. For example in some cases, ensuring the spread of BTX-A to the area of pain is more important (especially oral injection) than just increasing the dose itself.

Sometimes the advanced therapies may not be what patients need the most, along with the local medical conditions and patient acceptance. Compared to complicated surgical management, many patients and doctors in primary hospital were more interested in BTXA treatment. This method was safer, cheaper, simpler, easier to administer with fewer complications and better tolerated by patients.

Although it is impossible to eradicate pain, BTX-A is the most practical approach to deal with the problem

BTX-A in the treatment of trigeminal neuralgia currently shows a potential for broad applications, which requires efforts of experts around the world, and also needs support and help. Hopefully in the near future, BTX-A therapy for trigeminal neuralgia will also receive more attention and widespread use.

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