

Research Article

EFFECTIVENESS OF INTRADERMAL BOTULINUM TOXIN IN INTRACTABLE POSTHERPETIC NEURALGIA

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ABSTRACT

Objective: Post-herpetic neuralgia is not an uncommon complication of herpes. It is a type of neuropathic pain that is confined to the dermatome supplied by cutaneous nerves. A number of pharmacotherapies and other treatment modalities are tried in treatment of this type of neuralgia; however, still, a sizeable number of patients are refractory to treatment options. Botulinum toxin (BoNT) has been tried recently as one of the treatment option in intractable post-herpetic neuralgia (IPNH). **Methods:** Intradermal BoNT 2.5 units were given at multiple sites 2 cm apart in the affected region (face/trunk). **Results:** Five out of eight patients had significant pain relief on BoNT injections in dose range 50-100 units. **Conclusions:** Intradermal BoNT is an affective therapeutic option for IPNH.

Key words: Post-herpetic neuralgia, botulinum toxin, intractable post-herpetic neuralgia, intradermal Botulinum toxin

INTRODUCTION

Many individuals across the globe have been exposed to the *varicella-zoster* virus that causes chickenpox. After chickenpox has resolved, the virus remains latent in the dorsal root ganglia where it can re-emerge later in life as herpes zoster, otherwise known as shingles. Herpes zoster is a transient disease characterized by a dermatomal rash that is usually associated with significant pain. Post-herpetic neuralgia (PHN) is the term used for the condition that exists if the pain persists after the rash has resolved [1].

A variety of treatment modalities are used in postherpetic neuralgia [1-2]. Commonly used drugs are carbamazepine, tricyclic antidepressants, gabapentin or pregabalin etc. Intractable postherpetic neuralgia (IPHN) is not uncommon. A significant number of cases are refractory to these medications. Botulinum toxin (BoNT) has recently been tried as one of the treatment modality for pain management. In view of the favorable reports of BoNT in various neuropathic pain and headaches, an attempt was made to investigate the effect of BoNT in IPHN. This report includes 8 cases of IPHN treated successfully with intradermal BoNT.

MATERIAL & DESIGN

Eight cases of IPHN (Age range=50-80 years, M:F=5:3) were enrolled. Six had cranial trigeminal nerve (V1, V2) and two had segmental involvement (thoracic). The duration of IPNH ranged from 7 to 48 months (Mean: 16 months). IPHN was defined as severe, persistent pain which failed to respond to 2 or more maximally tolerated doses of conventional drugs. Pain severity was assessed using Visual Analogue Scale (VAS-0: no pain; 10: maximum pain). Ice cubes were applied for one minute before injecting BoNT to reduce injection associated pain. Intradermal BoNT (Botox-Allergan@ Inc. USA) 2.5 units were given at multiple sites 2 cm apart in the affected region (face/trunk). VAS was administered at baseline, and at weekly intervals.

RESULTS

Five out of eight patients had significant pain relief on BoNT injections. Two reported worsening of pain. Total BoNT dose ranged from 50-100 units. Onset of effect was on 7th day. Mean VAS score dropped from 8.14±0.90 to 2.29±0.76 (p< 0.0001, 95% CI4.6.82). Improvements also occurred in allodynia and dysaesthesia. Mean duration of effect was 74±21 days. No local or systemic side effects were noted.

DISCUSSION

Post-herpetic neuralgia is a chronic pain of neuropathic type which occurs as a sequel of herpes zoster infection. Treatment is often challenging. Onset of postherpetic neuralgia typically occurs 4 weeks after the skin lesions heal. An unfortunate minority of patients with acute herpes zoster (AHZ) experience pain beyond the typical 4-week duration, and roughly 10% develop the distressing complication of postherpetic neuralgia (PHN), often defined as pain persisting for > 4 months after the onset of the rash [1]. Elderly patients are at increased risk of PHN [1-2].

The pathophysiology of PHN is complex, likely involving both peripheral and central processes. This complexity may create opportunities for pharmacologic interventions with multiple differing mechanisms of action. Consequently, complementary combinations of pharmacologic agents are frequently more effective than any monotherapy [3].

Post-herpetic neuralgia (PHN) is a devastating complication of shingles [3]. Condition is often refractory to drug treatment. Treatment includes the lidocaine patch, opioid analgesics, nortriptyline, amitriptyline, and gabapentin². However, no treatment regimen fully eliminates the pain. Improvements in prevention include prompt recognition and treatment of high-risk herpes zoster (HZ) patients with antiviral and analgesic therapies. Even with these advances, PHN remains a debilitating and painful disease. Vaccines offer promise of long lasting relief.

The treatment of PHN with traditional pharmaceutical agents has various side effects³. Therefore, the treatment of intractable PHN is often very time consuming, mainly because the available treatments often lead to intolerable side effects before the efficient dose can be reached². A variety of treatment options including nerve blocks⁵ are used for treatment with variable success.

Evidence-based data indicate that administration of botulinum toxin in several human conditions can alleviate refractory pain⁶. Role of botulinum in IPNH has started emerging recently. Though exact mechanism of pain relief in IPNH by botulinum is not known but it probably involves purinergic type of receptors⁸. Moreover, the drug has been shown to affect release of neurotransmitters and neuropeptides.

Chronic pain is associated with excess pain fiber activity. When the site of this excess activity resides in the peripheral portion of the pain pathway, a condition of peripheral sensitization can establish. During this state, excess pain signaling reaches the central nervous system, which can then lead to a condition of central sensitization, manifesting as the symptoms associated with chronic pain (i.e. burning, electric pain, lowered pain threshold to normal stimuli, etc). Experimentally, botulinum toxin type A has been shown to reduce

neuropeptides and neurotransmitter release from treated cells or nerve endings and to attenuate nociception in both neuropathic and non-neuropathic pain models⁹. A single case report in an older patient of 82 years relived pain of IPNH⁹. BoNT showed statistically significant improvements in IHPN in the current study. These encouraging findings warrant double blind placebo controlled trials to fully establish its role in IPHN.

Table 1: Studies using BoNT in IPNH.

Authors/year	Sample size (n)	Study design & Dose of BoNT	Results	Conclusion	Side effects
Eleni Sotiriou et al' 2009 ⁴	3	Case series Dose=5 units per site	VAS pain scores decreased at day 3 and 2 months	All patients significantly improved	Pain & erythema at injection sites
Mhs. R Emad, M Emad, P Taheri'2011 ⁵	15	Case series; Dose=15 units per 10 cm ²	VAS pain scores decreased at day 2 and 25 days	All patients reported improvement	
Xiao L et al'2011 ⁶	60	Randomized, double-blind, placebo-controlled study. Dose=5 units per site	VAS pain scores decreased at day 7 and 3 months	Decrease in pain (p<0.01)	
Present study	8	Case series; Dose=2.5 units per site	VAS pain scores decreased at day 7 and 74±21 days	5 out of 8 improved (p<0.0001)	Initial Transient worsening of pain (2)

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