ORIGINAL ARTICLE

Subcutaneous Injection of Botulinum Toxin in Patients with Post Herpetic Neuralgia. A Preliminary Study

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Abstract

Background: Post Herpetic neuralgia (PHN) is neuropathic pain that occurs after herpes zoster infection. Several treatments have been suggested in the management of PHN. This study evaluates the efficacy of subcutaneous injection of botulinum toxin in patients suffering from PHN.

Methods: Nineteen patients suffering from PHN for more than 2 months were enrolled in the study. The severity of pain was assessed by visual analog scale (VAS). A total dose 500 units of BTX-A was injected around the site of pain. This was administered in about 25 sub-cutaneous injection around the site, delivering approximately 20U/ml of BTX-A per injection. The patients were followed at 1,2, 3,4,12 and 16 weeks after the administration of the drug.

Results: The mean age was 56 years (age range 36 to 63) for non-pregnant patients. The two pregnant patients of age 28 and 32 year old who were in their 28 and 30 weeks of gestation were also included. The mean duration of PHN was 4.78 wks. At each visit VAS was used to evaluate the degree of pain (0: painless; 10: maximum pain). There was a significant reduction in the severity of pain after the injection.

Conclusion: Botulinum toxin significantly decreases the severity of pain in PHN patients and last for 4-6 month of the period. This decrease is less prominent by passing time.

Introduction

Herpes zoster is an infection caused by varicella zoster virus. Anyone infected with varicella (chicken pox) virus in childhood is at risk for reactivation of dormant virus although it occurs with increasing frequency in the elderly as a result of waning of cell medicated immunity. Herpes zoster is rare in pregnancy and only found one in 20000 pregnancies. The most common complication of herpes zoster is post herpetic neuralgia (PHN) which can cause chronic and debilitating pain.[1] One of the reasons for the constant pain months after zoster infection is the increase in the number of P fibers and decrease in the number of the large fibers which suppresses the pain transmission.[2] The early treatment of PHN with botulinum toxin type A has shown promise in the long term pain control without any cognitive side effects.[3] Due to large size of molecule botulinum toxin A is not expected to be present in systemic circulation and hence does not cross the placenta. It is safer to use in the pregnancy.[4] One of the authors has the experience of using the Botulinum toxin in hyperhydrosis as dose dependent cosmetic effect.[5] In this study we aimed to evaluate the effect of botulinum toxin type A in PHN patients in both general and pregnant patients.

Material and Method

Based on previous trial and experience in cosmetic effect of botulinum in hyper hydrosis (5-6) 19 patients men or women with severe PHN resistant to usual therapeutic modalities in order to evaluate the efficiency of BTX-A in this conditions were studied. Two women were pregnant. Written informed consent was obtained from each patient. Clearance from ethical committee was obtained. The mean age was 56 years (age range 36 to 63) years in the non-pregnant group. 2 pregnant patients were 28 and 32 year old in their 28 and 30 weeks of gestation respectively. The mean duration of PHN was 4.78wks. Herpes zoster has been diagnosed in all patients based on the presence of unilateral dermatomal clinical findings. Three patients had herpetic eruption in ophthalmic division of trigeminal nerve, six in T4-T5 dermatome on anterior side and five in T3, T4 dermatome on posterior side, one T6, T7 and four in T12 -L1 dermatome distribution. Both the pregnant patients did not receive oral antiviral (Acyclovir) therapy.

Patients were counseled regarding the nature of the drug, its possible complications. Method of injection was explained and written consent obtained. Severity of symptoms determined through a visual analogue scale (VAS) as standard criteria for assessment of severity of pain.[6] At each visit VAS was used to evaluate the degree of pain (0= painless; 10= maximum pain).

Each sterile viral containing 500 units of BTX-A (Dysport, Speywood UK -Bharat serum and vaccine, India) was diluted with 5ml of sodium chloride, resulting in a concentration of 100 U/ml. The entire 500 units of the drug was delivered through subcutaneous route in a chess board fashion over the affected area at 25 points. Each of the injection delivered about 20U / ml subcutaneously. The patients were followed at 1, 2, 3, 4 and 12 and 16 weeks.

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Table 1: Patients demographic distribution, duration of PHN and VAS score at base line and follow up visits (weeks) after BTX-A therapy

Patient No.	Affected dermatome	PHN duration in months	VAS score baseline	1 wk	2 wk	4 wk	12 wk	16 wk
01	Ophthalmic	3	8	8	5	3	3	2
02	T4,T5	4	8	8	5	3	3	3
03	T3,T4(posterior)	3	9	8	5	5	2	2
04	T3,T4(posterior)	4	6	6	7	3	2	2
05	Ophthalmic pregnancy 28 wks	2	7	5	5	3	2	2
06	T4,T5 dermatome pregnancy 32wks	2	7	5	5	4	3	3
07	T4,T5	4	8	6	5	4	3	3
08	T4,T5	6	9	5	4	3	2	2
09	T4,T5	5	6	6	5	3	2	2
10	Ophthalmic	6	7	5	5	3	2	2
11	T3,T4 (posterior)	7	7	5	6	3	1	1
12	T12, L1	8	7	5	5	3	2	1
13	T4 T5	6	9	7	5	2	2	1
14	T3,T4 (posterior)	5	10	7	4	2	2	2
15	T12, L1	7	9	6	4	2	2	2
16	T6,T7	6	8	6	4	2	2	2
17	T12, L1	3	9	6	5	2	2	2
18	T3,T4 (posterior)	4	8	6	5	2	1	1
19	T12, L1	5	10	6	4	1	1	1

Software SPSS 16.0 version (Significant at 0.01 i.e. 1 % level of significance)

Result

There was decrease in the intensity of pain in all the patients including the pregnant patients. The magnitude of relief from pain varied from the patient to patient. It had no correlation with age of the patient, dermatomal involvement and duration of PHN. Except for erythema at the site of injection in 3 patients, no other immediate side effects were noted up to an observation for 24 hours. Table 1 shows dermatomal distribution and the changes in VAS score during follow up period in weeks. Mean VAS score dropped from 8.3 at base line to 2. The decrease in the severity of pain was noted after 2 weeks of administration and the peak effect were noted at 4-6 weeks. In both the pregnant patients, the pain lasted up to 16 weeks. Further follow up of the pregnant patients could not be under taken in the study. The pain recurred in the other patients (n=17). The drug was re-administered in 5 patients along with carbamazepine. However the pain intensity was less in these five patients as compared to pre-study period. The remaining patients (n=12) did not consent for re-administration in view of the cost involved.

Discussion

PHN pain is considered neuropathic in nature. It has a very complex mechanism, so different modalities of treatment medical and surgical has been suggested.[7] The variable pain relief with BTX-A, with or without combinations of drugs as in our patients was reported in literature.[8,9] Use of BTX-A in pregnancy is considered safe as it does not cross the placental barrier and enter systemic circulations due to large size of molecule.[10] The local peripheral BTX-A reaction may result in a reduction in various substances that sensitize nociceptors. This anti-nociceptive effect is associated with the inhibition of formalin-induced glutamate release and a possible reduction of the peripheral nociceptive input by inhibiting the release of substance -P and calcitonin – gene – related peptide, which plays a significant role in neurogenic inflammation.[11] However, some investigators believe that the beneficial of BTX-A in treating neuropathic pain is related not only to acetylcholine inhibition but also to a blocking action on the parasympathetic nervous system.

Temporary erythema which was observed could be due to multiple injections in a limited area. However, it disappeared by passage of time. The dose of BTX-A was fixed in all the cases in spite of variable dermatomal involvement, intensity of pain and duration of PHN as it was observed in one of the study of one of the author that effect of BTX-A was dose dependent[5] and our goal was to achieve in the reduction of pain intensity to a certain extent as to make patient comfortable.

The encouraging results of this small clinical study lead us to conclude that BTX-A could be an alternative therapeutic modality in treating PHN if not complete but at least in reducing the intensity. It can be given safely to pregnant patients as well.[4]

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