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EVALUATION OF THE EFFICIENCY OF BOTOX THERAPY IN A PATIENT WITH UNILATERAL IDIOPATHIC NEURALGY ON THE TRIGEMINAL NERVE

ЕВАЛУАЦИЈА НА ЕФИКАСНОСТА НА БОТОКС ТЕРАПИЈАТА КАЈ ПАЦИЕНТ СО ИДИОПАТСКА, УНИЛАТЕРАЛНА ТРИГЕМИНАЛНА НЕУРАЛГИЈА КОЈА ГИ НАПАЃА ТРИТЕ ДИВИЗИИ НА ТРИГЕМИНАЛНИОТ НЕРВ

Shushak Z.[1], Popovski V.[2], Mitikj J.[3], Baftijari D.[4]

[1]PhD, DDM, DDS - Faculty of Medical Sciences, UGD – Stip, Private health institution „Dentoria-1 Specialist practice for oral surgery and implantology“ Ohrid, Republic of North Macedonia, [2]PhD, MSD, MFS, DDM, MD – Faculty of Dentistry, „Ss. Cyril and Methodius“ University Skopje, Republic of North Macedonia, Clinic for maxillofacial surgery, [3]PhD, DDM, MSD, trainee in periodontology - Private health institution „Gudadent“ Skopje, Republic of North Macedonia, [4]PhD, MSD, DDM, MFS - Faculty of Medical Sciences, Tetovo University, Private health institution „Vita Dent - Implantology Center“ Tetovo, Republic of North Macedonia.

Abstract

Trigeminal neuralgia (**TN**) often known as „painful tick“ or *„tic douloureux“* is a neurogenic disease that affects the facial segment. According to the intensity and clinical parameters of the pain, it is one of the most severe pain that the patient experiences on a daily basis. Botox therapy in trigeminal neuralgia is a relatively new strategy (*innovative therapy for the treatment of orofacial pain*), which is still in the experimental phase worldwide. Positive results have been reported in middle-aged and elderly patients who have been receiving conservative treatment (medications), despite skepticism regarding the side effects and complications of surgical treatment. The purpose of this case report is to describe the effect of botox therapy and improve the quality of life in a patient with *idiopathic, unilateral trigeminal neuralgia which affects all three branches of the trigeminal nerve* and is one of the most severe forms of this disease. **Key words:** Botox therapy, idiopathic trigeminal neuralgia, trigeminal nerve.

Апстракт

Тригеминалната неуралгија (**TH**) позната уште како „болен тик“ т.е. (*„tic douloureux“*) е нервно нарушување (патологија) која го засега лицевиот сегмент. По интензитет и клинички параметри на болката се смета дека е една од најтешките преживеани состојби со кои пациентот секојдневно се соочува. Ботокс терапијата при тригеминалната неуралгија е релативно нова стратегија, која во светски рамки се уште е во експериментална фаза, особени позитивни резултати се евидентираат кај средовечни и постари пациенти кои се долго време на конзервативен третман (лекарства), а се однесуваат со скепса кон несаканите ефекти и компликации на хирушкиот третман. Целта на овој приказ на случај е презентирање на ефектот на ботокс терапијата и подобрување на квалитетот на живот кај пациентка со *идиопатска, унилатерална тригеминална неуралгија која ги напаѓа трите дивизии на тригеминалниот нерв* и е една од најтешките форми на ова заболување. **Клучни зборови:** Ботокс терапија, идиопатска унилатерална тригеминална неуралгија, тригеминален нерв.

Introduction

Trigeminal neuralgia (**TN**) is defined by International Headache Society as *„unilateral disorder characterized by brief pain similar to an electric shock, sudden painful attacks and interruption of attacks limited to the distribution of one or more branches of the trigeminal nerve“*[1]. According to International Association for the Study of Pain and International Headache Society, the latest classification distinguishes 3 etiological categories: idiopathic TN (without neurovascular contact (WNC) or WNC without morphological changes of the trigeminal nerve); *classic TN* (due to neurovascular compression with morphological changes of the trigeminal nerve) and *secondary TN* (due to major neurological diseases such as tumors and multiple sclerosis[2].

The treatment of TN remains a major challenge. The treatment principles remain basically the same, and widely

used medical treatment options include antiepileptic drugs, muscle relaxants and neuroleptic agents[3]. Botox therapy has been successfully applied as an adjunctive therapy for patients suffering from TN in the recent decades[4].

Botulinum neurotoxin is a complex protein produced by the gram-positive anaerobic bacteria Clostridium botulinum. To date, seven serotypes of the toxin, i.e. A-G have been identified, according to their antigenic characteristics, however only A and B serotypes are commercially available. The serotypes range in size from 300 to 900 kDa and are composed of a neuroactive entity called botulinum neurotoxin (BoNT) which helps stabilize the complex protein. Each of the seven serotypes has a similar structure and molecular weight, consisting of heavy (H) chain and light (L) chain bonded by disulfide bond[5].

Botulinum toxin type A, is regarded as the most powerful subtype. BoNT typ A is believed to be effective in the treatment of migraine and myofacial pain. Subcutaneous or mucosal (perineural) application of BoNT typ A is effective in adult TN patients. Numerous studies shown a decrease in average pain intensity and frequency with a maximal effect within 4 to 6 weeks[6-8].

The purpose of this case report is to demonstrate the efficacy of botox therapy and improve the quality of life in patients with trigeminal neuralgia.

Case Report

A 57-year-old patient is being treated with a conservative method at the Maxillofacial Surgery Clinic in Skopje for a period of 7 years. Anamnestic patient describes unilateral pain localized in three divisions of trigeminal nerve. The pain occurs daily and might last anywhere from a few seconds to a several hours. Occurs spontaneously and with touch provocations and feeding. According to the patient's medical history we learn that the patient is treated with a conservative approach - Tegretol 400 mg twice a day with insignificant results in the last period over the past year.

The patient has suffered from hypertension for 7 years and is currently receiving antihypertensive therapy ENAP 10 mg 1 tablet daily. Her blood pressure ranges between 90 and 130 and between 120 and 180 mmHg. Extraoral examination revealed pain in the trigger points (figure 1.), However the intraoral examination reveals complete loss of teeth on the affected side (partial tooth loss in the upper and lower jaw, caries-non-resistant dentition, poor oral hygiene and presence of periodontal disease). In the previous period, paraclinical examinations including X-ray orthopantomography, computed tomography (CT), and laboratory blood tests were performed. A diagnostic block anesthetic was also administered to assist in the determination, i.e. confirmation of diagnosis.

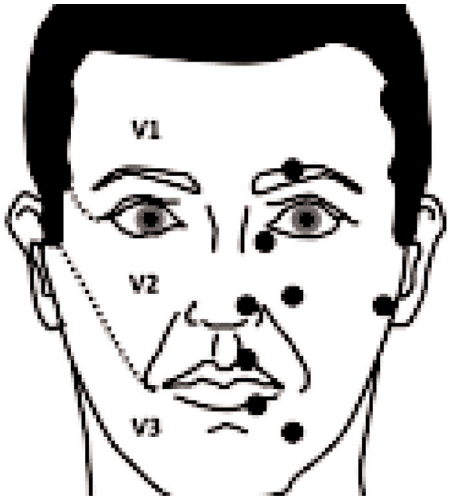

Figure 1. *Regimens and application points for botulinum toxin.*

We used Dysport (BoNT/A) 300 UI. The manufacturer is the company Ipses Biopharm Limited. The active ingredient of Dysport is Clostridium botulinum type A toxin – haemagglutinin complex (300 units). Before the administration, Dysport was dissolved in a physiological solution 0.9%. Our examination was carried out under in vivo conditions in order for the result to be a demonstration of the actual efficacy of botox therapy. The patient was examined by a therapist to exclude the subjective factors that would come from the work of several therapists. We gave the patient a questionnaire and she was asked to fill it out at zero, first, fifth and tenth week after the botulinum toxin application. **200 UI botulinum toxin type A.** (DYSPORT Botox® - Ipsen Biopharm Limited) (figure 2.), are administered in 3 regimens: **75 UI in the mental, 75 UI in the infraorbital** и **50 UI in the frontal region**. The Botox solution was applied perineurally to the mental region using the intraoral method of the technique for anesthetizing n. mentalis. The patient's mouth was closed, and the lower lip and cheek were retracted. The needle puncture was in the alveolar mucosa in the area of the mesial root of the first molar and moved along the bone towards the mental foramen. The Botox solution was applied perineurally in the infraorbital region, following the intraoral method of the infraorbital anesthesia placement technique. The patient's mouth was closed or slightly open. The upper lip was retracted and the needle puncture was in the alveolar mucosa above the second incisor. The movement of the needle was upwards, backwards and outwards. The angle of the needle is such that if applied simultaneously in both foramens the needles would cut at the incisal point. A bone border was felt at a depth of 1.5 to 2 cm. This area encompasses the infraorbital canal. The appli-

Figure 2. UI botulinum toxin type A (DYSPORT Botox® - Ipsen Biopharm Limited) and application set of botulinum toxin.

cation of the solution was implemented within the given region. In the frontal region, the Botox solution was applied subcutaneously at 3 points. The central point was in the center of the glabella, and the lateral ones were 2 cm away, above the supraorbital foramen. Pain evaluation and evaluation for improved quality of life have utilized the following parameters: visual analogue scale (VAS), numerical scale for assessing pain (NRS), facial expression rating scale (FRS), Wong - Baker scale, Hamilton's Anxiety Scale (HAM-A) and the Hamilton Depression Scale (HDRS).

Results

Table 1. Mental Region - pain evaluation and evaluation for improved quality of life parameters.

Mental Region	Week zero	First week	Fifth week	Tenth week
VAS-1	(0)	(7)	(6)	(3)
VAS-2	(10)	(3)	(3)	(8)
NRS	(10)	(4)	(3)	(7)
FRS	(8)	(4)	(3)	(7)
HAM-A	(severe form of anxiety)	(severe form of anxiety)	(moderate depression)	(severe form of anxiety)
HDRS	(severe depression)	(moderate depression)	(moderate depression)	(moderate depression)

Table 2. Infraorbital region - pain evaluation and evaluation for improved quality of life parameters.

Mental Region	Week zero	First week	Fifth week	Tenth week
VAS-1	(0)	(5)	(6)	(3)
VAS-2	(10)	(5)	(4)	(7)
NRS	(10)	(5)	(4)	(7)
FRS	(10)	(5)	(4)	(7)
HAM-A	(severe form of anxiety)	(severe form of anxiety)	(moderate depression)	(severe form of anxiety)
HDRS	(severe depression)	(moderate depression)	(moderate depression)	(moderate depression)

Table 3. Frontal region - pain evaluation and evaluation for improved quality of life parameters.

Mental Region	Week zero	First week	Fifth week	Tenth week
VAS-1	(0)	(8)	(9)	(6)
VAS-2	(10)	(2)	(1)	(4)
NRS	(10)	(2)	(2)	(4)
FRS	(9)	(2)	(2)	(4)
HAM-A	(severe form of anxiety)	(severe form of anxiety)	(moderate depression)	(severe form of anxiety)
HDRS	(severe depression)	(moderate depression)	(moderate depression)	(moderate depression)

Discussion

Trigeminal neuralgia is a relatively rare pathological condition (1/8000), which dramatically reduces the quality of life of affected individuals, not only due to pain attacks, but also due to other accompanying conditions, such as anxiety and depression[9]. TN is often undiagnosed or untreated in practice, and more attention has been paid to this disease in the last decade. Treatment can be difficult and unsatisfactory. It consists mainly of patient education and pharmacotherapy with tricyclic antidepressants. Anticonvulsants, analgesics and surgery did not show significant results in TN therapy. Other pain relief strategies include hot and cold compresses, acupuncture, splints[10].

Botulinum neurotoxin A is a powerful neurotoxin. It can inhibit the release of acetylcholine from neuromuscular junctions, resulting in muscle relaxation. It also inhibits vanilloid receptor expression TRPV1 on the surface of peripheral receptors responsible for inflammatory hyperalgesia. In addition, studies indicate that the analgesic effect of botulinum toxin is independent of its muscle relaxation.

Botulinum toxin has been used for over 20 years to treat various neurological diseases associated with pathologically increased muscle tone or impaired autonomic nerve regulation[11]. Our case has shown a positive effect of botulinum toxin on pain management in a patient with severe form of TN, which is consistent with studies of Piovesan and cop.[12]. A recently published meta-analysis concluded that botox therapy can be a safe and effective treatment option for patients with TN, with an average reduction in daily paroxysms to 29,8 %[13]. Jiangshan Wei and Xiangyu Zhu concluded in their meta-analysis that botox therapy is an effective and reliable method of treating TN. Due to the limited size and heterogeneity of the specimens, additional large and well-designed randomized controlled experiments are imperative in proving these results[14]. In the last decade, botulinum toxin has been used in numerous studies with the vast majority involving subcutaneous, intracutaneous, and perineural injections in the triger zones of the painful facial region[15-17].

In our case, the patient showed significant results in all parameters examined, with the greatest reduction in pain and other associated symptoms occuring in the fifth week, and the greatest improvement in quality of life occurring between the first to tenth weeks, accompanied by a period with a decrease in the degree of anxiety and depression severity.

Conclusion

This case report suggests that botox therapy for trigeminal neuralgia may be a useful method of pain management, improving the clinical picture and the quality of life in the most severe forms of the disease. Additional scientific studies are needed to confirm our results and further evaluate doses when applied, type and techniques of application, as well as duration of treatment.

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