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Original Research Article

Evaluation of Electromyoghraphy Guided Botolenium Toxin Type A Injection in Treating Chronic Migraine in Babylon Province

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Abstract

BOTOX is the first and only FDA-approved preventive treatment for chronic migraine. It's also the only treatment for people with chronic migraine. Current migraine preventive therapies are often unsatisfactory because of their limited efficacy, adverse effects, and drug interactions., Migraines typically present with pulsing head pain, nausea, photophobia (sensitivity to light) and phonophobia (sensitivity to sound).

The aim of this study to evaluate the benefit of Botox injection in patients presented with chronic migraine and to determine the efficacy and safety for this kind of treatment in Babylon province.

This was an interventional study of 37 subjects with a history of chronic migraine (28 female and the other 9 were male), The patients received botulinum toxin type A, 100 U into 21 intramuscular injections using a 0.5-inch-long needle EMG guided connected to the machine. and for 3 months following injection, subjects kept daily diaries in which they recorded headache frequency, duration, severity, and the occurrence of associated symptoms. The study were done during the period from January/ 2017 until July/2017.

There were significant differences in patients with chronic migraine before and after treatment , in which there is significant decrease in migraine attacks per month, with reduction severity of these attacks, a significant decrease of hours in each attack and reduced incidence of migraine-associated symptoms.

Pericranial injection of EMG guided BTX-A, 100U, was found to be a safe treatment that significantly reduced migraine frequency, duration, migraine severity, and reduced associated symptoms.

Key Words: Botox, migraine headache, Botolenium Toxin Type A.

تقييم حقن مادة البوتكس بواسطة تخطيط العضلات الموجه لمرضى داء الشقيقة المزمن في محافظة بابل

الخلاصة

يعد البوتكس المادة الوحيدة والاولى الموافق عليها من قبل اتحاد الدواء عالميا التي تستخدم كعلاج وقائي من داء الشقيقة المزمن. كما ويعد العلاج الوحيد لمرضى داء الشقيقة المزمن.

علاجات داء الشقيقة الوقائية التي تستخدم حاليا عادة غير مرضي بسبب فعاليتها المحدودة ، جوانبها السلبية و تفاعلاتها مع بقية الادوية.

تكون الام الرأس المصاحبة لداء الشقيقة من النوع النبضي و غالبا ما يصاحبه غثيان، قيء بالإضافة الى الخوف من الضوء والاصوات العالية.

لتقييم فائدة حقن مادة البوتكس السمية باستخدام تخطيط العضلات الموجه لمرضى داء الشقيقة المزمن ولتحديد فعاليته و سلامته لهؤلاء المرضى في محافظة بابل.

اجريت دراسة تداخلية ل ٣٧ مريضا مصابا بداء الشقيقة المزمن (٢٨ اناث و ٩ ذكور) تم حقن مائة وحدة لكل مريض لاحدى وعشرون منطقة في عضلات الرأس باستخدام نصف انج نيدل لتخطيط العضلات الموجه و الذي يتصل بشاشة عرض خاصة لتحديد مناطق الحقن بدقة متناهية و طلب من المرضى المعنيين تسجيل يومي مفصل لمدة ثلاثة اشهر بعد تأريخ الحقن عن نوبات الشقيقة من ناحية عدد مرات حدوثها خلال الشهر

الواحد و عدد ساعات كل نوبة و شدتها بالإضافة الى الاعراض المصاحبة لها وقد اجريت الدراسة للفترة من شهر كانون الثاني الى شهر تموز للعام ٢٠١٧.

سجلت هذه الدراسة اختلافات ذات اهمية معنوية لمرضى داء الشقيقة المزمن قبل وبعد العلاج حيث سجلت انخفاض واضح في عدد مرات حدوثها خلال الشهر الواحد ، وانخفاض ملحوظ في عدد ساعات كل نوبة بالإضافة الى قلة شدتها والاعراض المصاحبة لها بعد العلاج مقارنة بما سجل قبل العلاج.

وجد ان حقن مائة وحدة من مادة البوتكس السمية بواسطة تخطيط العضلات الموجه كان علاج آمن وله اهمية معنوية لمرضى داء الشقيقة المزمن قبل و بعد العلاج حيث سجلت الدراسة انخفاض واضح في عدد مرات حدوثها خلال الشهر الواحد، وانخفاض ملحوظ في عدد ساعات كل نوبة بالإضافة الى قلة شدتها والاعراض المصاحبة لها بعد العلاج مقارنة بما سجل قبل العلاج.

الكلمات المفتاحية: بوتكس، داء الشقيقة. سم البوجيولاينوم نوع أ.

Introduction

BOTOX is the first and only FDA-approved preventive treatment for chronic migraine and tension headache [1]. Current migraine preventive therapies are often unsatisfactory because of their limited efficacy, adverse effects, and drug interactions. Migraines typically present with pulsing head pain, nausea, photophobia (sensitivity to light) and phonophobia (sensitivity to sound).

Usually migraine attack affects one half of the head, which is pulsating in nature, and may last from 2 to 72 hours. And usually the attack became more worse by any exertion or physical activity [3].

Migraines may be due to a mixture of genetic and environmental factors. The majority of cases related to family history, hormonal imbalance, in which migraines affect women about two to three times more than men [4,5]. The exact cause of migraine are not well known. It is, however, contributed to a neurovascular disorder [6]. Migraine may be due to increase excitability of the cerebral cortex and abnormal neural control of trigeminal nucleus of the brainstem [7].

Migraines can also cause numbness of the skin. People with severe migraines also have nausea, vomiting and light sensitivity. Medications, certain foods, smells, loud noises and bright lights can all trigger a migraine headache [8].

Photophobia and visual symptoms are one of the most common associated symptoms of migraine [9] and grating patterns of definite spatial frequency may persist even between attacks [10,11].

Visual symptoms such as light flashes has been found in migraineurs with aura [12].

Some of the theories regarding the pathophysiology of migraine include Depolarization theory in which there is an electrical depolarization spreads to involve the whole cortex of the brain, in which there will be release of inflammatory mediators that cause irritation of the cranial nerve roots, specially the trigeminal nerve, which is responsible about the impulses conduction that concerned with head and face sensation. At the beginning of the attack, a large part of the brain involved by this depolerization, even the hypothalamus [13].

Vascular theory is another theory in which the wall of the head blood vessels contract and there will be spasm of the corresponding arteries leading to reduction in the blood flow mainly to the occipital lobe which give an explanation of aura that followed by migraine [14].

Neurotransmitter theory specially serotonin which acts as a mood stabilizer and pain regulator as well as its effect in the constriction and dilation of the brain blood vessels. This theory agreed with the fact that patient who suffer from migraine usually recorded low serotonin levels, [15].

Thyroid dysfunction mainly decrease level of thyroid hormones may be contributed to the cause of migraine attacks. In which decrease metabolic rate leads to fluid retention and mucin accumulation that affect the blood vessels and lead to the corresponding headache [16].

Botulinum toxin type A (BTX-A) used nowadays in majority of disorders which related to muscle contractions, such as spasticity, cervical dystonia, rectal sphincter spasm with fissure, blepharospasm, and achalasia as well as hyperhidrosis. In addition reducing pain associated with these conditions.

BTX-A is a neurochemical toxin, which effect the neuromuscular junction by blocking the ability of nerves in contracting the muscles. It means that it cause paralysis to the muscles [17].

In order to contract the muscle, the nerve endings release a neurochemical transmitter which represented by acety-lcholine at the neuromuscular junction that attached to a special receptors in the muscle fiber leading to contraction and relaxation of the muscles, so BTX -A prevents the release of acetylcholine in which it prevents contraction of the muscle fiber [18].

The aim of this study to evaluate the benefit of EMG guided BTX-A injection in patients presented with the main common primary headaches represented by chronic migraine and to determine the efficacy and safety for it regarding the frequency of the attacks, duration, intensity as well as other associated symptoms.

Materials and Methods

This study was carried out through the period from January 2017 to June 2017 , at Hilla city in Babylon province. By using the history, as a cross section observational study so it was an interventional study of 37 subjects with a history of chronic migraine diagnosed by neurologist ranging from (18-59) years with (28 females and 10 males), The patients were asked to note a daily diaries one month before the injection and three months after the injection including headache frequency per month, duration per hour for each attack, severity, and the occurrence of associated symptoms. A After dissolving 100 units of BTX-A (Allergan) in a 4 ml normal saline we select about 21 site for injecting the toxin by using a 0.5-inch-long needle EMG guided connected to the machine that it gives an important information about the exact site of injection by detecting the full interference pattern for the muscle contraction by the EMG machine in which the optimum point for injection could be localized. The mentioned muscles were injected: occipital (10 U for one site in each side; frontal (five U for seven sites); trapezius (five U in two sites for each side); temporalis (three and quarter U for two sites in each side); splenius capitis (two and a half U in one site for both sides); semispinalis (two and a half U in one site for both sides) [19], Following injection for three months later patients asked to record daily diaries in which they mentioned exactly the frequency of headache attacks in each month, duration of each attack by recording the number of hours, intensity for each attack and the occurrence of associated ymptoms such as nausea, vomiting , photophobia, photophobia, as it recorder previously.

The exclusion criteria were (1) any medical condition or any contraindication for BTX-A (2) a history of complicated migraine, (3) pregnant or lactating women (4) known allergy or sensitivity to BTX-A (5) patients with other types of headache (6) patient taking any prophylactic medication during the three months before and 3 months after BTX-A injections.

Statistical analysis were performed depending on SPSS version 19 [20].

Results

37 patients (28 female, 9 male) with chronic migraine involved in this study. Their weights ranged from 53 to 99 kg , while their heights from 155 to 190 cm , and their ages ranged from 18 to 59 years.

In this study table (1) and figure (1) shows the mean ± standard deviation frequencies of the migraine attacks of the involved patients before and after injection respectively (5.6 8± 2.08, 3.97 ± 1.8, 3.54 ± 1.83, 3.38 ± 1.77) in which there is significant decrease in the number of attacks per month.

Table 1 : Frequency of patients migraine attacks before and after Botox EMG guided injection

	Freq. before injection	freq. after injection during the 1st month	freq. after injection during the 2nd month	freq. after injection during the 3rd month
Mean ± SD	5.68± 2.08	3.97±1.8	3.54± 1.83	3.38±1.77
No: of patients	37	37	37	37

SD : Std. Deviation Freq: frequency No: number

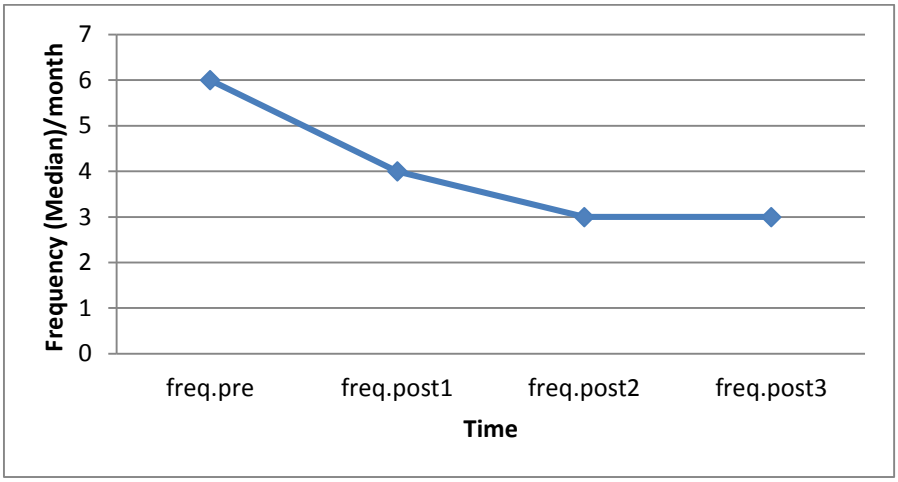

Figure 1: Frequency of patients migraine attacks before and after Botox EMG guided injection

While table (2) and figure (2) shows the duration of the patients attacks before and after Botox injection (10.05 ± 5.04 , 8.02 ± 4.77, 7.57 ± 4.56, 6.65 ± 4.24) respectively in which there is a significant reduced number of hours per each attack.

Table 2: Duration of patients migraine attacks before and after Botox EMG guided injection

	duration. before injection/hour	duration after injection during the 1st month	duration after injection during the 2nd month	duration after injection during the 3rd month
Mean ± SD	10.05 ± 5.04	8.02 ± 4.77	7.57 ± 4.56	6.65 ± 4.24
No: of patients	37	37	37	37

SD : Std. Deviation No: number

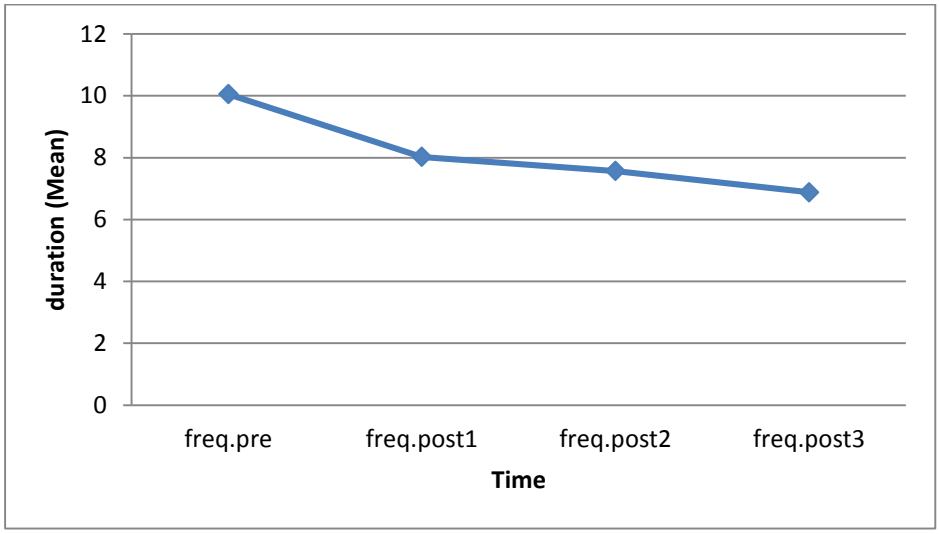

Figure 2: Duration of patients migraine attacks before and after Botox EMG guided injection

Figure (3) shows the decline in the intensity of the attacks before and after Botox EMG giuded injection.

Regarding the intensity of the attacks before EMG guided Botox injection there were 5 patients with mild attack, 23 patients with moderate attack, while only 9 with severe attack, during the 1st month post injection there were 18 patients with mild attack, other 18 with moderate attack and only one with severe attack, the same number were reported during the 2nd month post injection, while during the 3rd month post injection the intensity decline to become 20 patients with mild attack and 16 patients with moderate and only one remain severe without change, so there were significant reduction of the intensity of the attacks.

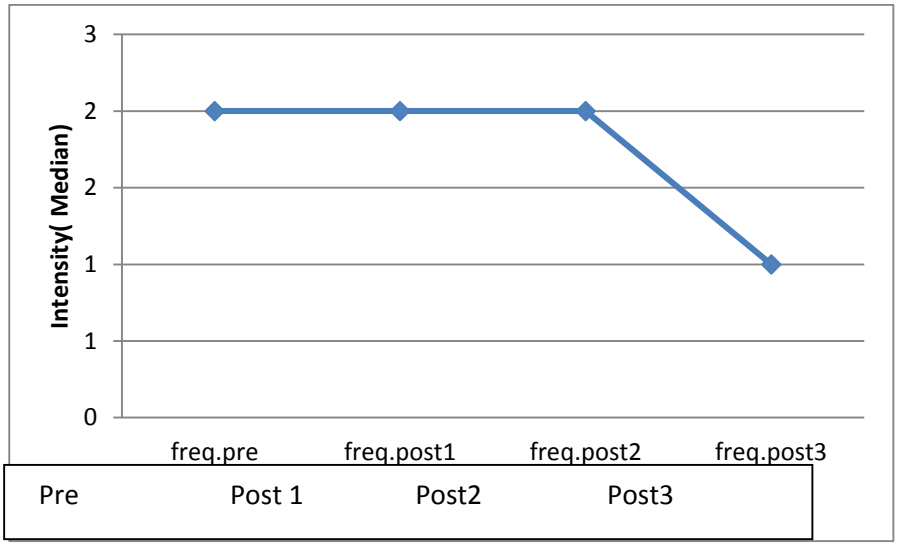

Figure 3: Intensity of the attacks before and after EMG giuded Botox injection

Regarding the associated symptoms, before EMG guided Botox injection there were 25 patients with these associated symptoms mainly nausea, vomiting, photophobea and phonophobia, while 10 with moderate associated symptoms and the remaining two patients presented with less symptoms. During the 1st month post injection 21 patients decrease their associated symptoms, while 12 patients

remain with the same associated symptoms and only 4 patients report increase in them. During the 2nd month post injection there were 21 patients with decrease associated symptoms and 13 the same and only three with increase associated symptoms, while during the 3rd month post injection 22 with decrease associated symptoms and 14 remain without change with the prevoius month , while there was only one patient free from these associated symptoms as shown in table (4) and figure (4), So there were significant reduction in these associated symptoms.

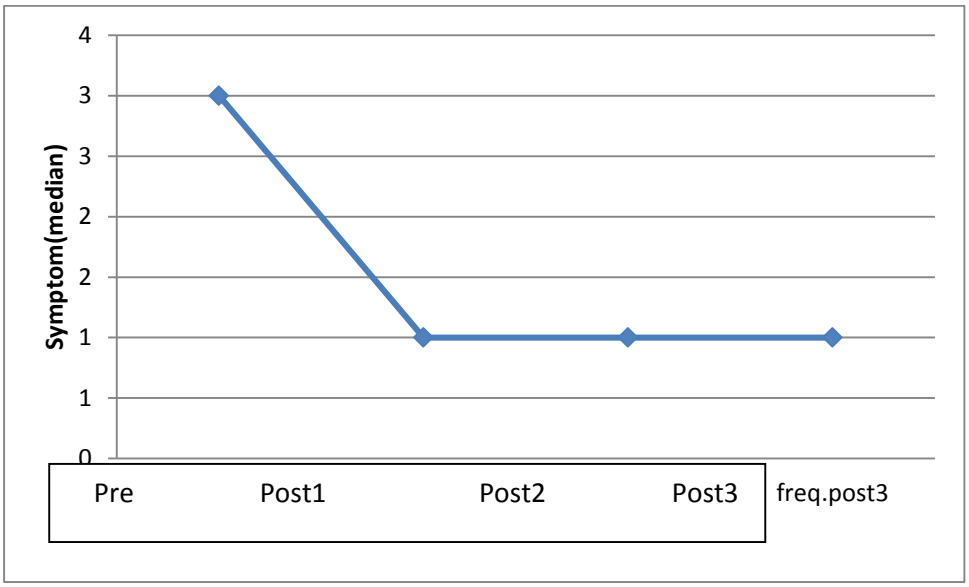

Figure 4: Associated symptoms before and after EMG giuded Botox injection

Discussion

The evaluation of EMG guided BTX-A injection in treating patients with the chronic migraine in this study found that it plays a role in decreasing the frequency of attacks per month before and after injection as well as the duration of the attacks, while there were decline in the intensity and severity of each attack after the injection. Regarding the associated symptom which may occur during each attack there were prominent decrease in them and these results consistent with many others who found the same results [21-23] while it disagreed with others who found that BTX-A failed to play a role in this kind of treatment [24].

The simplest explanation for this efficacy contributed to the effect of this toxin on the muscle contraction that plays a major role in the pathophysiology of migraine [25] as well as its powerful effect in reducing pain which gives an explanation for reducing migraine intensity and frequency. Even so it considered as an exocytotic inhibitors, [26] that gives its role in pain signals inhibition , in which the effect on the sensory system is unknown yet [27].

The role of BTX-A in treating chronic migraine was related to the release of acetyl choline at the neuromuscular junction and its attachment to the specific receptors which lead to muscle contraction , so this toxin will cause reduction of this attachment leading to muscle relaxation instead of contraction or its role in inhibiting the depolarization of the cerebral cortex of the central nervous system specially the trigeminal nucli in the brain stem as well as the hypothalamus which related to the associated symptoms.

In spite of its role for acting centrally in treating migraine, BTX-A can acts peripherally through inhibiting the peripheral sensory fibers in which the tingling and numbness of the corresponding skin related to it [21]. The role of this toxin in suppressing the sensory peripheral signals contributed to its effect in reducing the release of substance P from embryonic dorsal root

ganglion neurons [28], or CGRP from trigeminal ganglion neurons [29], or glutamate from the dorsal horn of the peripheral nociceptors [30]. Using quantitative sensory testing, however, [31] showed that the injection of this toxin cannot effect the threshold of pain to cold, heat ,as well as mechanical and electrical stimulation, giving the idea that BTX-A can exert its effect in blocking pain signals through neurochemical inhibition or anti-inflammatory action, rather than by direct peripheral anti nociceptive signals.

Regarding the mechanism of action of BTX-A on nervous system depends on whether it exert its effect peripherally or centrally and weather inside the cranium or outside the cranium. The pathophysiology of the extracranial tissue involvement has been mentioned before five decades ago [32,33] If so, it means that it works on the extracranial nociceptors that innervate the scalp.

Conclusions

EMG guided BTX-A injection was found to be effective treatment that significantly reduced chronic migraine frequency attacks, duration, severity, and associated symptoms in Babylon province.

References

[1] Kunkel, R, S, (2010) "Headache". Disease Management Project: Publications Cleveland Clinic. Retrieved Headache Reports, 14: 321.

[2] Piane, M., P. Lulli, I. Farinelli, S. Simeoni, S. De Filippis, F.R. Patacchioli, P. Martelletti, 2007.Genetics of migraine and pharmaco-genomics: some considerations. The journal of headache and pain, 8(6): 334-9.

[3] Stovner, L.J., J.A. Zwart, K. Hagen, G.M. Terwindt, J. Pascual, (2006). Epidemiology of headache in Europe. Eur J Neurol., 13(4): 333-45.

[4] Lay, C.L., S.W. Broner, (2009). "Migraine in women". Neurologic Clinics, 27(2): 503-11.

[5] Bartleson, J.D., F.M. Cutrer, (2010). "Migraine update. Diagnosis and treatment". Minn Med, 93(5): 36-41.

[6] Bartleson, J.D., F.M. Cutrer, (2010). Migraine update. Diagnosis and treatment. Minn Med, 93(5): 36-41.

[7] Dodick, D.W., Gargus, J.J. (2008). Why migraines strike. Sci. Am. 299(2): 5663.

[8] Cullom, Douglas, R., Benjamin Chang, A. Mark Friedberg and Christopher Rapuano, (2004). The Wills Eye Manual, Office and Emergency Room Diagnosis and Treatment of Eye Disease. J.B. Lippincott Company.

[9] Hay, K.M., Mortimer, M.J. Barker, D.C., Debney, L.M. and Good, P.A. (1994). 1044 women with migraine: the effect of environmental stimuli. Headache, 34: 166-168.

[10] Wilkins, A.J., M.I. Nimmo-Smith, A. Tait, C. McManus, S. Della Sala, A. Tilley, A. Arnold, M. Barrie, S. Scott, (1984). A neurological basis for visual discomfort. Brain, 107: 989-1017.

[11]Marcus, D.A., Soso, M.J. (1989). Migraine and stripe-induced visual discomfort. Arch Neurol, 46: 1129-1132.

[12]Wray, S.H., 1995. Mijovic-Prelec, D. and Kosslyn, S. M. Visual processing in migraineurs. Brain, 118: 25-35.

[13] Olesen, J., Bousser, M.G. , Diener, Dodick, H.C., First, D. M. Goadsby,P.J. et al. 2006. Headache Classification Committee. New appendix criteria open for a broader concept of chronic migraine. Cephalalgia, 26: 742-6.

[14]Bussone, G. 2010. Clinical considerations on chronic migraine, pharmacoresistance and refractoriness. Neurol Sci., 31(Suppl 1): S83-5.

[15]Adam, R.D., M. Victor, (1989). Principal varieties of headache migraine. Principles of neurology 4th ed. Singapore McGaw-Hill, pp: 138-144.

[16]Pearce JMS. Migraine. In: D.J. Weatherall, J.G.G. Ledingham, D.A. Warrell, (1996) Text book of medicine. Oxford: Oxford University Press, pp: 4024-4026.

[17]Bartelink, M.L., E. van de Lisdonk, H. van den Hoogen, H. Wollersheim, C. van Weel, (1993). Migraine in family practice: prevalence and influence of sex hormonal status. Fam Med., 25: 331-336.

[18]Foran PG, Mohammed N, Lisk GO, Nagwaney S, Lawrence GW, Johnson E, Smith L, Aoki KR, Dolly JO. Evaluation of the therapeutic usefulness of botulinum

neurotoxin B, C1, E, and F compared with the long lasting type A. Basis for distinct durations of inhibition of exocytosis in central neurons. J Biol Chem. 2003; 278: 1363–71

[19] Silberstein S, Mathew N, Saper J, Jenkins S. Botulinum toxin type A as a migraine preventive treatment. For the BOTOX Migraine Clinical Research Group. Headache. 2000;40:445–50.

[20] Siegel S. Nonparametric Statistics for the Behavioral Sciences. McGrow-Hill Kogakusha; Tokyo: 1956. p. 312.

[21] Aoki KR. Review of a proposed mechanism for the antinociceptive action of botulinum toxin type A. Neurotoxicology. 2005;26:785–93.

[22] Tfelt-Hansen P, Lous I, Olesen J. Prevalence and significance of muscle tenderness during common migraine attacks. Headache. 1981;21:49-54.

[23]Hohne-Zell B, Galler A, Schepp W, Gratzl M, Prinz C. Functional importance of synaptobrevin and SNAP-25 during exocytosis of histamine by rat gastric enterochromaffin-like cells. Endocrinol. 1997; 138:5518-5526.

[24] Vo AH1, Satori R, Jabbari B, Green J, Killgore WD, Labutta R, Campbell WW. Botulinum toxin type-a in the prevention of migraine: a double-blind controlled trial.

[25] Hansen I, Olesen J. Prevalence and significance of muscle tenderness during common migraine attacks. Headache. 1981; 21:49-54.

[26] Hohne-Zell B, Galler A, Schepp W, Gratzl M, Prinz C. Functional importance of synaptobrevin and SNAP-25 during exocytosis of histamine by rat gastric enterochromaffin-like cells. Endocrinol., 1997; 138:5518-5526.

[27] Blersch W, Schulte-Mattler WJ, Przywara S, May A, Bigalke H, Wohlfarth K. Botulinum toxin A and the cutaneous nociception in humans: a prospective, double-blind, placebo-controlled, rando-mized study. J Neurol Sci. 2002; 205: 59–63.

[28] Welch MJ, Purkiss JR, Foster KA. Sensitivity of embryonic rat dorsal root ganglia neurons to Clostridium botulinum neurotoxins. Toxicon. 2000;38:245–58.

[29] Durham PL, Cady R. Regulation of calcitonin gene-related peptide secretion from trigeminal nerve cells by botulinum toxin type A: implications for migraine therapy. Headache. 2004;44:35–42. discussion 42–3.

[30] Cui M, Khanijou S, Rubino J, Aoki KR. Subcutaneous administration of botulinum toxin A reduces formalin-induced pain. Pain. 2004;107:125–33.

[31] Blersch W, Schulte-Mattler WJ, Przywara S, May A, Bigalke H, Wohlfarth K. Botulinum toxin A and the cutaneous nociception in humans: a prospective, double-blind, placebo-controlled, randomized study. J Neurol Sci. 2002; 205: 59–63.

[32] Siegel S. Nonparametric Statistics for the Behavioral Sciences. McGrow-Hill Kogakusha; Tokyo: 1956. p. 312.

[33] Wolff HG, Tunis MM, Goodell H. Studies on migraine. Arch Internal Medicine. 1953;92:478–484.