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Botulinum Toxin-A For Management of Migraine: An Experience in Iraq

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Abstract

Background

Iraq as a country, doesn't have any facts or details about using botulinum toxin for the prevention of migraine. The main goal of this experience, is to study the clinical profile and response to treatment with botulinum toxin injection for migraine patients. Migraine is a headache illness identified by repeated attacks of moderate to severe pain, nausea, photophobia, and phonophobia. Botulinumtoxin A is used to prevent and treat migraine.

Aim of the study

To estimate the effectiveness of botulinum toxin-A injections for managing migraine and prove the usefulness and safety of botulinum toxin -A.

Materials and methods

The study sample included 23 patients aged 20-45, 8 males and 15 females, diagnosed with migraines for more than one year. Patients with neurological or cardiovascular disorders and pregnant women were not included from the study. Botox powder 150 units and a 30-gauge needle were used to inject 30 injections, with 5 units of botulinum toxin in each injection site.

Results

Ranging from non-responders (4.4%) to partial responders (4.4%), responders (26%) and high responders (65.4%). The constancy of migraine days revealed a clear reduction from the original percentage after three months of botulinum toxin injection.

Conclusion

Botulinum toxin A is a useful alternative for chronic migraine patients who do not benefit from other medications. In chronic migraine botulinum toxin, A is helpful in terms of quality of life, headache frequency, and pain intensity. Botulinum toxin A therapy is safe and tolerated.

Keywords

Orofacial pain, Migraine, Botulinum toxinA, Chronic migraine.

Orofacial pain syndromes, which affect the face, head, and neck, are very prevalent and incapacitating illnesses. These issues can be difficult for the doctor since the orofacial area is quite complicated and discomfort can occur . The doctor has to have a lot of information on the pain caused by these structures in order to give an appropriate diagnosis. Orofacial discomfort can be categorized as follows:

- Physical.
- Psychological.

Physical orofacial pain includes temporomandibular joint and musculoskeletal diseases, neuropathic pain (such as trigeminal neuralgia), and neurovascular illnesses (eg, migraine). Depression and anxiety disorders are symptoms of psychiatric illnesses. [1] [2].

1.2 Migraine

The most general form of headache condition is referred to as a migraine, which can be identified by recurring episodes of moderate to severe unilateral pulsing pain, which may also be accompanied by nausea, a fear of light or sound. A migraine with aura is identified by brief neurological symptoms (including vision impairment) that occur before the start of the headache and are created by changes in brain activity.[3] [4]. Migraine headaches are frequently seen present on one side that cause discomfort and suffering in the skull, neck, and behind the eyes. [5] [6].

Although the main cause of migraines is still unclear, there are additional variables, such as hereditary and environmental ones, that might potentially contribute to the development of migraines (the methylenetetrahydrofolate reductase gene defect, production of inflammatory substances around the nerves and cerebrospinal fluid, abnormal vitamin D levels, low level of serotonin, elevated calcitonin gene related peptide, mitochondrial disorders and low levels of metabolic enzymes are some of the main causes of migraine.) [7].

1.3 Epidemiology

An analysis of worldwide studies on the epidemiology of chronic migraine found a number of generality rates [8]. According to the term used and the population under study, these estimates range from 0% to 5.1% [9] [10]. Using the most recent HIS (The Indian Health Service) criteria, recent research find that the prevalence is 0.5% in Germany and 0.91% in the US population [11, 12]. Many studies in the main population and among chronic migraine sufferers have found that women are more prone than males to acquire chronic migraine.[13]. Adjusted prevalence rises in both men and women from childhood to midlife and begins to fall after the fifth decade of life. The disorder affects 1.89 percent of women between the ages of 40 and 49 [11]. Chronic migraineurs are likely to develop obesity, asthma, chronic obstructive pulmonary disease, heart disease, stroke, anxiety, and depression than episodic migraineurs [14]. Those who suffer from chronic migraines often abuse medications as a result of their frequent episodes. An interventional investigation found that between 40.9% and 50.4% of those with chronic migraine misused their medication. [15] [16].

1.4 Regulation And Pharmacologic Treatment :

The identification of chronic migraine is made using a neurological examination, the patient's medical past, including a headache record , and other factors. To rule out secondary headache causes, lumbar puncture and cerebral magnetic resonance imaging may be necessary in some circumstances. [17]. Lessening the effect that the disease has on the patient's life is the major objective of treating persistent migraines. So, it's important to keep attacks of migraine as brief and infrequent. Many non-pharmacological techniques, such as stress reduction, lifestyle migraines can be avoided with management, massage treatment, yoga, and a diet high in vitamins and minerals, particularly magnesium (B2,B3,B12,D). [18] [7] [19]. The treatment of persistent migraine with medication includes both acute migraine therapy and prevention care. The two treatments that are used to stop migraine episodes most commonly are triptans and nonsteroidal anti-inflammatory drugs (NSAIDs). Both medication groups have a lot of clinical evidence to back up their

effectiveness in stopping acute migraine episodes. As soon as a chronic migraine is detected, the preventative therapy may usually be started, and the choice of material to apply should take the patient's comorbidities into consideration. [20]. The medications specifically tested in people with persistent migraine include valproate, amitriptyline, gabapentin topiramate, ergotamine, and onabotulinumtoxinA. The only substance that has been authorized by the US Food and Drug Administration is onabotulinumtoxin - A . [21]

1.5 Onabotulinumtoxin-A (Botox) :

Oral anti-migraine medications are ineffective in about 40–50% of people and have unfavorable adverse consequences [22]. Nowadays, many people utilize botulinum toxin A to treat and prevent migraines. [23]. Botulinumtoxin A has been used for more than 20 years to treat a range of conditions related to skeletal and smooth muscle spasm. [24]. The gram-positive, anaerobic bacteria *Clostridium botulinum* produces the complex protein toxin known as botox. Botulinum toxins were developed by German doctor Justinus Kerner to address issues with autonomic dysfunction and hyperkinetic movements (1786-1862). The Food and Drug Administration (FDA) gave botulinum toxin A its approval in 1989. The eight primary serotypes of botulinum toxin are represented by the letters A through H. The only varieties used in therapeutic settings Classes A and B can be distinguished from one another by their prolonged duration of action. [23] [25]. Only chronic migraine, which is defined by headaches that last longer than four hours on average, fifteen days or more out of every month, is treated with botulinum toxin A. [26]

1.6 Mode Of Action Of Botulinumtoxin-A :

The exocytosis of proteins and neurochemicals from the motor and sensory systems, the exocytosis of proinflammatory cells, excitatory neuropeptides from the nervous system, such as substance P (peptide secreted mainly by neurons), CGRP (calcitonin gene-related peptide), and glutamate, as well as the inhibition of soluble N-ethylmaleimide-sensitive factor attachment protein receptors have all been linked to the action of botulinum toxin A [27]. Botulinum toxin A may have an impact on the central nervous system, according to recent investigations. [23]

1.7 Doses And Injections Sites :

OnabotulinumtoxinA injections should be given every three to nine months at 30–39 pericranial injection sites, including seven bilaterally afflicted head and neck muscle groups at each site [28]. Fig(1)

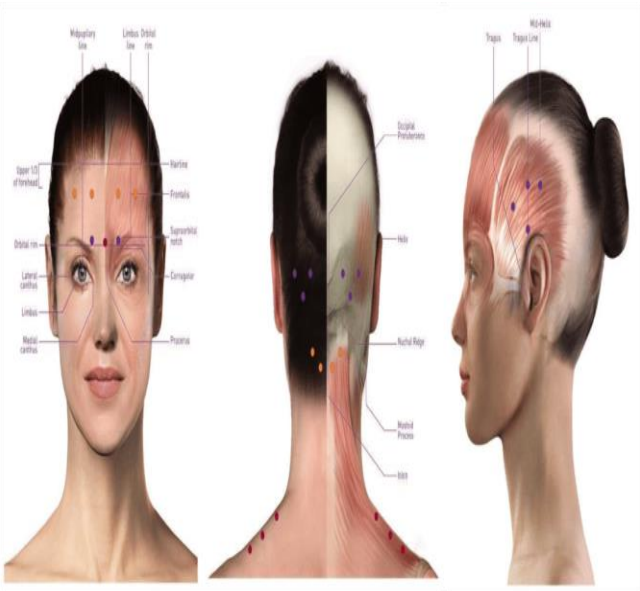


Fig. 1: Injection sites of botox for migraine. [35]

1.8 Safety And Tolerability:

Botulinum toxin A side effects that affect the entire body are rather rare and usually related to the injection [29]. Injection side effects are generally minimal, transient, and seldom result in patients ceasing to take their medication. The most commonly reported adverse effects, according the PREEMPT (The Phase 3 Research Evaluating Migraine Prophylaxis Therapy) studies [30], were neck discomfort (4.3%), injection site pain (2.1%), eyelid ptosis (1.9%), and muscle weakness (1.6%). The results of various clinical studies demonstrate the tolerability of onabotulinumtoxinA treatment. [31] [32]

Materials and Methods

2.1 Study Sample :

Eight men and fifteen women, totally (23) between the ages of 20 and 45, participated in the study.

pregnant women, individuals with neurological or cardiovascular disorders , and any previous botulinum toxin sensitivities, being pregnant or breastfeeding, or displaying symptoms of a mental disorder were also forbidden.

This clinical investigation was carried out from September 2022 to March 2023 in the college of dentistry-university of Tikrit's oral and maxillofacial surgery department.

The study was accomplished in accordance with the Declaration of Helsinki and was given the ethics committee's blessing.

2.2 Armamentarium (Instruments, Materials) :

A 30-gauge needle was used to administer 2.5 units of Botox per 0.1 mL diluted in 1 mL of 0.9% sodium chloride solution, in accordance with the recommended dilution and storage instructions. Figure (2).

Type A neurotoxic botulinum toxin, Kanada (100 units) powdered type. Figure (3)

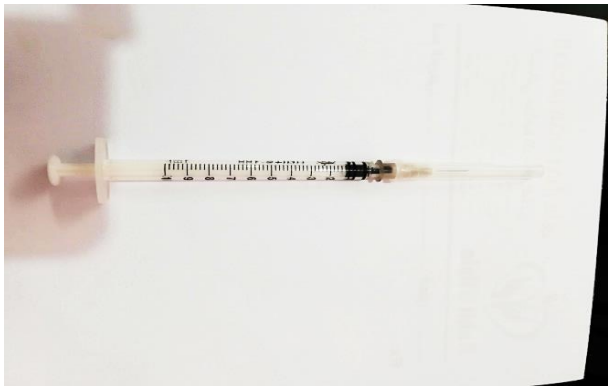


Fig.2: Disposable syringe, needle gauge 30.

Fig.3 : Botox vial .

2.3 Methodology :

During patient preparation, a total of 30 injections were performed, each containing five units of botulinum toxin. The muscles that involved were explained in tab. (1) , while the doses for each muscle explained in tab. (2)

Table 1 : number of injection sites for each muscle

Muscle	Number If Injection Sites
Frontalis	Five Injection Sites
Corrugator	Two injection sites one in each muscle
Procerus	Single injection site
Occipitalis	Three injection sites per side
Splinus Capitus	Three injection sites per side
Temporalis	five injection sites per side

Table 2: Dosing by Muscles for Chronic Migraine

Head/Neck Area	Recommended Dose (Number of Sites")
Frontalis	25 Units divided in 5 sites
Corrugator	10 Units divided in 2 sites
Procerus	5 Units in 1 site
Occipitalis	30 Units divided in 6 sites
Splinus Capitus	30 Units divided in 6 sites
Temporalis	50 Units divided in 10 sites
Entire Dose:	150 Units divided in 30 sites

Each injection site = 5 Units BOTOX *
Dose distributed bilaterally

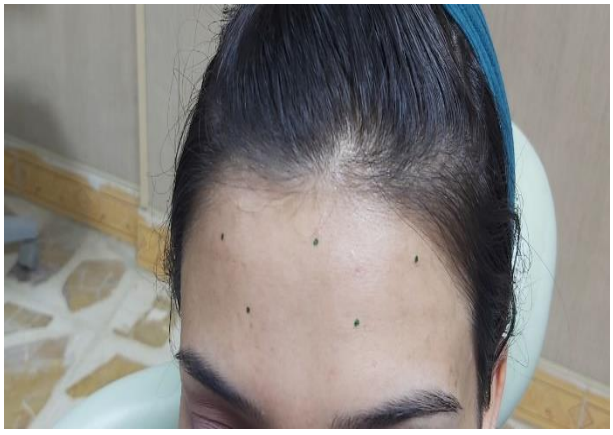


Fig.4 : Marking the injection sites.

Fig.5 : Injection technique.

2.4 Postoperative Instructions And Medication :

After injection, every patient is advised to relax, abstain from leaning over or vigorously washing their faces for at least 4 hours, forbidden from doing any sort of physical exercise, avoid heat exposure, avoid alcohol and painkillers, avoid wearing anything on the treatment area, no laying down after botox treatment, forbidden from touching the face or massaging the treatment area, and phone us or request an ambulance if any allergic symptoms are present

2.5 Follow up And Data Collection :

The Migraine Disability Assessment (MIDAS) questionnaire table (3) which was given to the patient at baseline and three months after receiving a botox injection, was used to assess the patient's way of living life is stated as a migraine-related impairment .

Table (3) : Migraine Disability Assessment (MIDAS) questionnaire

The Migraine Disability Assessment Test

The **MIDAS** (Migraine Disability Assessment) questionnaire was put together to help you measure the impact your headaches have on your life. The information on this questionnaire is also helpful for your primary care provider to determine the level of pain and disability caused by your headaches and to find the best treatment for you.

INSTRUCTIONS

Please answer the following questions about ALL of the headaches you have had over the last 3 months. Select your answer in the box next to each question. Select zero if you did not have the activity in the last 3 months. Please take the completed form to your healthcare professional.

_____ 1. On how many days in the last 3 months did you miss work or school because of your headaches?

_____ 2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? (Do not include days you counted in question 1 where you missed work or school.)

_____ 3. On how many days in the last 3 months did you not do household work (such as housework, home repairs and maintenance, shopping, caring for children and relatives) because of your headaches?

_____ 4. How many days in the last 3 months was your productivity in household work reduced by half of more because of your headaches? (Do not include days you counted in question 3 where you did not do household work.)

_____ 5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches?

_____ Total (Questions 1-5)

What your Physician will need to know about your headache:

_____ A. On how many days in the last 3 months did you have a headache? (If a headache lasted more than 1 day, count each day.)

_____ B. On a scale of 0 - 10, on average how painful were these headaches? (where 0=no pain at all, and 10= pain as bad as it can be.)

Scoring: After you have filled out this questionnaire, add the total number of days from questions 1-5 (ignore A and B).

MIDAS Grade	Definition	MIDAS Score
I	Little or No Disability	0-5
II	Mild Disability	6-10
III	Moderate Disability	11-20
IV	Severe Disability	21+

If Your MIDAS Score is 6 or more, please discuss this with your doctor.

Results

There was an amount of (23) individuals included in the study, the gender classificationz showed that (65.3%) of patients were females, while males represented only 34.7 % of the study population .

A seventeen patient grade (iv) according to MIDAS score and (6) grade (iii) , The number of migraine days showed a clear declination from baseline after 3 month botulinum toxin injection , the result explained in table (4)

15 patient drope to grade I (65.4%)
6 patient drope to grade ii (26%)
1 patient grade iii (4.4%)
1 patient grade iv (4.4%)

No side effect or complications was recorded in our study

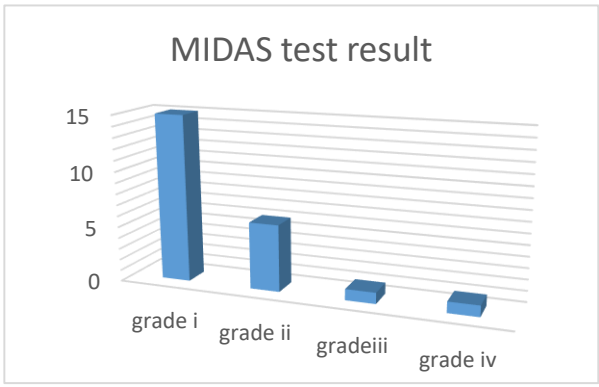


Fig. (6): The migraine disability assessment results.

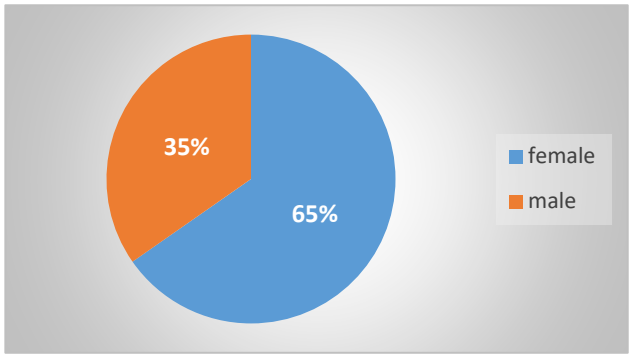
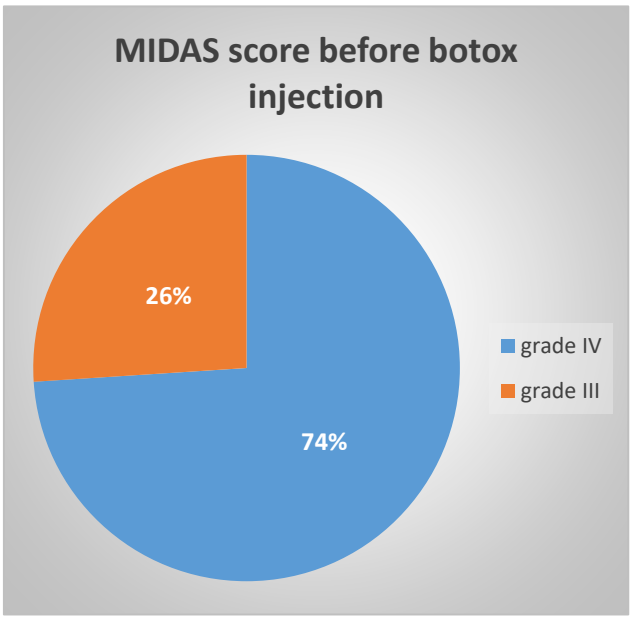


Figure 7: Female to male ratio.

Table 4: Clinical data of patients in our study with migraine treated with botulinum toxin-A injection.

Variables	Number (range)	%
Number of females	15	65.22 %
Number of males	8	34.78 %
Mean age	20±45 Years (range 20-50)	-
Female to male ratio	15:8	-
non responders	1	4.4 %
partial responders	1	4.4 %
responders	6	26 %
High Responders	15	65.4 %



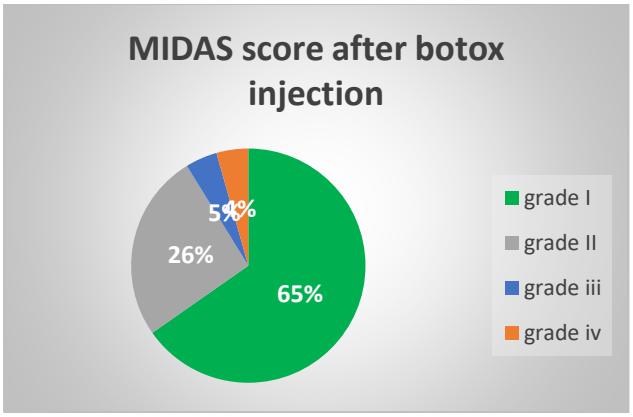


Figure 8: MIDAS score before and after 3 months of botox injection

Discussion

The migraine characterized by recurring episodes of moderate to severe unilateral pulsing pain. Furthermore, nausea, a fear of light or sound, or all three might be symptoms of migraines.[3]

There are many studies that explain the role of botox in the prophylaxis of multiple headache disorders including migraine [36]. A number of multicenter, double-blind

placebo-controlled trials were published since 2010, demonstrating the efficacy of botulinum toxin injection in the prevention of migraine. [37] [38] A current review studies proved the effectiveness of botox injection in chronic migraine only [36]. Our study is the first study done in iraq to explore the effect and evaluate the result from botox injection in patients with chronic migrane by using minimal dosing of botulinum toxin in comparism to traditional methods (avoid injection of trapezius muscles in our study) , our study disagree with **Ali Zandieh et al,. 2022 ,** [34] in their study that explaine the Increase in the onabotulinumtoxinA dose is associated with better headache control and independently improves the numbers of the headache and severe headache days.

The influence of gender in our study show that the female more affected by migraine than male, this in the same line with **Hussein Algahtani1 et al., 2020,**[39] who reach the same result in their study , hormonal disturbance considerd the main factor for aggravating migraine headache .

In our study we don't record any complications or major side effect , this mainly due to correct selection of patient and follow scientific protocol in preparing and injection of botox .

Conclusion

Botulinum toxin A is a highly effective alternative for chronic migraine patients who do not benefit from other medications. In chronic migraine botulinum toxin-A is helpful in terms of quality of life as well as headache frequency and pain intensity. Botulinum toxin-A therapy is safe and tolerated .

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