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Full Length Research Paper

The response rate in chronic migraine patients after the first session of Onabotulinumtoxin A injection, a single center experience from Saudi Arabia

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Chronic migraine needs a unique approach in management that includes oral prophylactic medications and eventually injection of Onabotulinumtoxin A (Onabot A) to improve patient outcome and quality of life. We aimed to find out the incidence of chronic migraine in a single center experience in Saudi Arabia in addition to the response of injection to Onabot A Retrospective analysis of the occurrence of chronic migraine in our patients. The data were collected to evaluate the response rate after the first injection of Onabot A with emphasis on pain relief in 30 days after the injection session. Among 212 migraine patients, 14 were labeled with the diagnosis of chronic migraine that received Onabot A. 12 of them were female with a mean age of 51.4 +/- 15.3 (25-86). 78.6% had excellent response with reduction of more than 50% of their migraine attacks and eventually changing into episodic migraine. We presented an excellent response rate of Onabot A injection in carefully selected chronic migraine patients after the first injection session.

Keywords: Migraine, chronic migraine, Onabotulinumtoxin A

INTRODUCTION

Background

Migraine in general has a global prevalence of 14.7% (Steiner et al., 2013) and is generally divided into episodic and chronic based on the total number of headache days per month.

Chronic migraine is defined as the occurrence of headaches for 15 or more days per month for more than 3 months, which has the features of migraine headache on at least 8 days per month (Headache Classification Committee of the International Headache Society (IHS), 2013).

It affects about 2% of the general population (Natoli et al., 2010).

For years, the right dose and right injection sites for Onabot A was not agreed upon until the publication of the PREEMPT I and II (phase III Research Evaluating Migraine Prophylaxis Therapy) (Diener et al., 2010; Aurora et al., 2010). The current practice is clear when it comes to the total dose of Onabot A and the location of injection of each site.

The PREEMPT study also evaluated the long-term response after 52 weeks of injection and reported it to be effective, safe, and well tolerated (Aurora et al., 2011).

There is excellent response of Onabot A reported on different ethnic groups (Grazzi and Usai, 2015; Vikelis et

Table 1. The effect of Onabot A injection at 30 and 90 days

Variables		Having Botox		Test	P value
		No	Yes		
Change to episodic migraine at 30 days	No	2 (100%)	1 (8.3%)	Chi square	0.03*
	Yes	0 (0.0%)	11 (91.7%)		
Number of monthly attacks at 30 days		24.0±2.0	11.0±7.0	Independent t test	0.02*
Number of monthly attacks at 90 days		24.0±2.0	4.0±2.0	Independent t test	0.01*

al., 2016). There is no data on the occurrence of chronic migraine or the efficacy of Onabot A in the Saudi population.

We aim to evaluate the occurrence of chronic migraine across our migraine patients and the response rate after the first session of Onabot A at 30 and 90 days.

METHODS

Retrospective analysis of all migraine patients presenting between June 2015 to June 2016.

The patients were seen and evaluated in a private clinic in Jeddah, Saudi Arabia over the study period.

All patients were seen and the injected by the same physician following the same injection sites in the PREEMPT study.

All migraine patients were included in the first search to ensure inclusion of all patients of interest. Then the subgroup of chronic migraine was recognized and included in the final analysis of the study.

All patients with migraine and chronic migraine were diagnosed based on the International Classification of headache disorders, third version (Headache Classification Committee of the International Headache Society (IHS), 2013).

All patients that had the diagnosis of chronic migraine and were injected with Onabot A were evaluated and the response rate after the first session of Onabot A was looked at.

The injection sites and total dose were given as specified in the PREEMPT trials (Diener et al., 2010; Aurora et al., 2010; Aurora et al., 2011).

The patients' response was evaluated at the time of follow up in the clinic or by phone contact and all variables of response were registered at the analysis date of 30 and then 90 days post injection.

The statistical analysis was done by using an SPSS 20 program with the use of chi square and independent t-test to find out if the reduction in headache days was significant at the specified interim analysis.

All other confounders of secondary headache disorders were excluded by appropriate clinical evaluation and respective investigations and only chronic migraine patients were included.

The primary objective of the study was to evaluate the occurrence of chronic migraine headache in our population and to evaluate the response rate of injection based on the total number of headache days at 30 days

Another analysis at 3 months were registered to evaluate the maintenance of response before the next dose of Onabot A was given.

RESULTS

212 migraine patients were identified and 80% of them fulfilled the criteria of migraine without aura. The majority of our group was female and represents about 85% of the total number of migraine patients. 14 patients fulfilled the criteria of chronic migraine. It represents about 6.6% of all migraine patients seen during the year. Two patients were excluded from the injection due to their preference to continue on oral medications rather than Onabot A injection.

12 patients were analyzed who received Onabot A.

12 (85.7%) of the total number of patients were female.

The mean age was 51.4 +/- 15.3 (range 25-86).

The shortest duration of chronic migraine headache before injection was 3 months and the longest was 12 months and the mean number of months prior to injection was 6 months +/- 3

The mean number of headache days per month was 24.4 +/- 5.9.

All patients were treated with prophylactic medications in the months prior to Onabot A injection. Topiramate was used in 57.1 % and amitriptyline was used in the rest of the patients as the first choice of prophylactic drug.

10 patients needed to use a second line prophylactic medication and 8 tried a third drug before getting the session of Onabot A injection.

At 30 days, 80% of the group reported dramatic response to the first dose of Onabot A injection. The number of headache days had a mean of 12.0 +/- 7.0 (p= 0.02) and each migraine attach was very responsive to a single dose of triptan drug to relive the pain.

At 90 days, the mean number of headache days per month was 4 +/- 2 (p=0.01).

All patient who stayed on oral treatment had still chronic migraine with no improvement in headache days despite the change between two prophylactic medications (table 1).

Both patients that did not respond to treatment has an active treatment for depression and were on medications for it.

DISCUSSION

Migraine occurs in 14.7% of all populations with variable ethnic background (Steiner et al., 2013). Chronic migraine patients are affected negatively by the pain, which has significant impact on their life and work.

It was found that it increases disability by impairing household activities and productivities (Bigal et al., 2008).

Multiple treatment protocols were suggested to break the cycle of patients' headaches and many of them has modest effect.

Onabot A is an FDA approved treatment that can be given if the patient qualifies for the diagnosis of chronic migraine. It works by altering sensitized peripheral nociceptors and eventually negative feedback on central sensitization that are highly active during migraine attack. This central sensitization is believed to be a major factor in chronization and transformation of episodic to chronic form (Whitcup et al., 2014; Szok et al., 2015).

Pooled analysis of the PREEMPT studies showed significant reduction in the mean frequency of headache days from baseline (week 4) to the primary end point at week 24 in addition to other variables such as frequency of migraine and cumulative hours of headache (Dodick et al., 2010).

It was suggested before that meaningful clinical response may take time to occur and that the percentage of first time responders to the third dose of Onabot A is around 10.3% (Burstein et al., 2014; Silberstein et al., 2015).

We are reporting the response rate of Onabot A after the first injection in Saudi Arabian chronic migraine patients.

It is obvious that chronic migraine do occur with almost the same rate as the international figures. As well the response rate to the first dose of Onabot A is very high.

Patients reported significant reduction in the total number of days affected by headache and maintenance of that effect in the first 30 days and 3 months after the first dose of Onabot A in comparison to no response at all in patients continuing on oral prophylactic medications.

Our limitations are the following:

First, the number of patients who were injected was low to draw clear conclusions despite the fact that the number of headache days was clearly lower in comparison to patients' baseline headaches. The headache has changed from being chronic to episodic migraine.

Second, it is an experience from single center, which has an embedded referral bias, and also a single person did the injections

Third, the design of the study is retrospective and we would love to evaluate this response rate in prospective fashion to find out if the results are replicated on a larger and well-designed study.

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