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Monoclonal Antibodies for Migraine Treatment. What do Brazilian Patients Want from them, Know about them and How Much Would they Pay for them?

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Abstract

Monoclonal antibodies (mAbs) against CGRP are a new hope for migraine. Better adherence rates, good tolerability and effectiveness have been demonstrated. As of this writing, two has been approved in Brazil and one is likely to be shortly, but none are available. The aim of this study was to evaluate among migraineurs being treated in a tertiary center what patients want from them, know about them and how much would they pay for them? Patients with episodic migraine were interviewed about their current treatment, satisfaction, expectations and knowledge about the use of mAbs for migraine and willingness to pay for it. Seventy-nine migraine patients (67 women and 12 men) were evaluated. Regarding the use of daily preventive medications, 34.2% of the patients were very satisfied, while 65.8% were unsatisfied with such intake. The mAbs were known as migraine prophylactic treatment by 48.1% of the patients. If they could eliminate headache attacks, 77.2% of patients would switch to this new option, regardless of price and route of administration. Regarding willingness to pay, 40.5% of patients would spend US$ 250, while 59.5% up to US$ 450 each month. The mAbs are still unknown to more than half of migraine patients, despite its current treatment in a headache clinic, but two-thirds of patients would change to these pharmacological agents, even injectable and more expensive if proven more effective.

Keywords: Migraine; Monoclonal antibodies; Willingness to pay; Treatment

Introduction

Migraine is a highly debilitating neurological disease. Despite its burden, migraine is underdiagnosed and undertreated [1]. Patients seeking help in primary care or in non-specialty centers do not receive comprehensive approaches or even preventive therapies, usually focusing their treatments in acute medications [2,3]. In addition, the diagnosis of migraine is based in a well-structured and time-taking history, which, in most cases, can't be carried out by physicians rushing to complete their productivity goal or simply not interested in headache [4].

The sole use of attack treatments may lead to overuse of symptomatic medications and chronification of migraine, therefore exacerbating its burden [5,6]. Monoclonal antibodies (mAb) anti-CGRP (calcitonin gene-related peptide) represents a new class of treatment for migraine, which have attractive efficacy figures and very good tolerability and treatment adherence. It is administered once a month or every three months in subcutaneous injections. Erenumab is the only mAb designed to block the CGRP receptor while fremanezumab, galcanezumab and epitnezumab aim at the peptide itself. CGRP is released during migraine attacks and the activation of the trigeminal vascular system. Its role in migraine is crucial and has been known since the nineties. In addition, the blood level of CGRP increases during migraine and decreases after its relief with the use of triptans. Chronic migraineurs have a higher circulating level of CGRP [7-12].

Although mAbs do not penetrate the blood brain barrier and seems to act in nuclei such as the trigeminal ganglion, these new therapeutic options represent the first time that mechanism-based treatments are created for migraine. Due to its particularities, mAbs will have a higher cost compared to traditional pharmacological agents used orally either for the preventive as well as the acute treatment of migraine [3].

Press releases and reports for lay media have been presented during the past two years in many countries like Brazil. Additionally, patients from tertiary clinics have been informed about these

upcoming options and the need for special reimbursements from insurance companies and health plans. The aim of this study is to evaluate what Brazilian patients from tertiary centers know about it, expect from it and are willing to pay for the new anti-CGRP therapeutic class including the monoclonal antibodies.

Methods

This was a prospective, cross-sectional and observational study in non-random sampling, consisting of 79 consecutive patients with episodic migraine who were evaluated at a tertiary care headache clinic in Brazil, from January to March 2019. All migraine patients met the diagnostic criteria of the International Classification of Headache Disorders, third edition (ICHD-3) [12] and the questions were asked by two neurologists with experience in headache. The study included migraine patients older than 18 years, during a regular follow-up visit at our clinic in patients under treatment for at least two months.

After the selection of patients diagnosed with episodic migraine (ICHD-3) [12] during a regular follow-up visit, a questionnaire regarding their current treatment performance, satisfaction, expectations as well as about having any knowledge regarding the use of monoclonal antibodies for migraine was presented and the questions performed by the treating physician. In addition, two arbitrary fiduciary values in local currency were presented, and willingness to pay for it was also asked.

All collected data were organized in database. The Statistical Package for Social Sciences (SPSS®) version 17.0 for statistical analysis was used. The quantitative variables were expressed as mean, standard deviation and minimum and maximum values. This study was approved by an ethics committee and all patients signed the informed consent form [13].

Results

The sample consisted of 79 migraine patients and was characterized by a mean age of 41.3, ranging between 19 and 59 years, of whom 67 were women (84.8%) and 12 were men (15.2%). No patient refused to answer the interviewer's questions. Most patients (64.6%) were in treatment for more than one year (Table 1).

Variables	n	%
Sex		
Female	67	84.8
Male	12	15.2
Follow up time (months)		
2	14	17.7
2 to 12	14	17.7
Greater than 12	51	64.6

Table 1: Distribution of sex and follow up time of 79 migraine patients.

Thirty-seven (46.8%) subjects were very satisfied with the overall treatment and twenty-two (27.9%) had a greater than 75% reduction in the frequency of headache attacks during the previous two to four months prior to the consultation, compared to the initiation of the treatment. Regarding the use of daily preventive medications, 27 (34.2%) of the patients considered themselves very satisfied, while 52 (65.8%) were unsatisfied with such intake. However, 29 (36.7%) studied patients reported not being bothered with the use of daily medications if no side effects would appear in the future (Table 2).

Variables	n	%
Satisfaction with general treatment		
Very satisfied	37	46.8
Unsatisfied	42	53.2
Satisfaction with prophylactic medication		
Very satisfied	27	34.2
Unsatisfied	52	65.8
Feel uncomfortable with daily medication use		
Yes	50	63.3
No	29	30.7
Reduction of headache attacks frequency		
>75%	22	27.9
>50%	27	34.2
Would change oral medication for injectable medication		
Yes	52	65.8
No	27	34.2

Table 2: Satisfaction analysis of 79 migraine patients with current prophylactic treatment.

In addition, 52 patients (65.8%) responded that they would exchange oral medication for an injectable drug, even much more expensive, if not to be used daily and if proved more effective than the current ones. Among the total sample of 79 patients, 38 (48.1%) had never heard of mAbs for prophylactic migraine treatment and 61 (77.2%) informed they would use any new medication, regardless of price and way of administration, if it could eliminate migraine attacks.

Regarding willingness to pay, and most of the medications used in Brazil by private patients even with health plans, are bought by the patients themselves, although sometimes with a co-pay or discount system, 32 (40.5%) subjects reported that they could pay up to R$ 1,000 (around US$ 250) per month whereas 47 (59.5%) sufferers could spend up to R$ 1,800 (around US$ 450) per month with the pharmacological agents prescribed if they proved able to finish their migraine attacks (Table 3).

Variables	n	%
Have you heard about mAbs		
Yes	41	51.9
No	38	48.1
Would use mAbs regardless of price and route of administration		
Yes	61	77.2
No	18	22.8
How much would you pay for this medication		
Up to R$ 1000 (about US$ 250)	32	40.5
Up to R$ 1800 (about US$ 450)	47	59.5
mAbs: monoclonal Antibodies		

Table 3: Knowledge analysis of 79 migraine patients on the use of monoclonal antibodies in migraine prophylaxis and willingness to pay for this treatment.

Discussion

Migraine is a neurological disease highly burdensome to individuals, families, economies and the society [14]. Productivity and even employment are severely impaired due to migraine, which often result in frequent and costly use of symptomatic medications as well as resource utilization across different countries [15,16].

Preventive treatment of migraine attacks, aiming at reducing not only the number of migraine days, but additionally, the functional disability, is recommended for most migraineurs who seek for medical care or have severe compromising of routine activities. However, adherence to migraine preventive treatments is low and lack of efficacy as well as poor tolerability leads to discontinuation of most prescribed agents after few months [17-19]. In addition, as suggested in our study, at least half of the patients are not satisfied with the daily use of preventive agents and may be not satisfied at all with approaches from general practitioners and unnecessary requesting of complementary examinations or imaging studies [20]. Although we believe that treatment adherence issues can be improved in migraine through a model that combines the patient's perceived severity of migraine, their beliefs regarding the safety of daily and acute medications, and factors related to the physician-patient relationship to manage medication adherence problems as described by Katić, et al. and practiced by our center, there will be those not following treatment prescriptions and/or switching doctors and treatments in a quest for better tolerated pharmacological agents [21].

In such a view and considering the various unmet needs for migraine treatments, the use of monoclonal antibodies represents a new era of headache management [22]. Up to now, and with the results of nearly 4-year experience with erenumab and nearly 3-year with fremanezumab and galcanezumab, there is a clear-cut point to an unprecedented safe and reasonably effective way of preventing migraine [23]. Few patients discontinued due to adverse events and because the mAbs are injected once a month, figures of adherence are very interesting as well [23,24].

Although injectable medications for migraine are not highly preferred by Brazilian patients, those having received comprehensive approaches with thorough explanations about migraine, its nature and potential for progression or development of chronification, as practiced in most tertiary clinics, usually adhere to the treatment even with rational combination of drugs and injectable medications [2,25,26]. In addition, there is a trend for patients seeking help in tertiary clinics of our country, to have a higher economic standard and therefore, being able to bear with the costs of more expensive approaches even with questionable efficacy, as onabotulinum toxin A [27-29].

Since options like monoclonal antibodies are expensive compared to most of the available medications and patients from more specialized centers tend to receive more efficient treatment options, at least regarding prevention, we aimed at evaluating among this limited subpopulation of migraine sufferers whether, despite their ongoing treatments, new therapeutic classes with different administration routes and higher costs could be accepted in an easier way, which was demonstrated regardless of the absence of a control group [29-31].

It should be emphasized that conclusions from this study can't be used for the whole migraine population or even for population of patients from primary care or general practitioners, since most of the sufferers don't have access to a neurologist and fewer to a headache specialist. In addition, the public health system in Brazil doesn't pay or hand out expensive medications for migraine and not even topiramate is available for public system migraine patients if not purchased by the patients in private drugstores. This study was not intended to fundament definitive policies regarding dispensation of mAbs to the general population in Brazil, but rather, to prepare tertiary centers for a better approach and delivering more comprehensive information for patients and professionals.

Conclusion

The mAbs are still unknown to more than half of migraine patients, but two-thirds of these patients would switch to these new drugs, even if they are injectable and more expensive if proven more effective.

Conflict of Interest

There is no conflict to declare.

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