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ORIGINAL ARTICLE

Experience with botulinum toxin in chronic migraine☆,☆☆

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Abstract
Objective: The purposes of this study were to describe our 16-month experience with onabotulinumtoxinA (OnabotA) for the treatment of chronic migraine (CM) in the Spanish province of Segovia, evaluate its benefits, and determine clinical markers of good response to treatment.
Patients and methods: Prospective study of patients with CM who received OnabotA for 16 months. The effectiveness of OnabotA was evaluated based on the reduction in the number of headache days, pain intensity, and side effects. We used two-way analysis of variance to assess the effects of treatment according to the time factor. We studied the correlation between treatment effects and other variables using a linear regression model to establish the clinical markers of good response to treatment.
Results: We included 69 patients who met the diagnostic criteria for CM. Patients underwent an average of two infiltrations. Mean age was 43 years; 88.4% were women. The number of headache days and pain intensity decreased significantly ($P < .005$); improvements remained over time. We found a negative correlation between the reduction in pain intensity and the number of treatments before OnabotA.
Conclusion: The beneficial effects of OnabotA for CM continue over time. OnabotA is a safe and well-tolerated treatment whose use for refractory CM should not be delayed since early treatment provides greater benefits.

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PALABRAS CLAVE
Migraña crónica;
Toxina botulínica A;
Estudio prospectivo

Experiencia con toxina botulínica en la migraña crónica

Resumen
Objetivo: Describir la experiencia con la administración de toxina botulínica tipo A (OnabotA) en el tratamiento de la migraña crónica (MC) en Segovia durante 16 meses, evaluar su beneficio y buscar marcadores clínicos que sirvan para predecir una mejor respuesta al tratamiento.
Pacientes y métodos: Estudio prospectivo de pacientes con MC que recibieron infiltraciones con OnabotA durante 16 meses. Se evaluó la eficacia de OnabotA comparando la reducción en el número de días de cefalea, en la intensidad y efectos adversos. Se comparó el efecto del tratamiento con el factor tiempo mediante un análisis de la varianza de dos vías (ANOVA). Se estudió la correlación del efecto del tratamiento con el resto de las variables mediante un modelo de regresión lineal para buscar marcadores clínicos que sirvan para predecir una mejor respuesta.
Resultados: Se incluyó a 69 pacientes que cumplían criterios de MC. Se les realizó una media de 2 infiltraciones. La edad media fue de 43 años, el 88,4% fueron mujeres. La frecuencia de los días de cefalea y su intensidad se redujeron de forma significativa ($p < 0,005$) y esta mejoría se mantuvo a lo largo del tiempo. Se encontró una correlación negativa entre la reducción de la intensidad y el número de tratamientos previos a la administración de la toxina.
Conclusión: El efecto beneficioso de la OnabotA en la MC se mantiene en el tiempo, siendo un tratamiento seguro y bien tolerado. No debe retrasarse su uso en MC refractaria, ya que su beneficio podría ser mayor cuanto antes se administre.

Introduction

Chronic migraine is an extremely complex and severely disabling neurological disorder which causes a profound impact on patients' quality of life.[1] The third edition of the International Classification of Headache Disorders (ICHD-3) defines chronic migraine as migraine occurring on at least 15 days per month for more than 3 months, which has the features of migraine headache with or without aura on at least 8 days per month or responds to migraine treatment. The complex pathogenic mechanisms of chronic migraine affect multiple sensory pathways, emotional networks, autonomic systems, and cortical functions. The condition has a prevalence of 1.4-2.2%.[3]

The use of botulinum toxin type A (OnabotA) for prophylaxis has considerably changed the management of chronic migraine. The efficacy of this treatment for chronic migraine was confirmed by the results of the PREEMPT programme. The programme demonstrated the efficacy of OnabotA in decreasing the frequency of headache days per month, reducing medication use, and improving quality of life. The PREEMPT trials also showed the treatment's safety and tolerability and the low incidence of associated adverse reactions.[4–6] Subsequent studies have confirmed the efficacy, safety, and long-term effect of the drug, as well as its positive impact on quality of life and healthcare cost savings.[7,8]

Although the analgesic effect of OnabotA is not fully understood, the drug is thought to act not only by inhibiting acetylcholine release at the presynaptic level, relaxing the pericranial muscles, but also through an effect on other pathways. OnabotA inhibits the release of nociceptive mediators such as calcitonin gene-related peptide, glutamate, and substance P from afferent peripheral nerve fibres. This, in turn, inhibits neurogenic inflammation and consequently peripheral nociceptive fibre sensitivity, reducing the transmission of peripheral pain signals to the central nervous system. This decreases central sensitisation, which is responsible for progression to chronic migraine.[9,10]

In this study, we describe our experience with OnabotA for the treatment of chronic migraine at Complejo Asistencial de Segovia over a period of 16 months. We evaluate the treatment's capacity to reduce pain intensity and frequency and attempt to identify possible clinical markers of good response to treatment.

Patients and methods

Study design

We conducted a prospective study with a sample of patients aged 18 years and older who visited our hospital's neurology department between 1 October 2013 and 1 April 2015; all participants met ICHD-3 diagnostic criteria for chronic migraine.[2]

All patients received OnabotA injections according to the PREEMPT injection paradigm (155 U in 31 sites) every 3-4 months for 16 months. We gathered patients' demographic and clinical data, including age, sex, history of psychiatric disorders, previous preventive treatments, number of headache days per month, and pain intensity. Patients were asked to complete a headache diary, in which they