Botulinum toxin type A in chronic migraine with medication overuse: the experience of the Headache Centre of "Spedali Civili Brescia"

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Objectives: Botulinum toxin type A (BoNT-A) has shown to be effective in the treatment of chronic migraine (CM) with or without medication overuse (MO). The aim of this study was to examine its efficacy and tolerability in the real-life setting.

Materials: We reported a post-marketing experience of patients with CM with MO, diagnosed according to the International Headache Society diagnostic criteria, which started treatment with BoNT-A at the Headache Centre of the Neurology Unit, "Spedali Civili Hospital", Brescia, between September 2014 and April 2016.

Methods: BoNT-A was injected following the PREEMPT protocol, at the dosage of 155 UI for 31 fixed-sites or using a "follow-the-pain" strategy. No withdrawal treatment was carried out before starting BoNT-A.
Clinical assessment comprised headache frequency and analgesic consumption, which were collected from the patients' headache diaries during pre-treatment period and throughout the study. Disability was documented with the Migraine Disability Assessment Score Questionnaire (MIDAS).

Results: We enrolled 30 consecutive CM patients (83%females) with a mean age of 49.1±9.9 years, mean disease duration of 9.9±6.6 years and a median past migraine prophylaxis treatment of 4 (range 1-9) (**TABLE 1.)**

5 (16.6%) patients discontinued therapy in the fist year for lack of improvement after a median of 3 infusions (range 2-4); no relevant adverse events were recorded.

An analysis was performed on the 13 patients who received at least 3 injections during a follow-up of 6 months.

TABLE 1. *Demographic and clinical characteristics of study population*

	Subjects (n= 30)
Mean (SD) age, y	49,1 (9.9)
Female, n (%)	83
Mean disease duration CM (SD),y	9.9 (6.6)
Median (range) number of migraine prophylaxis treatment, n	4 (1-9)
Mean (SD) number of migraine days per month, n	21.0 (5.1)
Mean (SD) number of days with mild headache per month, n	9.3 (8.5)
Mean (SD) number of days with moderate-severe headache per month, n	11.5 (8.5)
Mean (SD) number of migraine attack treatments per month, n	25.9 (16.3)
Mean value of MIDAS (SD)	55.9 (52.5)

TABLE 2. *Variations in the efficacy outcomes at 6 months after the start of therapy*

Variables	**Baseline**	**After 6 months**	***P value* interaction**	***P value* post-botulinum**
Number of migraine days per month	20.23 ± 4.04	13.31 ± 8.08	**0.001**	**0.01**
Number of days with mild headache per month	9.31 ± 6.47	5.85 ± 5.71	**0.015**	0.071
Number of days with moderate-severe headache per month	10.6 ± 6.89	7.46 ± 7.80	**0.015**	0.171
Number of migraine attack treatments per month	20.08 ± 4.91	15.69 ± 9.17	**0.139**	**0.021**
MIDAS	55.9 ± 52.5	45.3 ± 39.2	**0.5**	0.856

Results are expressed as mean +/- SD

The Botulinum Toxin intervention elicited statistically significant changes in days with headache over time ($F_{(2,24)}$=11.572, p<0.001, partial η2=0.491); there was a significant decrease in days with headache from 20.23±4.04 to 13.3±8.08 (p=0.01) from the first to the third session of therapy.
Similarly, BoNT-A treatment reduced medication intake over time ($F_{(2,24)}$=4.989, p<0.015, partial η2=0.294) with a significant decrease in analgesics from 20.08±4.91 to 15.69±9.17 (p=0.021). A non-significant improvement was observed in the MIDAS score (p=0.856) (**TABLE 2).**

Discussion: Our data are in line with previous studies. However, despite the effectiveness and tolerability of the treatment, there was not an improvement in the perception of disability related to migraine during BoNT-A treatment, probably due to the inclusion of patients with a highly disabling headache at baseline, in addition to the short duration of the study.

Conclusion: Treatment with BoNT-A is effective and well-tolerated in patients with CM associated to MO; however, there are still open questions surrounding duration of treatment and possible identification of response predictors.

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