Use of non-invasive vagus nerve stimulation for acute migraine attack

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Objectives: Non-invasive vagus nerve stimulation (nVNS) has been studied in several primary headache disorders. We investigated the effects of nVNS for acute treatment of migraine attacks in patients with high-frequency episodic and chronic migraine (HFEM and CM), associated to medication overuse (MO).

Materials and Methods: 14 patients with HFEM (n=9) and CM (n=5), complicated by MO, were enrolled in this 2-month, prospective, two-phase study **(TABLE 1)**. All patients received training on the proper use of the device, through a practical demonstration and an instructional video. In the first phase (phase A), attacks that occurred during a 1-month period were treated with two 90-second trials of nVNS at 15-minute intervals, delivered to the right cervical branch of the vagus nerve. Patients were allowed to take a rescue medication if they perceived no reduction in pain 2 h after nVNS treatment. In the second phase (phase B), patients treated all attacks with medication, as they usually did, without using the nVNS **(FIGURE 1)**. At the end of the two phases of the study headache frequency and analgesic consumption were collected from the patients' headache diaries and health- and migraine-related quality of life were documented with the Short Form Health Survey (SF-36) and the Headache Impact Test (HIT-6), respectively.

Results: During phase A, 177 attacks were reported and all were treated with nVNS. Only 24 (13.5%) attacks required medical treatment within 2 hours of the onset of migraine while 70 attacks (39.6%) did not require the use of a rescue medication **(TABLE 2)**. When all attacks (n=177) were considered, the pain-free rate was 5% at 30 minutes and 18% at 2 h, whereas the sustained pain-free rate was 62.1% at 24h. The device was very well tolerated with no relevant adverse events. At the end of the two phases, no significant differences were observed in the mean number of attacks, in HIT 6 score and in all SF-36 items. In phase B, 175 attacks were reported and all required medical treatment **(TABLE 3).** We observed a non-significant increase in the mean number of medication intake during phase B (from 11.9 to 14.1, *p*=0.211).

Discussion: our study showed that nVNS reduced the number of attacks requiring medical treatment (39.6%), while in phase B all attacks required analgesics (100%).

Conclusion: nVNS might potentially provide an effective and well-tolerated solution for the treatment of acute migraine attacks. Its use is desirable in order to reduce medication overuse and medication-associated adverse events.

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

	Subjects N=14
Mean (SD) age, y	38.4 (7.7)
Female, n (%)	10 (71.4)
Mean (SD) number of migraine days per month, n	20.4 (5.5)
Mean (SD) number of migraine attack treatments, n	21.4 (10)
Mean (SD) number of migraine prophylaxis treatment, n	2.4 (1.6)
Concomitant prophylaxis, n (%)	11 (78.6)

FIGURE 1. *Study flowchard*

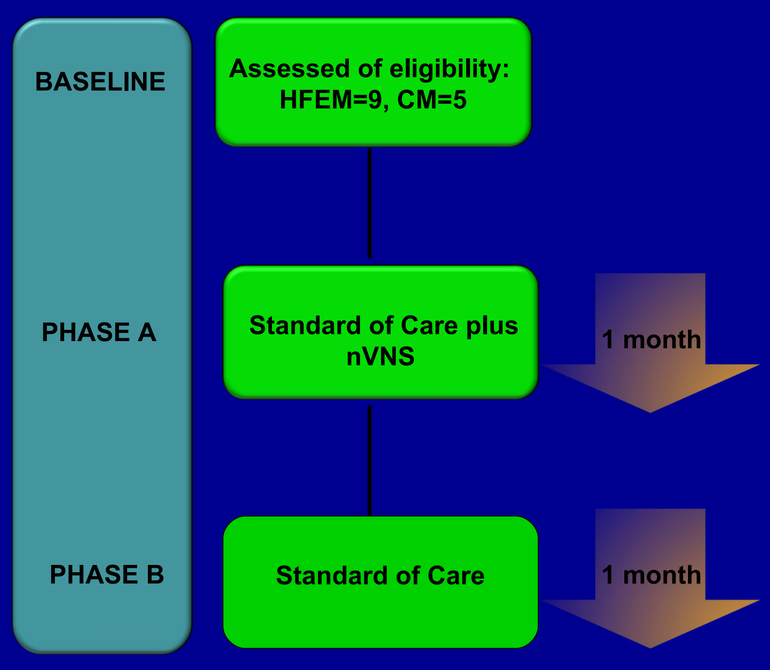

TABLE 2. *Clinical data of Phase A*

PHASE A	
Mean (SD) number of migraine attacks, n.	12.7 (4.4)
Total migraine attacks, n.	177
Attacks type, n. (%)	
Mild	64 (36.1)
Moderate	90 (53.1)
Severe	34 (19.2)
Mean value of HIT 3 (SD), n	61.5 (7.2)
Mean (SD) number of migraine attack treatments, n	11.9 (9.0)
	107 (60.4)
Rescue medications in all attacks, n (%)	24 (13.5)
Medications within the first 2 hours, n (%)	

TABLE 3. *Clinical data of Phase B*

PHASE B	
Mean (SD) number of migraine attacks, n.	12.5 (4.4)
Total migraine attacks, n.	175
Mean value of HIT 3 (SD), n	64.2 (2.7)
Mean (SD) number of migraine attack treatments, n	14.0 (6.6)

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