Neurological Sciences

Official Journal of the Italian Neurological Society

Editor in Chief Antonio Federico

SUPPLEMENT

XLIX Congress of the Italian Neurological Society

Rome 27-30 October 2018





tion was associated with higher odds of a positive response to candesartan (OR 1.04, 95% CI 1.01-1.08, p=0.02) in a model adjusting for age, presence of aura, type of migraine and the total number of preventive therapies tried by patients.

Discussion: Candesartan is effective for migraine prevention in episodic and chronic migraine patients. Longer disease duration was the only independent predictor of a positive response to candesartan in migraine patients. The number failed preventives up to nine did not predict treatment failure.

Conclusions: Candesartan is effective for migraine prevention, irrespective of previous failed preventives.

OF DIAGNOSIS THE HERALDING HEADACHE NEUROSARCOIDOSIS

C. Lisotto, L. Toma, E. Mampreso, G. Zanchin

¹Headache Centre, Azienda Ospedaliera Friuli Occidentale (Pordenone); ²Department of Neurology, Arcispedale Sant'Anna (Ferrara); ³Department of Neurology, ULSS 6 Euganea (Piove di Sacco-PD); ⁴Department of Neurosciences, Headache Centre, University of Padua (Padova)

Objectives: Sarcoidosis is a multi-organ granulomatous disease of unknown aetiology, characterized pathologically by multiple non-caseating granulomata in the absence of a defined infective or toxic trigger. Sarcoidosis involving the nervous system (the so-called neurosarcoidosis) is infrequent and headache may be the presenting symptom [1]. The diagnosis of headache attributed to neurosarcoidosis is challenging and requires particular attention from headache specialists.

Material and methods: The medical records of patients admitted in the past 15 years to our Department of Neurology for recent-onset headache with a final diagnosis of neurosarcoidosis were retrospectively reviewed. The diagnosis of headache attributed to neurosarcoidosis was made according to the International Classification of Headache Disorders, 3rd edition (ICHD-3) [2].

Results: Four patients, two males and two females, mean age at observation 40 years (range 31-49), were included in our review. In all the subjects headache was the onset symptom, occurred acutely or subacutely. Two patients (one male and one female) reported headache as the only symptom; the pain was diffuse, severe, non-pulsating, with daily or nearly-daily occurrence, mimicking tension-type headache. In the remaining two cases the headache was unilateral, periorbital, intense and sharp, associated with third cranial nerve paralysis, resembling Tolosa-Hunt syndrome. All the patients underwent brain magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) examination. MRI showed non-enhancing periventricular white matter lesions, enhancement of the leptomeninges with predilection for suprasellar and frontal basal meninges and involvement of cavernous sinus ipsilateral to pain in the patients with third cranial nerve palsy. CSF examination revealed lymphocytic pleocytosis and elevated protein. All the patients were treated with oral prednisone, starting from 1 mg/kg daily, with rather rapid clinical improvement. In three patients chest radiography was abnormal, showing bihilar lymphadenopathy; on bronchoalveolar lavage CD4:CD8 lymphocyte ratio was more than

Discussion: The headache in our patients was clinically similar to tension-type headache in two cases and to Tolosa-Hunt syndrome in the other two. ICHD-3 criteria for headache attributed to neurosarcoidosis imply that the clinical features of this secondary headache have a wide range of presentations. As for differential diagnosis versus Tolosa-Hunt syndrome, our patients obtained a remission within 10-14 days, a longer time than 72 hours for pain and paresis resolution, as required by ICHD-3 diagnostic criteria for this syndrome.

Conclusions: Headache may rarely herald the diagnosis of neurosarcoidosis. New case series continue to broaden the phenotype of

neurosarcoidosis, reinforcing the need for a systematic approach to diagnosis and management.

References:

- Radwan W, Lucke-Wold B, Robadi IA, Gyure K, Roberts T, Bhatia S. Neurosarcoidosis: unusual presentations and consideration for diagnosis and management. Postgrad Med J (2017);93:401-5
- Headaché Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. Cephalalgia (2018);38:1-211
- Ibitoye RT, Wilkins A, Scolding NJ. Neurosarcoidosis: a clinical approach to diagnosis and management. J Neurol (2017);264: 1023-8

HEADACHE IN DIFFERENT AGES

F. Pietrocarlo

University La Sapienza Roma (Latina)

Objectives: Find an efficient therapy for headache.

Patients and methods: 3 cases in different ages and situations. 1. female 40-year-old: headache for cervical trauma; cervicodynia, tracted with fans. no neurological deficits, EEG, RX and TC negative. 2. female 45-year-old, attacks also in menses, tracted with rizatriptan. visus alteration, fotofobia, nausea and vomiting. 3. female 81-year-old: headache from the age of 15 also during menses, tracted with fans, metamizolo cloridrato at 35/50 triptan: sumatriptan by os and intramuscolar. After isterectomy the attacks were fewer.

Results: Pain improved but not totally. Discussion: It is possible to use an off label?

Conclusions: Not always elective drugs are used, but aspecifics or off label, such as amitriptilina.

PRELIMINARY EFFICACY STUDY IN PROPHYLAXES TENSION CEPHALA AND HEMICRANIA OF EPISODIC WITHOUT AURA USING A COMBINATION OF MAGNESIUM, L-TRIPTOFANO, BOSWELLIA SERRATA CASPEROME® NIACINA, RIBOFLAVINA AND VITAMIN D COMPARED WITH AMITRIPTILINE

L. Balzano¹, B. Ciccone²

¹Headache Surgery, ASL Naples 3 Sud (Torre Del Greco-NA); ²Clinic Headaches, Athena (Saviano-NA)

Introduction: Open-label efficacy study in prophylaxis therapy using Magnesium 225 mg, L-Tryptophan 150 mg, Boswellia Serrata Casperome® 100 mg, Niacin 16 mg, Riboflavin 1.4 mg, Vitamin D 10 μg (Normorelax®=NRX) to Amitriptyline (AM) in patients with CTE and ESA [1-3]. Outcomes of th study are: pain modulation (NRS scale), monthly attacks number and monthly analgesic-triptans consumption.

Patients and methods: 200 patients with CTE and ESA using ICHD-II were selected: 100 CTE and 100 ESA. 50 CTE assuming NRX (two tablets per day) compared to 50 assuming AM (20 mg evening). 50 ESA assuming NRX, compared to 50 assuming AM. Results were evaluated at T1 (60 days) and T2 (120 days). The longitudinal variatons of the three outcomes were analyzed through the GEE (Generalized Estimating Equations) modeling in order to check the correlation induced by the repeated measures. In all the Group factor , the time induced by the repeated measures. In all the models the Group factor, the time factor (as a categorical variable) and their interaction were included as predictors.

Results: Both groups show statistically significant changes from TO to T2 for all the outcomes considered. In CTE patients of NRX and AM group results are, respectively: NRS reduces by 2.4 (p<0.001) and by 3.5 (p<0.001) points, attacks number reduces from 9.5 to 5.7 (p<0.001) and from 9.6 at 4.7 (p<0.001); analgesics frequency is reduced by an average of 3.1 (p<0.001) and 4.9 (p<0.001). Patients percentage showing a reduction in attacks frequency \geq 50% from baseline is 24% in NRX and 40% in AM group. In ESA patients in NRX and AM group, results are, respectively: NRS reduces by 3.3 (p<0.001) and by 3.7 (p<0.001) points; attacks number reduces from 9.7 to 5.2 (p<0.001) and from 9.3 to 4.2 (p<0.001); analgesics frequency is reduced by an average of 4.9 (p<0.001) and 7.2 (p<0.001); patients percentage showing a reduction in attacks frequency \geq 50% from baseline is 40% in NRX and 60% in AM group.

Discussion and conclusions: Results confirm the improvement of all the outcomes in patients treated with NRX. The greater treatment efficacy with AM compared to NRX is confirmed; there is no statistically significant difference in patients with ESA vs CTE in monthly attacks reduction, with NRX advantage for no side effects and greater patient compliance.

References:

- Ciccone B, D'Otolo G, Balzano L. Efficay of Oral Supplement Compared with Amitriptyline in the Prophylaxis of Episodic Tension Type Headache and Migraine without Aura. Curr Neurol Neurosci (2018);1(1):1-2
- Leone M, Grazzi L, D'Amico D, et al. A review of the treatment of the primary headaches. Italian J Neurol Sci (1995);16:577-86
- Silberstein SD. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology (2000);55(6):754-62

HEMICRANIA CONTINUA-LIKE HEADACHE REVEALED A SUBACUTE INTERNAL CAROTID ARTERY DISSECTION IN PATIENT WITH UNRECOGNIZED CONNECTIVE TISSUE DISORDER

S. Ricci, V. Annese, M. Turazzini, G. Salomone, A. Polo

Neurology Department, Mater Salutis Hospital (Verona)

Background: It is widely accepted that internal carotid (ICA) dissection could simulate a cluster headache attack. Conversely, clinical features resembling hemicrania continua (HC) occurring after cervical artery dissection have rarely been reported in the literature. We described the case of a patient who developed typical HC-like headache after carotid artery dissection.

Case presentation: On February 2018, a 43-year-old man presented to our emergency department because of the onset, four days before, of severe continuos right trigeminoautonomic cephalgia with Horner's syndrome and elevated blood pressure. His familiar and personal medical history were unremarkable except for the cluster headache involving the left side few years ago. Neurological examination revealed acute headache fulfilling all IHS criteria for HC (apart from the time criterion) unresponsive to habitual medication for migraine associated with right tongue deviation. The routine laboratory test, CT brain scan and ultrasound examination of neck vessels were normal. Indomethacin 200 mg i.v improved the headache but we decided to admit the patient to our department because of the continuity of pain. Over the next two days there was complete relief with oral indomethacin 200 mg per day and an improvement of the Horner's syndrome, nevertheless the patient developed progressive dysphagia, dysphonia, and weak left-turning of the head suggesting 9th through 12th cranial nerve palsy. He underwent brain magnetic resonance imaging (MRI) with MR angiography of head and neck that showed a right ICA dissection with extension into the petrous segment and intramural hematoma causing mass effect upon the internal jugular vein; no hyperintensity was found in DWI sequences. The patient was started on acetylsalicylic acid 100 mg daily. An extended CT angiography showed extensive luminal irregularities in the main renal arteries, with aneurysm formations and

irregularities of iliac vessels. Due to his new diagnosis of arterial hypertension and the other findings we assumed the possibility of a connective tissue disorder and we performed a genetic counseling with test for Ehlers-Danlos syndrome variants. So far, the results received were negative but other test are still ongoing and fibromuscolar dysplasia (FMD) is strongly considered.

Conclusions: ICA dissection may result in an HC-like headache syndrome. The history of cluster headache, a specific response to indomethacin and the absence of neurological focal signs does not rule out dissection as underlying pathology. Screening for connective tissue disorder and extracranial manifestations of FMD should be considered even if the brain vasculature is normal.

References:

- Ashkenazi A, Abbas MA, Sharma DK, et al. Hemicrania continualike headache associated with internal carotid artery dissection may respond to indomethacin. Headache (2007);47:127-30
- Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia (2013);33:629-808
- O'Connor S, Poria N, Gornik H. Fibromuscular dysplasia: An update for the headache clinician. Headache (2015);55:748-55

EFFICACY AND SAFETY OF ERENUMAB IN EPISODIC MIGRAINE PATIENTS WITH 2-4 PRIOR PREVENTIVE TREATMENT FAILURES: RESULTS FROM THE PHASE 3B LIBERTY STUDY

U. Reuter¹, P. Goadsby², M. Lanteri-Minet³, M. Ferrari⁴, S. Wen⁵, J. Klatt⁶

¹Department of Neurology, Charité Universitäts Medizin Berlin (Berlino-D); ²NIHR-Wellcome Trust Kings Clinical Research Facility, King's College London (London-UK); ³Department of Pain-CHU Nice, FHU Inov - Côte Azur University (Nizza-F); ⁴Department of Neurology, Leiden University Medical Centre (Leiden-NL); ⁵Novartis Pharmaceutical Corporation (East Hanover-USA); ⁶Novartis Pharma AG (Basel-CH)

Objective: To assess the efficacy and safety of erenumab in patients with episodic migraine who have failed 2-4 prior preventive migraine treatments (PMTs).

Material and methods: LIBERTY (NCT03096834) was a 12-week, double-blind, randomized study. Patients (n=246) were randomized (1:1) to receive erenumab 140mg and placebo. The primary endpoint was the proportion of patients achieving ≥50% reduction in mean monthly migraine days (MMDs) during Weeks 9-12 (Month 3). Secondary endpoints included change from baseline to Month 3 in MMDs and monthly acute migraine-specific medication days (MS-MDs) and safety/tolerability.

Results: At baseline, proportion of patients who failed 2, 3, and 4 prior PMTs were 38.6%, 37.8%, and 22.8%, respectively. The mean (SD) MMDs and MSMDs were 9.3 (2.64) and 4.6 (2.89), respectively. At week 12, the proportion of patients achieving ≥50% reduction in MMD was higher in those treated with erenumab 140mg vs placebo (30.3% vs 13.7%; OR [95% CI]: 2.73 [1.43, 5.19]; p=0.002). At week 12, there were greater reductions in MMDs and MSMDs with erenumab 140mg vs placebo (mean difference [95% CI] in MMD: -1.61 [-2.70,-0.52]; p=0.004; mean difference (95% CI) in MSMD:-1.73 [-2.46,-1.01]; p<0.001). Safety and tolerability profile of erenumab was comparable to placebo. No patients in the erenumab group discontinued due to adverse events.

Discussion: Erenumab is a fully human monoclonal antibody that inhibits the canonical CGRP receptor. Clinical studies have demonstrated the efficacy and safety of erenumab in patients with episodic and chronic migraine. Current oral preventive therapies are associated with low adherence rates due to the lack of efficacy and/or poor tolerability. It is therefore important to assess the safety and efficacy of

STUDIO PRELIMINARE DI EFFICACIA DI UNA ASSOCIAZIONE DI MAGNESIO, L-TRIPTOFANO, BOSWELLIA SERRATA CASPEROME®, NIACINA, RIBOFLAVINA E VITAMINA DA CONFRONTO CON AMITRIPTILINA NELLA TERAPIA DI PROFILASSI PER CEFALEA TENSIVA EPISODICA ED EMICRANIA SENZA AURA

L. Balzano¹, B. Ciccone²,

1 Neurologist – Clinic for the diagnosis and treatment of headaches – Torre del Greco (NA) ASL NA3 SUD 2. Neurophysiopathologist - Clinic for the diagnosis and treatment of headaches ATHENA Saviano (NA)

Mail: neurogino@yahoo.it

OBIETTIVI

Studio in aperto di efficacia in terapia di profilassi con una associazione di "Magnesio 225mg, L-Triptofano 150mg, Boswellia Serrata Casperome® 100mg, Niacina 16mg, Riboflavina 1.4mg, Vitamina D 10mcg (Normorelax®=NRX) verso Amitriptilina (AM) in pazienti con CTE e ESA (1-2-3) utilizzando come outcome: modificazione del dolore (scala NRS), del numero di attacchi/mese e del consumo di analgesici-triptani/mese.

MATERIALI E METODI

Selezionati pz con CTE e ESA secondo ICHD-II: totale 200: 100 CTE e 100 ESA. Di questi 50 con CTE in terapia con NRX (1 cp mattina e sera) confrontati con 50 in terapia con AM (20 mg sera). Mentre 50 con ESA in terapia con NRX, confrontati con 50 in terapia con AM. Il confronto è avvenuto a T1 (60gg) e a T2 (120gg) di trattamento.

Le variazioni longitudinali dei tre outcome sono state analizzate attraverso la modellistica GEE (Generalized Estimating Equations) così da controllare la correlazione indotta dalle misure ripetute. In tutti i modelli sono stati inseriti come predittori il fattore Gruppo, il fattore tempo (come variabile categorica) e la loro interazione.

RISULTATI

In entrambi i gruppi si osservano variazioni statisticamente significative da T0 a T2 rispetto a tutti gli outcome considerati.

Nei pz con CTE rispettivamente nel braccio NRX e AM: la NRS si riduce di 2.4 punti (p<0.001) e di 3.5 punti (p<0.001);il numero di attacchi passa da 9.5 a 5.7 (p<0.001) e da 9.6 a 4.7 (p<0.001); la frequenza di analgesici si riduce in media di 3.1 (p<0.001) e di 4.9 (p<0.001). La percentuale di pazienti in cui si osserva una riduzione nella frequenza di attacchi pari ad almeno il 50% del valore basale è del 24% nel braccio NRX e del 40% nel braccio AM.

Nei pazienti con ESA rispettivamente nel braccio NRX e AM: la NRS si riduce di 3.3 punti (p<0.001) e di 3.7 punti (p<0.001); il numero di attacchi passa da 9.7 a 5.2 (p<0.001) e da 9.3 a 4.2 (p<0.001); la frequenza di analgesici si riduce in media di 4.9 (p<0.001) e di 7.2 (p<0.001); la percentuale di pazienti in cui si osserva una riduzione nella frequenza di attacchi pari ad almeno il 50% del valore basale è del 40% nel braccio NRX e del 60% nel braccio AM.

DISCUSSIONE E CONCLUSIONI

I risultati confermano il miglioramento nei pazienti in trattamento con NRX di tutti gli outcome considerati. Si conferma la maggiore efficacia del trattamento con AM rispetto al NRX che tuttavia non presenta differenza statisticamente significative nei pz con ESA rispetto a quelli con CTE nella riduzione degli attacchi al mese con cefalea, con il vantaggio di minori effetti collaterali e maggiore compliance da parte dei pazienti.

BIBLIOGRAFIA

- 1 Ciccone B, D'Otolo G and Balzano L, Efficay of Oral Supplement Compared with Amitriptyline in the Prophylaxis of Episodic Tension Type Headache and Migraine without Aura Current Neurology and Neuroscience An open access journal, Vol 1(1): 1-2, feb 2018
- 2. LEONE M. et al., A review of the treatment of primary headaches, in Italian Journal of Neurological Science, 16 (1995), 577-586.
- 3.SILBERSTEIN S.D., Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology, in Neurology, 55, 2000.