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INVITED SPEAKER PRESENTATIONS

A1

Kynurenine pathway metabolites in migraine

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Kynurenine pathway (KP), the quantitatively main branch of tryptophan metabolism, has long been considered a source of nicotinamide adenine dinucleotide, although several of its products, the so-called kynurenines, are endowed with the capacity to activate glutamate receptors, thus potentially influencing a large group of functions in the central nervous system (CNS). In fact, Kynurenic Acid and Quinolinic Acid are able to interact with ionotropic glutamate receptors and Cinnabarinic Acid has been reported as an orthosteric agonist of metabotropic glutamate receptors (mGlu4), and Xanthurenic Acid has been recently demonstrated to be a putative agonist of metabotropic glutamate receptors 2/3 (mGlu2/3). Moreover, 3-HK and 3-HANA have mainly been studied, since they have been shown to induce neurotoxic effects by increasing oxidative stress and the production of free radicals or through excitotoxicity. Migraine has a complex pathophysiology in which both central and peripheral components of the trigeminal pain pathway play a central role. The trigemino-vascular activation during the attack has largely been described, and recently the brainstem nuclei, called "migraine generators", have been reported to be involved in migraine. Moreover, a series of destabilizing events within the brain trigger a cortical spreading depression (CSD), responsible for the aura phenomena and for trigeminal activation. The role of glutamate is heavily supported both in the trigemino-vascular as well as in brainstem nuclei activation, and furthermore in the CSD initiation and propagation. Some of the KP metabolites able to interact both with ionotropic and metabotropic glutamate receptors might be involved in migraine pathophysiology. Despite the large number of studies conducted on migraine etiopathology, the KP has only been recently linked to this disease. Nonetheless, some evidence suggests an intriguing role for some kynurenines, and an exploratory study on the serum kynurenine levels has been helpful to better understand possible alterations of the kynurenine pathway in patients suffering from migraine.

A2

Disability, ICF biopsychosocial model and burden of migraine

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When defining the burden of migraine it is important to consider patients' disability and clinical and public health perspectives. Migraine sufferers often have severe under recognized and underdiagnosed health burden and reductions in social activities and work capacity. Health professionals focus on diagnosis as a key element to effective treatments, however the majority of clinicians still tend to perceive migraine, and headache disorders in general, as minor complaints. Ten years ago a possible way to increase awareness and diminish the burden was described[1]. However epidemiological data of headache disorders, despite the international Lifting the Burden Campaign, is still scarce in many parts of the world and inconsistent because of the sampling frames and of how prevalence rates are defined and the physical, emotional, social and economic burdens of headaches are still poorly acknowledged. Uncertainty about the prevalence distribution reflects that there is still need of instruments for classifying migraine in a comparable manner across populations and that more studies must be undertaken to classify the disability due to the disorder using reliable outcome measures[2]. Estimation of needs for health services, their costs and effectiveness require indicators that go beyond measures of death rates or of diagnosis alone, and include the "functioning" of people. The biopsychosocial model of the WHO Classification of Functioning, Disability and Health (ICF) provides the model, as well as the classification system, that allows to measure all dimensions of functioning and disability[3]. More than ten years of research with ICF in migraine sufferers shows that it allows data comparability and the evaluation of the role of environment. According to ICF construct any health condition, in an unfavourable environment, can cause disability. Environmental barriers for migraine sufferers are lack of health care facilities, of accurate diagnosis, of drugs, but also difficulty in being taken seriously. Steiner[4] drew attention to the high number of people with disability due to headache who do not receive health care. The barriers responsible for this might vary throughout the world, but poor awareness of headache in a context of limited resources generally was still constantly among them. Describing and accounting the burden of migraine worldwide is not enough anymore, we need to change our paradigm again and to move towards new pathways. The opportunity is provided by the biopsychosocial approach of the ICF. To reduce the burden of millions of migraine and headache sufferers once we cannot change the disease, we should change the environment and global efforts should focus on the new development of drugs but mainly on improving the response of health care systems.

Conflict of interests: The authors certify that there is no actual or potential conflict of interest in relation to this article.

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Headaches and other cranio-oro-facial pains are widely distributed in the general population. Unfortunately, there is very little evidence regarding the impact of these conditions in patients admitted to rehabilitation units, regardless of the disease or syndrome requiring rehabilitation. The availability of diagnostic and therapeutic guidelines, as well as the increasing number of data coming from controlled clinical trials, should be implemented in these patients to reduce the burden of pain and improve their global outcome.
The Italian Society for Neurorehabiltation, in collaboration with the Italian Society of Physical Medicine and Rehabilitation, has promoted the Consensus Conference on Pain with the aim to foster attention on pain also in the rehabilitative field (http://www.doloreinneuroriabilitazione.it/).
The working group has proposed the following recommendations:
- Standard methods or criteria exist to evaluate head and cranio-facial pain in terms of intensity (B);
- Standard methods exist to evaluate migraine in terms of disability (A);
- It is important to evaluate the impact of cephalic and cranio-facial pain in neurorehabilitation (D);
- Standard methods or criteria exist to diagnose head and cranio-facial pain (GL);
- It is important to identify predictive factors associated with the development of cephalic and cranio-facial pain in association with a condition requiring neurorehabilitation (D);
- Effective pharmacological treatment exists for primary headaches and for trigeminal neuralgia (GL);
- Manual therapy is indicated in the management of migraine and tension-type headache (GL);
- Manual therapy may be effective in TMD-associated pain (D);
- Botulinum toxin A is effective in the treatment of idiopathic trigeminal neuralgia (B);
- Botulinum toxin A is effective in the treatment of hemifacial spasm (B);
- Topical capsaicin is effective in chronic neuropathic pain (B);
- Evidence is needed to evaluate the impact of treating cephalic and cranio-facial pain on the outcome of patients undergoing neurorehabilitation (D).
The recommendations are presently under evaluation by the Consensus Conference panel.

A133

O005. Efficacy of oral supplement compared with amitriptyline in the prophylaxis of episodic tension-type headache and migraine without aura

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Introduction: We conducted an observational study of patients attending our outpatient headache clinic, suffering from episodic tension-type headache (ETTH) and migraine without aura (MO). The purpose of the study was to compare the efficacy of magnesium bisglycinate, L-tryptophan, niacin, vitamin B2 and vitamin D, pineal tens (PT) and amitriptyline (A) in the prophylaxis [1-4] of these primary headaches using as outcomes: pain modification with visual analogue scale (VAS); the change in the number of attacks/month; the change in the consumption of analgesics/month.
Patients and methods: ETTH and MO were diagnosed according to the International Classification ICHD-II criteria. We studied a total of 200 patients: 100 patients were diagnosed with ETTH and 100 with MO. Of these patients, 50 with a diagnosis of ETTH (15 M, 35 F; mean age: 34 years) were treated with PT (1 sachet morning and evening) and were compared with 50 patients (17 M, 33 F; mean age: 39 years) undergoing amitriptyline therapy (20 mg in the evening). Fifty patients with MO (15 M, 35 F; mean age: 37 years) were treated with PT (1 sachet morning and evening), and compared with 50 patients (8 M, 42 F; mean age: 40 years) taking A (20 mg in the evening).
Results: The VAS modifications, the number of attacks and the number of analgesics taken during the study are shown in Figure 1 for the patients diagnosed with ETTH. The group treated with PT clearly showed a reduction in all treatment outcomes during the study compared to the group taking A.
VAS modification, the number of attacks and the number of analgesics taken during the study are shown in Figure 2 for the patients diagnosed with MO. The group treated with PT clearly showed a reduction in all treatment outcomes during the study compared to the group taking A.
Conclusions: Our clinical observation of an improvement in headache in patients receiving PT led us to conduct this cohort study comparing PT with A therapy. Although this study is obviously limited because of the absence of patient randomization, its results confirm the clinical impression of an improvement in the primary headache in patients with PT in terms of improvement in VAS, reduction in the number of attacks/month, and the consumption of analgesics/month. In fact, PT treatment was found to be more efficacious when compared to A treatment in many outcome measures.
Written informed consent to publish was obtained from the patient(s).

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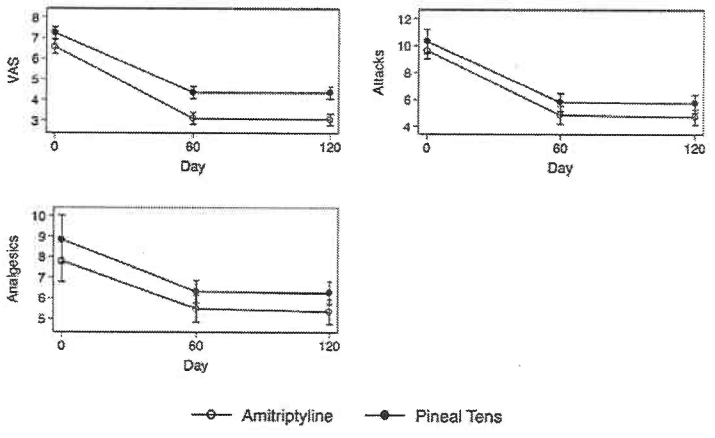
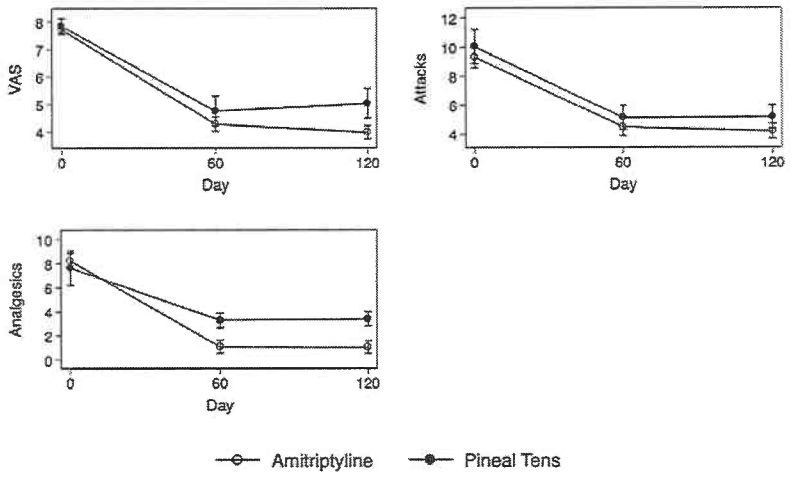


Values are means and 95% confidence intervals estimated from linear regression (VAS) or Poisson regression (attacks, analgesics) for repeated measures.

Figure 1(abstract A133) Patients with ETTH



Values are means and 95% confidence intervals estimated from linear regression (VAS) or Poisson regression (attacks, analgesics) for repeated measures.

Figure 2(abstract A133) Patients with MO

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A134

O006. Efficacy of prophylactic therapy in chronic primary headache with use of biofeedback

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Introduction: Retrospective study of patients with chronic tension headache (CTH) and chronic migraine (CM).
Objective: To compare the efficacy of biofeedback (BFB) compared to only prophylactic therapy in these primary headaches [1-4].
Materials and methods: We evaluated a total of 8 patients with CTH and 8 patients with CM. All patients had a history of primary headache and had never undergone prophylactic therapy. The observation period lasted 90 days. Four CTH patients and 4 CM patients underwent only prophylactic therapy (amitriptyline 20 mg daily), the remaining 4 CTH and 4 CM prophylactic therapy and BFB training sessions. Assessment tools outcome measures were:
- Headache diary to assess days per month with headache;
- Analgesic consumption and/or triptans;
- Score of the visual analogue pain scale (VAS);
- SEMG parameter for patients who carried out BFB training.

Results: At the end of the 90 day observational period there was a significant improvement (reduction in headache days per month, in VAS score, in analgesic consumption and in SEMG parameter) in CTH and CM patients that had undergone both BFB training and prophylactic therapy when compared to the group of patients treated only with prophylactic therapy drug.
Discussion and conclusions: The overall data confirmed the efficacy of the BFB training in the prophylaxis of primary headaches, further supporting the benefits already possible with the therapy of only pharmacological prophylaxis (Table 1). The data also showed a clear dominance of efficacy, especially in the forms of chronic tension headache (Table 2).
Written informed consent to publication was obtained from the patient(s).

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POSTER PRESENTATIONS

A135

P067. Multimodal therapy in the management of MOH: a 3-year experience

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Table 1(abstract A134) Overall differences between the two groups after 90 days of therapy

	Frequency	VAS	Analgesic consumption	Triptan consumption	SEMG
CTH	-58%	-37%	-62%		
CTH BFB	-75%	-67%	-86%		-54%
CM	-53%	-34%	-60%	-50%	
CM BFB	-61%	-43%	-75%	-63%	-54%

EFFICACIA DI INTEGRATORE ORALE A CONFRONTO CON AMITRIPTILINA NELLA PROFILASSI DI CEFALEA TENSIVA EPISODICA ED EMICRANIA SENZA AURA

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INTRODUZIONE

Abbiamo condotto uno studio osservazionale su pazienti afferenti ai nostri ambulatori cefalea, affetti da Cefalea Tensiva Episodica (CTE) ed Emicrania Senza Aura (ESA). Lo scopo dello studio era confrontare l'efficacia del Magnesio bisglicinato, L-triptofano, niacina, Vitamina B2 e Vitamina D, Laborest Italia spa = PT e dell'amitriptilina nella profilassi[1-2-3-4-5-6-7-8-9-10-11-12-13-14-15] di queste cefalee primarie utilizzando come outcome:

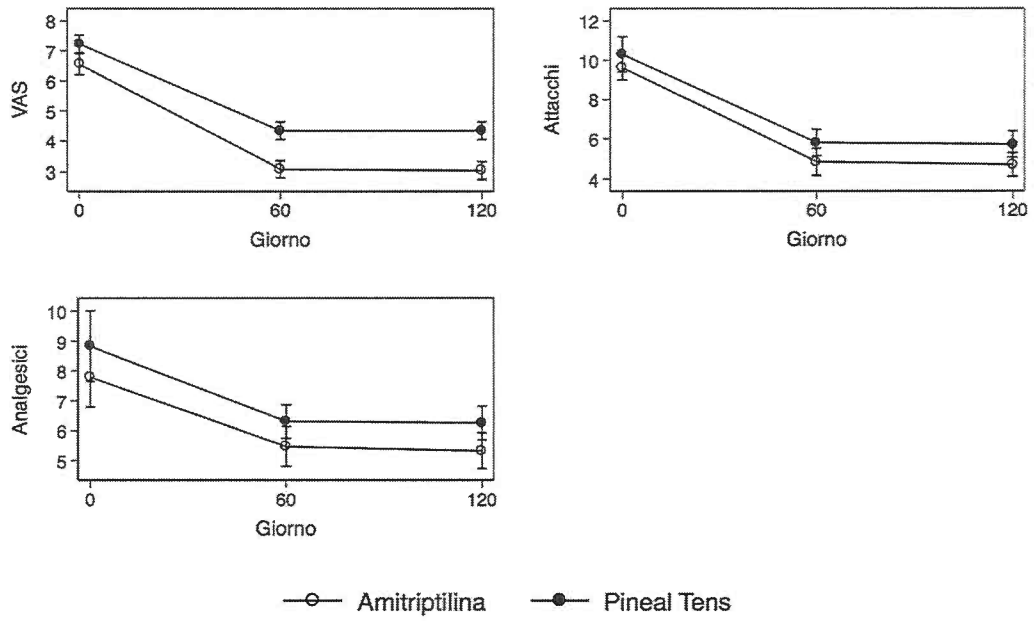
- la modificazione del dolore (scala VAS);
- la modificazione del numero di attacchi/mese;
- la modificazione del consumo di analgesici/mese .

PAZIENTI E METODI

La CTE ed ESA sono state diagnosticate secondo i criteri della classificazione internazionale ICHD-II. Sono stati studiati in totale 200 pazienti: 100 pazienti con diagnosi di CTE e 100 con ESA. Di questi 50 pz con diagnosi di CTE (età media 34 anni, 15M e 35F) erano in terapia con PT (1 bustina mattina e sera) e sono stati confrontati con 50 pz (età media 39 anni, 17 M e 33 F) in terapia con A (20 mg la sera). Mentre 50 pz con diagnosi di ESA (età media 37 anni, 15M e 35F) ed in terapia con PT (1 bustina mattina e sera), sono stati confrontati con 50 pz (età media 40 anni, 8M e 42 F) in terapia con A (20 mg la sera).

RISULTATI[16-17]

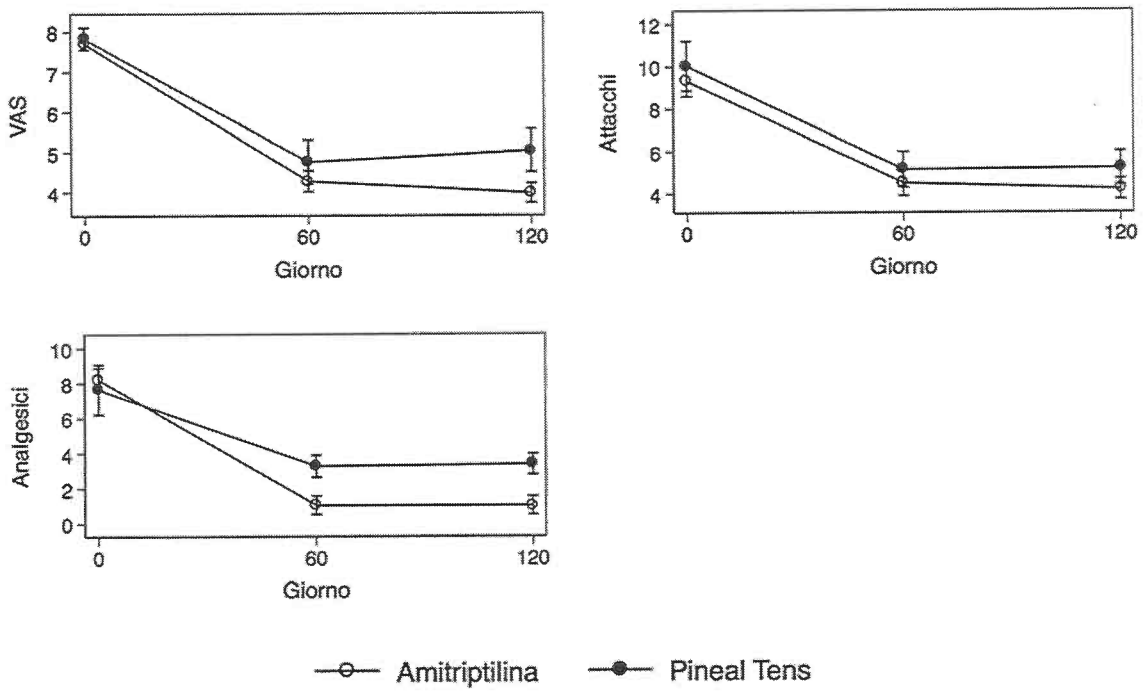
Figura 1 pazienti con CTE



I valori sono medie e intervalli di confidenza al 95% ottenuti da regressione lineare (VAS) o da regressione di Poisson (attacchi, analgesici) per misure ripetute.

Le modificazioni della VAS, del numero di attacchi e del numero di analgesici nel corso dello studio sono riportate in **Figura 1 per i pazienti con diagnosi di CTE**. È evidente la riduzione di tutti gli outcome nel corso dello studio sia per il gruppo A sia per il gruppo PT.

Figura 2 pazienti con ESA



I valori sono medie e intervalli di confidenza al 95% ottenuti da regressione lineare (VAS) o da regressione di Poisson (attacchi, analgesici) per misure ripetute.

Le modificazioni della VAS, del numero di attacchi e del numero di analgesici nel corso dello studio sono riportate in **Figura 2 pazienti con diagnosi di ESA**. È evidente la riduzione di tutti gli outcome nel corso dello studio sia per il gruppo A sia per il gruppo PT.

CONCLUSIONI

Abbiamo riportato i risultati di uno studio di coorte scaturito dall'osservazione clinica di un miglioramento della cefalea in pazienti in trattamento con PT. Ciò ci ha portato a confrontare il PT con A tramite uno studio osservazionale. Anche se questo studio ha l'evidente limite dell'assenza di randomizzazione dei pazienti, i suoi risultati confermano l'impressione clinica di un miglioramento della cefalea primaria nei pazienti in trattamento con PT in termini di miglioramento della VAS, di riduzione del numero di attacchi/mese, e del consumo di analgesici/mese. Infatti, il PT è risultato di efficacia comparabile all'A per molti degli outcome.

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