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**CEFALEE,
NEUROLOGIA E
INNOVAZIONE**

GENOVA
28-30 Novembre 2024
Starhotel President



ABSTRACT

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COMUNICAZIONI ORALI

Venerdì 29 Novembre 2024

8.00-9.00

COMUNICAZIONI ORALI 1

Moderatori: E. Arena, F. Valguarnera

Results from the 2nd Italian Interim Analysis of the PEARL Study: Response Rate and Maintenance of Response over 12 Months of Fremanezumab Treatment

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Background

The Pan-European Real-Life study (PEARL; EUPAS35111) is a 24-month, prospective, observational study aiming to assess the real-world effectiveness of fremanezumab in patients with episodic (EM) and chronic migraine (CM). This subgroup analysis performed in the Italian population of patients with high frequency episodic migraine (HFEM) and CM investigates fremanezumab effectiveness in terms of response rate over 12 months of follow up.

Methods

This subgroup analysis included 354 Italian patients with HFEM and CM enrolled in 30 headache centers who had failed ≥ 3 prior preventive treatments and had been prescribed fremanezumab (225 mg monthly/675 mg quarterly). All patients received ≥ 1 fremanezumab dose and were considered for safety analysis; 343 patients (HFEM/CM: 124/219) were included in the full analysis set. Endpoints investigated in the analysis were: proportion of patients with $\geq 50\%$ reduction in monthly migraine days (MMDs) over 6 months (primary endpoint of the PEARL study); $\geq 50\%$, $\geq 75\%$, and 100% response rate at Months 1, 3, 6 and 12; proportion of patients with sustained response ($\geq 50\%$ MMD reduction) from Month 3 to 12; and safety and tolerability of the treatment within 12 months of follow up.

Results

Overall, 61.2% of patients (207/338) achieved a $\geq 50\%$ reduction in MMDs over 6 months. Over 12 months of follow up, $\geq 50\%$ response rates were 59.2% at Month 1, 60.9% at Month 3, 66.6% at Month 6, and 60.1% at Month 12. At the same timepoints, $\geq 75\%$ response rates were 33.5%, 35.3%, 38.2%, and 34.7%, respectively, and 100% responder rates were 16.3%, 10.6%, 14%, and 12.5%. Notably, 42.9% of patients achieving a response at Month 3 maintained the response status at Month 12. This trend was similar across patients with HFEM (44.6%) and CM (41.9%). Furthermore, 29.1% of patients achieved a sustained response throughout the entire treatment duration (uninterruptedly from Month 3 to 12), a pattern consistent among patients with EM (28.6%) and CM (29.4%). Drug-related AEs occurred in 35 (9.8%) patients. The most common AEs reported were related to site-injection reactions (5.5%) followed by gastrointestinal disorders (constipation, 2.8%; nausea, 1.1%).

Conclusions

Over 12 months of follow up, treatment with fremanezumab provided sustained effectiveness, safety, and tolerability in the Italian subpopulation of patients with HFEM or CM and ≥ 3 prior preventive treatment failures.

Acknowledgements

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GLP-1 Agonists for the treatment of chronic migraine: a pilot prospective observational cohort study

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Introduction

Migraine, affecting 14.7% of the global population, often lacks effective treatment. Glucagon-like peptide-1 receptor (GLP-1R) agonists, used for diabetes and obesity, control fluid secretion, influencing cerebrospinal fluid (CSF) production in the brain's choroid plexus. Studies show GLP-1R agonists reduce intracranial pressure (ICP) in rodents, surpassing common IIH drugs in effectiveness (1). Clinical trials have confirmed their ability to lower ICP and improve headache frequency in IIH patients. There is evidence that reducing ICP benefits not only IIH patients but may also be beneficial to those with borderline normal CSF pressure, indicating that even isolated intracranial compliance reduction might be crucial in migraine development (2). Interestingly, GLP-1R agonists have also been found to suppress pain pathway sensitization in trigeminal nucleus caudalis (3). This study explores GLP-1R agonists as a novel migraine treatment, focusing on their efficacy in reducing migraine frequency.

Methods

This is a pilot prospective observational cohort study, aiming at evaluating the effectiveness of subcutaneous Liraglutide, 1.2 mg daily for the treatment of chronic migraine. We enrolled 12 patients with chronic migraine and a concomitant BMI equal or greater than 27 at the Headache Centre of University Federico II of Naples. Exclusion criteria included the presence of papilledema to rule out idiopathic intracranial hypertension. Duration of follow-up was 6 months. We assessed mean monthly days with headache by reviewing standardized paper patient headache diaries. We also assessed patient's weight every month.

Results

A significant decrease in mean monthly headache days was observed throughout the observation period (baseline: 23.17 ± 5.98 ; after 1 month: 12.08 ± 7.19 , after 6 months: 9.42 ± 6.27 , for all $p < 0.001$). We observed a statistically significant decrease in MIDAS score as well (baseline: 63.58 ± 15.07 ; after 1 month: 32.5 ± 20.12 , after 6 months: 24.33 ± 13.06 , for all $p < 0.001$). Conversely, we did not observe any significant weight reduction (baseline: 99.83 ± 18.49 ; after 1 month: 98.42 ± 17.88 , after 6 months: 94.42 ± 14.74 , for all $p > 0.05$). During the 6 months' treatment period, none of the 12 patients discontinued treatment due to adverse events.

Conclusion: this pilot study suggests that GLP-1 agonists may be a suitable and effective treatment for chronic migraine and that efficacy is unrelated from weight loss. This may shed new light on migraine physiopathology and its relation with CSF volume and pressure homeostasis.

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Phenotyping ictal and perictal migraine patients according to clinical and psychophysical characteristics

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Background

This study aims to 1) identify different migraine phenotypes according to clinical and psychophysical characteristics, and 2) assess the clinical validity of the different migraine phenotypes.

Methods

This observational study included Episodic Migraine (EM) patients assessed in the ictal, preictal, and postictal phases and Chronic Migraine (CM) assessed in the ictal phase and was divided into two parts. In part 1, headache frequency, disability, cervical active range of motion (AROM), pressure-pain threshold (PPT) over temporalis, two cervical areas (C1/C4 vertebral segments), and two distal pain-free areas(hand/leg) were assessed and used to subgroup migraine patients into different Clusters. In part 2 clinical characteristics (multiple questionnaires), somatosensory function (comprehensive quantitative sensory testing (QST)), and cervical musculoskeletal impairments (cervical musculoskeletal assessment) were assessed and compared across headache clusters and a group of 56 healthy controls matched for sex and age.

Results

Part 1: 100 patients were included, and two clusters were identified. Cluster-1.1 No Psychophysical Impairments (NPI, 19%) and Cluster-1.2 Increased Pain Sensitivity and Cervical Musculoskeletal Impairment (IPS-CMD, 81%). Cluster 1.1 had a higher percentage of men and lower disability compared to Cluster 1.2 (all, $p < 0.037$). Cluster 1.2 had reduced AROM in flexion, extension, and left/right lateral flexion, and lower PPT value in all areas compared to Cluster 1.1 (all, $p < 0.037$).

Part 2: Cluster-1.2(IPS-CMD) had higher headache intensity, worse headache-related and neck-related disability, worse quality of life, higher symptoms related to sensitization and psychological burden (all, $p < 0.048$) vs. Cluster-1.1(NPI). Cluster-1.2(IPS-CMD) had 1) reduced cervical active and passive range of motion reduced functionality of deep cervical flexors, and reduced values in all QST (higher sensitization) vs. controls (all, $p < 0.023$); and 2) reduced active mobility in flexion, left/right lateral flexion, and reduced values in QST vs. Cluster-1.1(NPI) (all, $p < 0.045$). Cluster 1.1 (NPI) had reduced functionality of deep cervical flexors and higher QST values (lower sensitization) vs. Controls (all, $p < 0.049$).

Conclusion

In the ictal/perictal phase, two clinically relevant clusters were identified according to clinical and psychophysical characteristics, with one group showing no psychophysical impairment, and one with increased pain sensitivity and cervical musculoskeletal dysfunctions

Phenotyping ictal and perictal migraine patients according to clinical and psychophysical characteristics



Comparison of efficacy and safety of monoclonal antibodies targeting CGRP for migraine prevention and sub-groups analysis: a 12 months, multicenter, prospective, real-life study
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Introduction

Limited data exists on the efficacy and safety of anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) for migraine prevention across different age groups. Our previous single-center study demonstrated the effectiveness and safety of 3 and 6 months of erenumab therapy in patients over and under 65 years, without significant differences. This study aims to explore the influence of patients' age on the efficacy and safety of mAbs targeting the CGRP pathway.

Methods

Prospective enrollment of migraine patients was conducted as part of the I-GRAINE registry, a national multicentric project. Patients were categorized into age quartiles, resulting in 4 subgroups. Clinical data were collected at baseline (T0) and at 3 (M3), 6 (M6), and 12 (M12) months, including monthly headache (MHD) and migraine (MMD) days, abortive treatment usage in terms of days (AMD) and pills (AMP), HIT-6, MIDAS, NRS, ASC-12 scores, and side effects assessment.

Results

A total of 1890 migraine patients participated in this multicentric, observational study, predominantly females (80%) with a median age of 49 years (IQR: 18 – 80). Migraine characteristics included chronicity (62%) and comorbidities such as medication-overuse headache (MOH, 58%) and psychiatric conditions (32%). All age groups exhibited significant improvements in clinical variables at M3, M6, and M12 ($p < 0.001$). At M12, patients aged >57 years experienced a greater reduction in MHD, MMD and AMP ($p < 0.001$). Adverse events (AEs) occurred in 3% of patients during mAb treatment, with constipation (39%), local reactions (33%), and systemic symptoms (28%) being the most common. AEs predominantly occurred in the first trimester (63%), decreasing to 17% at M12. No statistically significant differences were found among age groups regarding the frequency of AEs ($p > 0.05$).

Conclusions

This multicentric study, involving more than 25 Italian Headache Centers, is the first to investigate real-life efficacy and safety of CGRP-targeting mAbs across different age groups. Our results confirm the consistent effectiveness of mAbs across all ages, particularly in elder patients, and suggest their suitability for older patients with potential contraindications to oral preventive drugs. These findings support clinicians in confidently recommending mAb treatment for advanced-age patients and reinforce the favorable safety profile of these therapies.



Application of Machine Learning in the diagnosis of headache and migraine in children and adolescents

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Rational

Headache in childhood is underdiagnosed and poorly recognized, both by family members and doctors. This leads to a delay in diagnosis. Furthermore, it is not always possible to meet the diagnostic criteria indicated by the ICHD-3 classification, which mainly refer to adulthood. A correct diagnosis allows for early therapeutic-rehabilitative interventions with the possibility of a better prognosis. Objectives and methods: This exploratory study aims to improve the diagnosis through an "ad hoc" questionnaire and Machine Learning (ML) methods. The free description of "headache" and its graphical representation were analyzed using Natural Language Processing (NLP) and image analysis techniques, respectively. The patients included were aged 6-18 years, of both gender, having their first/follow-up visit for migraine/primary headache. Patients with secondary migraine/headache, neurological/psychiatric pathologies, medium-severe intellectual disability were excluded.

Results

The preliminary analysis was based on 63 patients, 9 of whom were excluded from this preliminary step as they had a mixed form (tension and migraine). Cluster analysis was based on questionnaire answers: the number of clusters (n=4) was defined based on the best optimization of the algorithm on the data currently available. Words most associated with headache and migraine were also identified. Image analysis has not yet started.

Conclusions

Two clusters, with a similar distribution of diagnoses (~80% migraine), differed in some characteristics: mode of onset, aggravating factors, accompanying symptoms. The third cluster was characterized by a greater presence of accompanying sensory symptoms. The fourth cluster collected headache sufferers aged 8-14, excluding adolescents, more frequently affected by migraine. Future steps: refine clustering algorithms on new data, implement mixed headache features into models and improve NLP lemmatization.



COMUNICAZIONI ORALI **Sabato 30 Novembre 2024**

8.00-9.00

COMUNICAZIONI ORALI 2

Moderatori: M. Aguggia, T. Tassinari

Happiness in Migraine Disease

G. Fiorentini^{1,2}, S. Ardis³, M.C. Tonini⁴ and The Migraine Happiness Group (M. Albanese, C. Aurilia, M. Autunno, M. Bandettini, P. Barbanti, M. Bartolini, M.L. Bartolozzi, S. Cevoli, V. Drago, R. Altavilla, F. Frediani, F. Giambattistelli, L. Giani, A. Lerario, S. Massari, M. Padroni, F. Perini, A. Ranieri, N. Rebaudengo, C. Rubino, M.G. Saracco, M. Secchi)

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Introduction

Positive health is defined as the science that studies health resources. Measurements of subjective well-being, such as overall happiness, life satisfaction and health satisfaction, along with positive and negative affects, are crucial for understanding the impact of illness on quality of life. In particular, little is known about these aspects in the context of migraine.

Objective

To assess subjective well-being in individuals with episodic migraine with and without aura using validated questionnaires.

Materials and Methods

This is an ongoing multicenter cross-sectional study conducted in 16 Headache Centers across the country, evaluating positive health in individuals with episodic migraine with and without aura through specific scales measuring overall happiness, life satisfaction, emotional well-being, resilience, gratitude, and hope. Additionally, the MIDAS, HIT-6, HAM-D, and BAI questionnaires were administered.

Results

Preliminary results from a sample of 278 subjects (243 F and 35 M), with an average age of 45.12 years (SD ± 13.38), consisting of 89% females, show a significant disparity in terms of life satisfaction (LS) to the detriment of migraine patients compared to the general Italian population. The mean LS score for migraine patients is 6.31 points (SD ± 2.22), whereas for the general Italian population it is 7.2 points ($p = 0.000$). An inverse correlation between the number of migraine days and LS was found to be significant.

Conclusions

Preliminary results indicate that individuals with migraine experience a significant disparity in subjective well-being compared to the general population. The inverse correlation between the number of migraine days and life satisfaction suggests that attack frequency may partly explain this disparity. We hope that assessing subjective well-being through the analysis of all administered questionnaire results at the end of the study will allow for a better quantification of the impact of treatments on patients' quality of life.



Reduction of spontaneous EEG alpha power and TMS-evoked potentials in the right occipital area after administration of Galcanezumab in migraine patients

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Migraine is a neurovascular disorder characterized by abnormal excitability of the cerebral cortex. The calcitonin gene related peptide (CGRP) is a vasodilator involved in pain transmission released from both peripheral and central nervous system terminals. It plays a key role in the pathogenesis of migraine attacks and has been suggested to contribute to many features of the migraine brain.

CGRP and its receptor are a target for a class of drugs that specifically act on the CGRP-linked trigeminal pain activity (anti-CGRP therapies). Galcanezumab is a safe, rapid, effective and well tolerated anti-CGRP monoclonal antibody (anti-CGRP mAb) that binds the circulating CGRP reducing its biological activity and, consequently, lowering frequency and intensity of migraine attacks. Although it is unlikely that Galcanezumab trespasses the blood-brain barrier in a significant proportion, some studies suggest that it could have central effects.

To understand whether Galcanezumab can affect electrical cortical activity, we recorded both resting electroencephalogram (EEG) and Transcranial Magnetic Stimulation combined with EEG (TMS-EEG), a non-invasive technique that allows to directly measure cortical excitability. Specifically, we acquired resting EEG and TMS-evoked potentials (TEPs) in 6 migraine patients in eyes closed (EC) and eye open (EO) conditions, before (T0) and one week after (T1) the first intake of Galcanezumab. With TMS-EEG, we targeted right and left occipital and motor areas. We found that EEG alpha power in EC condition was reduced in T1 compared with T0 in all subjects. Notably, the amplitude of TEPs in the right occipital area was reduced in T1 with respect to T0 in the 4 patients who reported a better clinical improvement, whereas TEPs in the left occipital area did not show reproducible changes. TEPs in both left and right motor areas did not show any significant changes.

These preliminary results suggest that Galcanezumab can modulate cortical excitability in migraine patients. Moreover, patterns of cortical excitability modulation can be different for responders compared to non-responders.



Migraine and Irritable Bowel Syndrome (IBS): may the CGRP be the link?

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Background

CGRP is the pivotal molecule that starts the migraine attack inducing the neurogenic inflammatory cascade. CGRP is involved in the regulation of many gastrointestinal functions including motility, mucosal ion transport, enzyme secretion, neuronal excitability, and the inflammatory and immune response. It facilitates peristaltic activity and stimulates water secretion into the intestinal lumen. Irritable Bowel Disease (IBS) patients frequently complaint of diarrhea or constipation. A relationship between IBS and migraine was observed and CGRP may be the link.

Aims

To evaluate the IBS prevalence among migraineurs treated with antiCGRP monoclonal antibodies and to evaluate antiCGRP effects on IBS symptoms.

Results

200 migraine patients, consecutively treated with antiCGRP were asked to fill an ad hoc questionnaire on IBS symptoms. 102 of them (90F and 12 M, age range 18–67 years) returned the questionnaire. IBS could be diagnosed in 50 out of these 102 patients (49%), more than double that in the general population. Among these 102 subjects, recurrent abdominal pain was reported by 53 patients (in 7/53, the antiCGRP increased and in 9/53 reduced the frequency of abdominal pain attacks); recurrent loose or poorly formed stools were referred by 48 (in 9/48 antiCGRP reduced the problem); recurrent urgent defecations were reported by 32 people (in 9/32 reduced by antiCGRP); food intake and stressing situations worsening IBS disturbances in 47 subjects (in 10/47 this was reduced by antiCGRP); recurrent constipation was observed in 48 patients, recurrent diarrhea in 15 and diarrhea/constipation alternation in 19. Constipation improved with antiCGRP in 8 patients, worsened in 13 and appeared in 7 cases. Patients reporting a significant reduction of migraine frequency with antiCGRP treatment had a statistically significant reduction of IBS symptoms in respect of non-responders.

Discussion and conclusions

IBS is very frequent among refractory migraine patients, and CGRP modulating therapies seem to ameliorate both migraine and IBS. The CGRP may be considered as the pivotal molecule of both conditions. High CGRP levels may possibly cause or worsen both migraine and IBS, and CGRP down-modulation may help both conditions.



Exploring Glymphatic Involvement in Idiopathic Intracranial Hypertension before and after treatment: A DTI-ALPS Study

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Background

Glymphatic system is currently the subject of much scientific attention, and fast-growing evidence suggests an integral role in maintaining central nervous system function. In 2017, Taoka et al. proposed a noninvasive non-contrast MRI-diffusion-based method to study the glymphatic system indirectly: the “Diffusion Tensor Image-Analysis aLong the Perivascular Space (DTI-ALPS). This method has been mostly applied to neurodegenerative conditions and to a lesser extent to CSF circulation disorders such as idiopathic intracranial hypertension (IIH). This is a neurological disorder resulting from persistently high levels of intracranial pressure in the absence of obvious causative factors. Its pathogenesis remains unclear and although invasive methods have suggested a glymphatic involvement in its pathogenesis, no studies have evaluated the DTI-ALPS pre and post lumbar CSF tap test in these patients.

Methods

This observational prospective study included all patients with a suspected diagnosis of Idiopathic Intracranial Hypertension evaluated at Bologna Headache Center between February 2021 to December 2023 who underwent a lumbar puncture for CSF opening pressure measurement and tap-test. We performed a contrast enhanced Brain MRI (3T) for diagnosis confirmation (i.e., exclusion of secondary intracranial hypertension) with DTI sequences for DTI-ALPS calculation before and after the lumbar puncture with CSF removal.

Results

To the date of December 2023, a total of 18 patients were screened. We confirmed diagnosis and completed the protocol in 10 patients. We performed a calculation of DTI-ALPS pre and post tap test, along with venous outflow evaluation.

Conclusions

We present the first data of pre and post treatment, Glymphatic function evaluation in IIH patients using the DTI-ALPS methodology.



Lasmiditan as symptomatic treatment for hemiplegic migraine: case report on efficacy, safety and future perspectives

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The treatment of hemiplegic migraine represents a challenge since the use of specific anti-migraine drugs such as triptans is generally not recommended for symptomatic treatment¹ even if some case series suggest a possible use².

Here we present the case of a young 28-year-old patient with hemiplegic migraine who used lasmiditan as symptomatic treatment for attacks she had over a three-month period of clinical observation. The diagnosis of hemiplegic migraine was formulated after a clinical episode occurred at the age of 20 when a severe migraine attack has been preceded and accompanied by moderate hemiparesis in the left limbs, visual and sensory aura ipsilateral to the paresis; at that time the patient was hospitalized and underwent an exhaustive diagnostic work-up aimed at excluding vascular, infectious and autoimmune etiologies. Two years after the first episode, a second attack of hemiplegic migraine occurred and since then, on average, she presents 1-2 attacks per month characterized by visual and sensory aura associated in approximately half of the cases with a slight reduction in strength in a hemisome; attacks were ineffectively managed and poorly tolerated by nonsteroidal anti-inflammatories. The patient was never told to treat the episodes with triptans due to the hypothetical reduced vascular safety. In September 2023, after a reassessment of the case, it was recommended to treat the attacks with lasmiditan 50 mg, due to the safety on the vascular side demonstrated in the pivotal studies³. In 3 of the 4 reported attacks the patient reported complete resolution of the headache within 2 hours, in 1 out of 4 attacks the headache resolved within 24 hours; no other medication where been necessary. All 4 attacks treated with lasmiditan recorded the presence of mild adverse symptoms such as dizziness and drowsiness. Patient satisfaction was very good.

References

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POSTER

Venerdì 29 Novembre 2024

13.00-14.00

SESSIONE POSTER A

Moderatori: F. Tazza, A. Coccia

Anxiety and Depression in Chronic Migraine Patients Treated with Atogepant: A One-Month Follow-Up Study

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Chronic migraine is often accompanied by psychiatric comorbidities. This study evaluates the impact of atogepant, a novel CGRP receptor antagonist, on anxiety and depression levels in chronic and refractory migraine patients over a one-month period. Using the Hospital Anxiety and Depression Scale (HADS) and the Migraine-Specific Quality of Life Questionnaire (MSQ), we assessed changes in these psychological and quality-of-life parameters pre- and post-treatment. Additionally, the Patients' Global Impression of Change (PGIC) was used to evaluate overall patient perceptions of improvement.

Introduction

Chronic migraine is frequently associated with psychiatric comorbidities, including anxiety and depression. Traditional migraine treatments, often fail to provide adequate relief for some patients. Atogepant, offers a promising alternative for migraine prophylaxis. This study aims to evaluate the effects of atogepant on anxiety and depression levels in chronic and refractory migraine patients who have failed at least four prior therapies and to assess their overall impression of change using the PGIC and quality of life using the MSQ.

Methods

Participants: seven patients (aged 20-65) with a diagnosis of chronic and refractory migraine, were recruited for this study.

Procedure: participants received atogepant 60 g per die, and their anxiety (HADS-A) and depression (HADS-D) scores were recorded at baseline (T0) and after one month of treatment (T1). The Patients' Global Impression of Change (PGIC) and the Migraine-Specific Quality of Life Questionnaire (MSQ) were also assessed at T1.

Discussion

The results of this study suggest that atogepant treatment over a one-month period does not lead to significant changes in anxiety, depression, or quality of life levels in patients with refractory migraine. While some individual patients showed notable changes, the overall trends were not statistically significant. The small sample size and the limited observation time limits the ability to detect significant differences. Additionally, the PGIC responses varied, with some patients reporting moderate improvements while others noted little to no change.

Conclusions

This preliminary study indicates that one month of atogepant treatment does not significantly affects anxiety, depression, or quality of life levels in chronic and refractory migraine patients. The variability in PGIC responses suggests that while some patients perceive improvement, the overall impact on anxiety, depression, and quality of life may be limited.



CSF-hypotension related headache: an atypical presentation

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Objective

To describe an atypical case of CSF hypotension headache.

Methods

A 46-year-old patient with a history of hypercholesterolemia currently not on therapy, dysmenorrhea treated with estrogen-progestogens for 2 months; no history of headache. In March 2023 acute onset, during the night, of intense headache at the top, thunderclap-type, which woke her up from sleep; nausea and vomiting, phono and photophobia were associated. For this reason, she had hospitalization and practiced CT + angioCT, which were negative; the neurological examination at the time of access showed no signs of ongoing neurological pathology. Discharged with indication to perform brain MRI with angio sequences, practiced 7 days after onset and negative.

Results

The patient came to our observation for diplopia due to VI cranial nerve palsy that began 15 days after the onset of headache. She performed in emergency CT and angio-CT, negative, and was admitted to the Neurology department. The MRI carried out at our department highlighted an apparently somewhat stretched aspect of the ventricles with subdural bihemispheric subdural seroematic effusion predominantly parieto-occipital, interhemispheric and tentorial; diffuse thin smooth dural thickening with enhancement after contrast; interpeduncular angle of about 37°, pontomesencephalic angle of about 43°, perioptic liquor film was not clearly demonstrable; all these findings oriented, at least in the first instance for phenomena related to CSF hypotension. She underwent a blood patch procedure, completed without complications. The clinical control at 30 days showed complete regression of the cephalalgic symptoms type thunderclap, diplopia in the lateral gaze over 45 degrees laterally for VI deficiency; MRI control brain showed no signs of residual intracranial hypotension.

Discussion

The clinical presentation of the patient did not suggest, given the lack of anamnestic elements (trauma, intense physical exertion), the onset of a CSF hypotension headache. Other causes (e.g. cerebral venous thrombosis associated with estrogen-progestogen use) were more likely, with focal neurological deficits coexisting.

Conclusions

The symptoms of SIH resemble intracranial hypotension from other causes such as postdural puncture, postsurgical and post-traumatic CSF leaks, but in SIH the leak occurs spontaneously in the spine at a site which is unknown at the time of presentation. Our case presents clinical particularities related to onset and neurological symptoms not associated with evidence of risk factors for CSF hypotension.



Beyond the Initial Relief: Sustained Benefits and Tolerability of Galcanezumab in Migraine Prevention

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Background

Galcanezumab has proven to be a highly effective and well tolerated Migraine preventive medication since its approval. Although the abundant real-world scientific production on this topic confirmed long-term tolerability, most studies have relatively short follow-up. Hence, longer follow-up data with a high level of surveillance for efficacy and safety are warranted in a potential life-long using medication.

Methods

This observational prospective study included all patients with a diagnosis of Episodic or Chronic Migraine who started treatment with Galcanezumab between December-2019 to August-2020. Patients were followed up with a minimum of two outpatients' evaluations per year and for a total duration of three years. Mean Headache days (MHD), pain intensity and acute medication consumption were collected throughout the study period as well as adverse events.

Results

A total of 20 patients were included. Sixty percent of patients were Chronic Migraineurs with Medication Overuse Headache. After the first year of treatment, 40% of the total cohort showed a sustained reduction of at least 50% (50%RR) in MHD and the 80% of the cohort continued the treatment. Four patients dropped out from the treatment due to inefficacy whereas zero patients dropped out due to side effects. During the subsequent therapy cycles, we observed a relative stabilization of dropouts (four drop out per year) and a significant relative increase in 50% responders (68.7% during 2° cycle versus 40% in 1° cycle). The fifty-five percent of the initial cohort started the ongoing third cycle. No baseline feature was predictive of long-term response.

Conclusions

In our cohort, Galcanezumab has proven to be an exceptionally tolerated pharmacological agent (zero adverse events) and remarkably efficacious in the prolonged prophylaxis of migraine, resulting in a minimal attrition rate from the therapeutic regimen.



Is Erenumab effective and safe in long term treatment of migraineurs? Three-year observational study results

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Background

Erenumab has proven to be a highly effective and well tolerated Migraine preventive medication since its approval in 2018. Although the abundant real-world scientific production on this topic confirmed long-term tolerability, most studies have relatively short follow-up. Hence, longer follow-up data with a high level of surveillance for efficacy and safety are warranted in a potential life-long using medication.

Methods

This observational prospective study included all patients with a diagnosis of Episodic or Chronic Migraine who started treatment with Erenumab between May-2019 to August-2020. Patients were followed up with a minimum of two outpatients' evaluations per year and for a total duration of three years. Mean Headache Days (MHD) were collected throughout the study period as well as adverse events.

Results

A total of 164 patients were included. After the first year of treatment, 34% of the total cohort showed a sustained reduction of at least 50% (50%RR) in MHD and 84/164 (50.9%) continued the treatment. Three patients dropped-out due to side effects (1.8% of the total cohort) whereas 23/164 patients dropped-out due to inefficacy. During the subsequent therapy cycles, we observed a relative stabilization of dropouts (64/84 patients started the 3rd cycle) and a slight relative increase in 50% responders (50.9% 1° cycle, 55% 3° cycle). No baseline feature was predictive of long-term response.

Conclusions

We observed a halving of the treated patients at 1 year, followed by a stabilization of dropouts and a 'selection' of the most responsive patients, with a very high 50%RR at the end of the third year.



Headache and cerebrospinal fluid dynamics: spontaneous CSF rhinorrhea in Idiopathic Intracranial Hypertension. Case report and literature review

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Spontaneous cerebrospinal fluid (CSF) rhinorrhea, characterized by the unexplained leakage of CSF from the nose, is a rare and clinically intriguing condition. Trauma accounts for 80-90% of cases, other causes are postoperative (10%), spontaneous (4%), neoplastic (2%), inflammatory (2%). When not associated with other factors, it is termed spontaneous, and it is at high risk of bacterial meningitis and cerebral abscesses. Diagnosis involves clear unilateral rhinorrhea and confirmation through fluid analysis (Beta-2 transferrin, glucose). Radiological examination, preferably CT with potential MRI, is crucial. Treatment entails surgical closure of the osteomeningeal defect, but it's insufficient for overall management, for the frequent underlying chronic idiopathic intracranial hypertension (IIH). Chronic IIH and spontaneous CSF leakage are suggested to be linked, sharing demographic similarities, increased intracranial pressure (ICP) after repair, elevated risk of recurrence, and heightened risk with tumor-associated IIH. Uncontrolled IIH increases the risk of repair failure or recurrence. IIH involves increased ICP without secondary causes, presenting symptoms like headache, papilledema, and visual disturbances. Its association with spontaneous CSF rhinorrhea is uncommon, providing sparse literature, necessitating further exploration for enhanced understanding and optimal management. Case: a 51-year-old woman with a seven-year history of IIH, managed with acetazolamide, was admitted due to spontaneous rhinorrhea following a sneeze, with intense headache and retro-orbital pain, worsened by orthostatism. Imaging revealed meningeal invaginations and fistulous tracts. Fiberoptic laryngoscopy confirmed secretion at specific intranasal sites, leading to fistula closure surgery. This case raises questions about the IIH-CSF leakage association and calls for multidisciplinary management. The connection has gained recognition, but opinions on assessment and management vary. Scientific literature hints at a potential link between pathology and compromised CSF barrier stability, urging further exploration of the ICP-CSF barrier relationship. A multidisciplinary approach is recommended for accurate diagnosis, treatment, and follow-up. We aim to assess clinical implications of the case and conduct a literature review on the IIH-spontaneous CSF leakage association, emphasizing the need for a unified and comprehensive approach to patient care.



Efficacy of Onabotulinum Toxin A (BonNT-A) in the Management of Hemicrania Continua, unremitting subtype: A Case Report

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Background

Hemicrania continua (HC) is a primary headache disorder characterized by continuous strictly unilateral head pain with episodic exacerbations associated with ipsilateral cranial autonomic symptoms. The HC typically have a dramatic response to indomethacin, but his use can lead to side effects, necessitating alternative treatments. For this reason, BonNT-A has emerged as a potential therapeutic option.

Materials and Methods

A 52-year-old female patient with a 15-year history of complained of a continuous, strictly left-sided headache moderate to severe in intensity, with superimposed paroxysms of short-lastingshooting pain in the same area and autonomic symptoms. Diagnosed as migraine without aura, she was treated with propranolol, topiramate and rizatriptan to the need, without benefit. After a rapid response to indomethacin, according to the International Classification of Headache Disorder criteria (ICHD-3), a diagnosis of HC was made. After a few months, gastrointestinal side effects appeared, which led to medication discontinuation. So, we decided to administer 100 units of BonNT-A (unilateral on occipitalis, cervical paraspinal, trapezius and temporalis muscles; bilateral on corrugator and frontalis muscles). Efficacy was assessed using Migraine Disability Assessment (MIDAS), Headache Impact Test-6 (HIT-6), Pittsburgh Sleep Quality Index (PSQI) and Hospital Anxiety and Depression Scale (HADS). Evaluations were conducted before treatment and 3 months post-treatment.

Results

Before treatment, the patient had high scores on the MIDAS and HIT-6, indicating severe headache impact and disability, alongside poor sleep quality according to the PSQI scores. High HADS score showed an underlying anxious-depressive syndrome. After BonNT-A, the patient experienced complete resolution of continuous headache pain and a significant reduction in the frequency and intensity of pain in migraine attacks. However, she continued to experience mild autonomic symptoms.

Discussion and Conclusions

This case highlights the effectiveness of BonNT-A injections in managing HC, particularly in patients who cannot tolerate indomethacin more. The significant reduction in MIDAS, HIT-6, HADS and PSQI scores suggests that BonNT-A can substantially alleviate the impact of headaches on daily functioning and overall quality of life. However, the persistence of autonomic symptoms suggests that these might be mediated by mechanisms not fully addressed by BonNT-A. So, we need further research to understand their underlying mechanisms and develop targeted treatments.



Phenotyping interictal migraine patients according to clinical and psychophysical characteristics

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Background

This study aims to 1) identify different migraine phenotypes according to clinical and psychophysical characteristics, and 2) assess the clinical validity of the different migraine phenotypes.

Methods

This observational study included Episodic (EM) and Chronic Migraine (CM) patients assessed in the interictal phase and was divided into two parts. In part 1, headache frequency, disability, cervical active range of motion (AROM), pressure-pain threshold (PPT) over temporalis, two cervical areas (C1/C4 vertebral segments), and two distal pain-free areas (hand/leg) were assessed and used to subgroup migraine patients into different Clusters. In part 2 clinical characteristics (multiple questionnaires), somatosensory function (comprehensive quantitative sensory testing (QST)), and cervical musculoskeletal impairments (cervical musculoskeletal assessment) were assessed and compared across headache clusters and a group of 56 healthy controls matched for sex and age.

Results

Part 1: 98 patients were included, and three clusters were identified. Cluster-2.1 No Psychophysical Impairments (NPI, 18%), Cluster-2.2 Increase Pain Sensitivity (IPS, 45%), and Cluster-2.3 Increased Pain Sensitivity and Cervical Musculoskeletal Dysfunctions (IPS-CMD, 37%). Cluster-2.1 had a higher percentage of men compared to clusters-2.2 and 2.3 ($p=0.009$). Cluster-2.3 had higher headache frequency, and disability compared to Cluster-2.2, and higher disability compared to Cluster-2.1 (all, $p<0.010$). Cluster-2.3 had reduced AROM in all directions compared to Clusters-2.1 and 2.2 ($p<0.029$). Clusters-2.2 and 2.3 have lower PPT values in all areas compared to Cluster-1.1 ($p<0.001$).

Part 2: Cluster-2.3 (IPS-CMD) had 1) longer disease duration, higher headache frequency, disability, and psychological burden vs. Cluster-2.2 (IPS) (all, $p<0.027$) and 2) higher headache-related disability, neck-related disability, and higher symptoms of sensitization vs. Cluster-2.1 (NPI) (all, $p<0.018$). Cluster-2.3 (IPS-CMD) had reduced cervical active and passive range of motion and reduced functionality of deep cervical flexors, vs. Controls, Cluster-2.1 (NPI), and Cluster 2.2 (IPS) (all, $p<0.034$). Cluster-2.2 (IPS) and 2.3 (IPS-CMD) had reduced QST values vs. controls ($p<0.001$) and Cluster-2.1 ($p<0.039$).

Conclusion

In the interictal phase, three clinically relevant clusters could be identified, with one group showing no psychophysical impairment, one increased pain sensitivity, and one increased pain sensitivity and cervical musculoskeletal dysfunctions.



Migrain-like headache: a manifestation of cerebral venous thrombosis

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Patient of 22 years old, obese, who started suffering with a migraine-like headache at the beginning of November 2023, pulsating, in left fronto-orbital site, associated with photo-phonophobia and nausea, poor responsive to common analgesics. An ophthalmoscopic evaluation revealed a bilateral papilledema for which the patient was admitted to the Emergency Unit. The neurological evaluation was normal, patient was symptomatic only for headache. A CT without contrast has been done, showing nothing relevant, and the exam was completed with an angio CT showing a possible thrombosis of right sigmoid sinus until jugular vein, without venous infarct. Blood samples revealed no increase of D-dimer level. Patient was admitted to the neurologic unit, started an anticoagulant therapy with enoxaparin 20000U/day and subsequently it was shifted to an oral anticoagulant therapy with coumadin. The thrombosis has been confirmed with an angio-MRI. A few days later headache improved with resolution and ten days later a venous CT showing a complete resolution of the thrombosis. Finally, blood samples showed a positivity to antiphospholipid antibodies and the patient was discharge with a closed follow up. Cerebral venous thrombosis (CVT) is a rare form of deep venous thrombosis, yet a leading cause of stroke in young adults, associated to headache, D-dimer increase and venous infarct. Headache is the most frequent symptom. They do not have particular characteristics and can mimic other numerous varieties of headache. Despite this, headache of our patient was migraine like, associated with papilledema (sign of intracranial hypertension). Most patients with an acute CVT have a D-dimer level greater than 500 µg/L. However, a low D-dimer level does not rule out CVT in patients with high suspicion or in the subacute/chronic phase of the disease since the D-dimer levels decline with time from onset of symptoms¹. The patient had low levels of D-dimer, probably because it was in the chronic phase. Finally, the rate of recanalization is around 85% and almost 50% of cases achieve a complete recanalization after a median time of 6 months (mainly in the first months)²; recanalization of our patient was in the first 10 days, before than literature data.

In conclusion:

- Do not underestimate a headache in a young woman;
- always look at the fundus of the eye;
- a negative D-dimer does not exclude a thrombosis;
- complete recanalization can occur even in the first days of therapy.

¹Crassard I et al, Headache in patients with cerebral venous thrombosis, Rev Neurol, 2005;

²M. Capecchi et al, Cerebral venous sinus thrombosis, Journal of Thrombosis and Haemostasis, 2018.



Real-world effectiveness of atogepant for the preventive treatment of episodic migraine: a single center study

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Atogepant, is approved oral calcitonin gene-related peptide receptor antagonist for the preventive treatment of episodic migraine. The drug is indicated for migraine prophylaxis in adults who have at least 4 migraine days per month. Refractory migraine is defined by having failed all of the available preventatives and suffer from at least 8 debilitating headache days per month for at least 6 consecutive months. Beyond the registration studies, we evaluated the efficacy in daily clinical practice in a group of patients with refractory migraine.

Materials and methods

We conducted a prospective study involving 11 who had previously failed all of the available preventatives treatment regimens. Patients were evaluated at baseline (T0), and subsequently at one, three, and six months after initiating treatment with atogepant 60 mg per day. During each visit, patients self-administered the HEADACHE IMPACT TEST (HIT-6) SCORE, MIGRAINE DISABILITY ASSESSMENT (MIDAS) score, Numeric Rating Scale (NRS) and patients' global impression of change scale (PGIC) to assess headache impact, disability, severity, and global impression of change. Headache diaries were maintained by all patients to monitor attack frequency, acute therapy use, and time to clinical benefit after treatment intake.

Results and conclusions

At baseline (T0), patients reported an average of 19 migraine days per month, significantly impacting their quality of life. Over the course of the study, there was a statistically significant reduction in migraine frequency, improvement in latency to symptomatic treatment response, and improvement of headache-related disability. The amelioration was observed consistently across the follow-up periods at one, three, and six months. Notably, patients with significant anxiety-depressive components experienced similar benefits compared to those without greater psychiatric comorbidities, albeit to a lesser extent. Our study confirms that atogepant shows promise as an effective treatment option for patients with refractory migraine. The significant reduction in migraine frequency and associated disability underscores its potential clinical utility in improving quality of life for these patients. Further research with larger cohorts and longer follow-up periods is warranted to confirm these real life data and elucidate the optimal use of atogepant in migraine management.



Trigemino-cervical pain sensitivity during the migraine cycle depends on headache frequency

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Background

This observational study assessed differences in pain sensitivity across chronic migraine (CM), low-frequency (LFEM), high-frequency episodic migraine (HFEM), and controls.

Method

Quantitative sensory tests (QST) (Wind-up ratio (WUR), pressure pain threshold (PPT) from the trigeminal area, and PPT from the upper-cervical spine) were recorded. CM were assessed ictally and interictally and compared vs controls. LFEM and HFEM were assessed in the interictally, preictally, ictally, and postictally and compared vs. 1) each other's, matched for the phase; 2) CM (ictal LFEM and HFEM were compared vs. ictal CM; postictal, interictal, preictal LFEM and HFEM were compared vs interictal CM); 3) control.

Results

A total of 56 controls, 32 CM, 105 LFEM, and 74 HFEM were included. Compared to controls: 1) ictal CM had lower trigeminal and upper cervical PPTs ($p < 0.001$), and higher trigeminal WUR ($p = 0.020$); no differences were observed with interictal CM; 2) preictal HFEM had lower upper-cervical PPT ($p = 0.014$); ictal HFEM had lower trigeminal ($p = 0.002$) and upper-cervical ($p = 0.009$) PPTs, and higher trigeminal WUR ($p = 0.002$); postictal HFEM had lower trigeminal ($p = 0.004$) and upper-cervical ($p = 0.010$) PPT. No differences were observed with interictal HFEM; 3) interictal LFEM had lower trigeminal ($p = 0.002$) and upper-cervical ($p = 0.016$) PPTs; preictal LFEM had lower upper-cervical PPT ($p = 0.014$); postictal LFEM had lower upper cervical PPT ($p = 0.006$). No differences were observed with ictal LFEM. Ictal LFEM had higher trigeminal ($p = 0.013$) and upper cervical ($p = 0.012$) PPTs compared to CM. No other differences were observed between HFEM and LFEM or HFEM and CM.

Conclusion

This study suggested that HFEM patients have a sensory profile matching CM better than LFEM.



Observational pilot study on the efficacy of Anti CGRP antibodies on quality of sleep and depression

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Migraine is a neurological disease affecting 15% of the general population. Chronic migraine patients are more likely to suffer from anxiety and depression compared with people without migraine as well as reporting poor sleep quality.

Objective

To study the influence of Ab anti CGRP therapy over time on the migraine disability assessment scale (MIDAS) and the association between anxiety, depression and sleep quality on migraine burden.

Material and methods

Twenty-four patients affected by Chronic Migraine have been selected in our Headache Clinic throughout the 2021-2023 period. All the patients were treated with Anti CGRP antibodies. We collected the following variables: MIDAS, HAD1 (anxiety scale), HAD 2 (Depression scale) Pittsburgh sleep scale at baseline (T0) and after 12 and 24 months follow up (T1 and T2).

T-Tests have been conducted to compare the disability burden (MIDAS) over time (T0 vs T1 and T1 vs T2). A Pearson correlation test has been run to investigate the potential relationship between migraine disability, anxiety, depression and quality of sleep. The sampling distribution was normal.

Results

The average MIDAS score was 168.71 (DS=92.196) at T0, 12.21 (DS= 3.413) at T1 and 7.05 (DS= 2.269) at T2. The t-test comparison between T0-T1 and T2 indicated a significant reduction of burden disability, anxiety and depression over time as well as an improvement in quality of sleep.

Conclusions

Our results seem to indicate an efficacy of the treatment on the disability burden as well as a correlation between migraine disability burden and sleep quality in patients affected by Chronic Migraine after one year of treatment. A correlation trend seems to emerge between disability burden and anxiety and depression scale.



From OnabotulinumtoxinA to Monoclonal Anti-CGRP Antibodies in patients with Chronic Migraine and Medication Overuse Headache

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Chronic migraine, often associated with Medication Overuse Headache (MOH), represents a challenge for headache center neurologists due to its disabling nature and comorbidities. OnabotulinumtoxinA (OnaB-A) was approved for chronic migraine prophylaxis; recently anti-calcitonin gene-related peptide monoclonal antibodies (anti-CGRP mAb) emerged as effective preventive treatment in high-frequency episodic and chronic migraine. Combining anti-CGRP mAb with OnaB-A can be effective when single treatments failed. In clinical practice, OnaB-A administration may present some critical issues: repetition every three-months by trained personnel, dedicated outpatient facilities not equally accessible throughout the Italian territory, subcutaneous injection intolerance and delayed benefits for some patients (10-24 weeks). These issues influence neurologists' treatment decisions, especially for patients with inadequate responses.

A case series review at San Paolo Hospital's Headache Center assessed 46 patients (38 females, 8 males; mean age 50, SD 12) with chronic migraine and MOH treated with OnaB-A. Efficacy, measured by Migraine Disability Assessment Score (MIDAS) improvement and patient/neurologist impressions, categorized patients as non-responders (39.1%), low-responders (23.9%), good-responders (17.4%), and excellent-responders (19.6%). Of OnaB-A-treated patients, 28.3% switched to anti-CGRP mAbs (5 non-responders, 5 low-responders, 3 excellent-responders with subsequent reduced efficacy). Of these 84.6% experienced rapid improvement, one discontinued due to constipation, and one had no benefit. Conversely, two OnaB-A non-responders had previously tried erenumab without success.

Switching to anti-CGRP mAbs in our case series resulted in rapid clinical improvement in most OnaB-A-treated patients, evident in disability reduction (MIDAS score), fewer headache days and decreased analgesic intake. Patients tolerated anti-CGRP mAb therapy better.

These findings suggest a potential treatment sequence for chronic migraine patients, emphasizing the importance of considering anti-CGRP mAbs as a viable alternative, particularly for those with suboptimal responses to OnaB-A.



Characterization of sleep and neuropsychological assessment in subjects with migraine treated with ketogenic diet

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Introduction

Migraine and sleep disorders have a high prevalence in the general population and are often related. Cognitive abilities are also often compromised in migraine patients, in particular attention and memory deficits. Ketogenic diet therapy (KDT) is gaining importance given the relatively low response rate of preventive therapies traditionally used for migraine. It has been hypothesized that KDT works by stabilizing the cell membrane, restoring neuronal excitability, improving cellular metabolism and thus counteracting neuroinflammation. Furthermore, the mood-stabilizing and neuroprotective effect of KDT could impact the neuropsychological profile and sleep quality of migraine patients. Objectives: The study aims to evaluate the effectiveness of ketogenic therapy on migraine and investigate the effects of KDT on quality of life, quality of sleep, micro and macrostructure of sleep and on neuropsychological functions (attention, memory) in subjects with migraine.

Methods

Subjects of both sexes (13-18 years) diagnosed with primary headache were recruited into the study. The initial evaluation of the patient and the expected follow-up at 3 and/or 6 months was carried out through neuropsychiatric and nutritional evaluation with related instrumental tests, subjective and objective sleep evaluation through self-administered questionnaires, execution of nocturnal polysomnogram and actigraphy study; evaluation of attention and executive functions, evaluation of memory and quality of life through standardized tests.

Discussion and results

Six patients (F:4; M:2) aged between 13 and 18 years were recruited in this study. The results showed that dietary therapy was effective in controlling migraine attacks in the majority of patients. Polysomnographic data before and after 3 months of KDT showed a slight increase in total sleep time and sleep efficiency along with a reduction in waking time during the night. Regarding sleep stages, a trend towards a decrease in NREM stage 1 and an increase in REM was observed. From our work it was also possible to outline the neuropsychological profile of pediatric patients with migraine, which was characterized by deficits in visual attention, working memory and sustained attention. Future studies should aim to comprehensively evaluate the effects of KDT on migraine, sleep and executive functions and the influence of possible individual and dietary characteristics, and related biochemical changes.



Efficacy of Mindfulness added to treatment as usual in patients with Chronic Migraine and Medication Overuse Headache: a randomized clinical trial, early results

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Objective

To assess the efficacy of a six-session mindfulness-based treatment added to treatment as usual (TaU) on headache frequency reduction and medication intake.

Materials

177 patients from the third-level headache center IRCCS "C.Besta", with Chronic Migraine and Medication Overuse Headache (CM and MOH) were enrolled in between November 2018 and December 2021. Methods This is a phase-III single blind RCT single-center study. Patients were randomized 1:1 to either TaU or mindfulness added to TaU (TaU+MIND) and followed-up for 12 months. Exclusion criteria were psychiatric comorbidities; pregnancy; secondary headaches; withdrawal from MOH at least twice in the previous two years; previous experience with mindfulness. TaU consisted of withdrawal from overused drugs, patients' education, and prescription of prophylaxis. Patients attending mindfulness sessions were taught to focus their attention on the present and enhance awareness of body sensations, which enabled tackling the pain-pill automatism, and were encouraged to engage in a 7-10 minute/day self-practice. The primary endpoint was the achievement, at 12 months of $\geq 50\%$ headache frequency reduction compared to baseline. Secondary endpoints included medication intake.

Results

Out of the 177 participants (median age 47.9 years [Q1-Q3: 40.1-54.2]; 19 [11.3%] males; median CM duration 14.6 years [Q1-Q3: 4.9-22.2]) 89 were randomized to TaU and 88 to TaU+MIND. Patients in the TaU+MIND group outperformed those in TaU for the primary endpoint, achievement of $\geq 50\%$ headache frequency reduction (78.4% vs 48.3%; $p < 0.0001$). They also showed superiority in some secondary endpoints, namely headache frequency and medication intake.

Discussion

Our results show that the addition of mindfulness-based behavioral approaches to usual treatment options is a suitable option for the most difficult patients among migraineurs.

Conclusion

These findings show that a six-week mindfulness-based treatment as add on to TaU is superior to TaU for the treatment of patient with CM and MOH.



Efficacy and tolerability of rimegepant and lasmiditan in the acute treatment of migraine: a real-life study

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Objective

To assess the efficacy and tolerability of two newly developed drugs, rimegepant and lasmiditan, for the acute treatment of migraine attacks.

Methods

We prescribed lasmiditan 50mg and 100 mg or rimegepant 75 mg to those migraineurs for whom triptans were contraindicated or ineffective, instructing them to treat two migraine attacks. Patients were asked to complete a diary to record headaches and other symptoms such as photophobia, phonophobia, osmophobia, nausea or vomit, any rescue medication taken, and any adverse events that occurred during each attack. Our primary endpoints were pain freedom and freedom from other symptoms at two hours, along with the persistence of pain freedom at 24 hours. Our secondary endpoints included pain relief at two hours, the efficacy of lasmiditan and rimegepant in triptans non-responders, and the presence of adverse events after the dose.

Results

Twenty patients met the inclusion criteria (M:7, F:13). None of these patients were included due to a contraindication to triptans. 12 patients were treated with lasmiditan (24 attacks), and 8 with rimegepant (16 attacks). In the lasmiditan group, freedom from pain within two hours was achieved in 50% of migraine attacks (12/24 attacks), with a persistence of pain freedom at 24 hours observed in 94% of attacks (17/18 attacks). Regarding the most bothersome symptoms, freedom from photophobia within two hours was observed in 64% of attacks (7/11 attacks), while freedom from nausea in 70% of attacks (7/10 attacks). In rimegepant group, two-hour pain freedom was achieved in 37,5% of attacks (6/16 attacks), with a persistence of pain freedom at 24 hours noted in 100% of attacks. Two-hour freedom from photophobia, the most related symptom, was attained in 56% of attacks (5/9 attacks). For what concerns tolerability, dizziness was reported in 25% of the attacks treated with lasmiditan. In contrast, in the rimegepant group, only one patient reported side effects (mental fog).

Conclusions

This analysis, conducted in a real-life context, confirms that rimegepant and lasmiditan represent two viable therapeutic options for patients in whom triptans are not recommended or prove ineffective. Besides, rimegepant seems to be better tolerated than lasmiditan.



POSTER

Venerdì 29 Novembre 2024

13.00-14.00 SESSIONE POSTER B

Moderatori: M. Bandettini di Poggio, E. Malara

Psychological adaptation to migraine as prerequisite for tailored care: an observational study in young patients

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Background

Lifestyle, psychosocial factors and perceived stress play a crucial role in the development and progression of migraine. Aim: The aim of this study was to evaluate whether emotions regulation skills can influence migraine-related disability.

Methods

We performed a prospective observational study in 51 patients aged 18 to 55 years (F=42, M=9; mean age $\pm$ SD 33.8S $\pm$ 10.91) with episodic migraine, enrolled in the S. Salvatore Hospital L'Aquila Headache Center. Participants were investigated through a clinical and psychological battery including the Headache Impact Test (HIT-6) questionnaire, the Migraine Disability Assessment (MIDAS) questionnaire, the Depression Anxiety Stress Scales Short Version (DASS-21), the Nepean Dysphoria Scale (NDS-I), the Difficulties in Emotion Regulation Scale (DERS-18) and the Pain Self-Efficacy Questionnaire (PSEQ). Participants were divided into two groups based on disease duration (median value: 36 months): a short disease duration (SDD) group (disease duration<36 months; n=25) and a long disease duration (LDD) group (disease duration>36 months; n=27).

Results

One-Way ANOVA showed a significant difference between groups with respect to NDS and DERS-18 scores: the SDD group showed a greater emotional distress as compared to LDD group. The Pearson's test showed a positive correlation between HIT-6 and (NDS) irritability ($r=0.425$; $p=0.002$), interpersonal resentment ($r=0.337$; $p=0.016$), surrender feelings ($r=0.292$; $p=0.038$) and (DASS-21) depression ($r=0.441$; $p=0.001$) and stress ($r=0.441$; $p=0.001$). A negative correlation was found between HIT-6 and pain self-efficacy (PSEQ) ($r=-0.727$; $p<0.001$) scores.

Conclusion

Individual adaptation to migraine through emotions regulation skills may influence the quality of life of patients and their disability. Patients with a shorter disease duration could benefit from an emotional training to encourage adaptability.



A jump in the past: a new complex neuropsychological symptom of migraine with aura?

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Background

Migraine is often associated to complex cognitive symptoms. Although episodes of temporal misperception have been reported in complex conditions associated to migraine, isolated episodes of temporal misperception during a headache attack were never reported.

Case report

A 23-year-old lady, diagnosed with migraine with aura. Her auras usually last 3-6 hours (prolonged auras), frequently with visual, somatosensory and aphasic disturbances. These auras occurred during menstruation which stopped in such situations. The genetic workup for hemiplegic forms was negative. EEG and brain MRI were irrelevant. A TMS-EEG investigation of V1 and V2/V3 between attacks showed high amplitude response within the occipital natural frequency. It has never been possible to perform TMS-EEG during an aura. In January 2020, she experienced a derealization episode characterized by a wrong temporal perception of herself, in a sort of temporal displacement in which she was persuaded to live her 7 years prior life. At about 1 am, she woke up from sleeping with a throbbing headache. She took triptan and went back to bed. One hour later, her mother heard she was calling her for the increasing pain. The patient appeared slightly emotional but not confuse. She recognized the mother but she felt her house unfamiliar. She asked her mother where her father (who died in 2013) was. In the ER (4 am) vitals and body temperature were in the range. She was convinced she was 16 years old, still attending high school, and reported other personal details coherent with the life of that time. The context she was reporting was coherent with that period of her life. During the morning, after a brief sleep, all symptoms vanished and the cognitive and psychological condition was completely restored. In the following years she complained of other prolonged auras but no other temporal disperceptions happened.

Discussion and conclusions

In our knowledge, this is the first report of an episode of an isolated temporal misperception associated with migraine with aura. The duration of psychiatric symptoms seems to be excessive for seizure and EEG was normal. Considering prolonged aura recurrence during the menstrual period, a possible hormonal effect on cortical excitability, able to induce in one case the temporal disturbance, may be hypothesized.



Familiar persistent aura without infarction (PAWOI)

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Background

Persistent aura without infarction (PAWOI) is included in the international classification of headache at the 1.2.4 paragraph. It is a rare condition that may appear in patients with migraine with aura. When it happens, typical aura symptoms, started in the usual way for that subject, go on for more than one week and they may last for months or years. The diagnosis requires that brain MRI does not show any lesion

Case report

A 40-year-old man diagnosed with migraine with aura had been complaining for a long time of a small visual aura in his right visual field that interferes in particular with reading. He describes the disperception as a round shaped scotoma of few millimeters that is perceived especially in the close-up vision and less relevantly from afar. The image is perceived also with closed eyes. The visual problem started 15 months before with a typical progressively enlarging scotoma, but never resolved even after an initial progressive dimensional reduction as usual for the patient. A 3T MRI did not show any lesion confirming the diagnosis of PAWOI. The element of novelty is the neurological history of his mother: in the past she complained of a persistent visual aura that she describes as an hemianopsia, that persisted for about two years. Also in her case, neurological investigations and brain imaging were normal. Two years later, her hemianopia suddenly disappeared. After resolution of the campimetric disturbance, she experienced other migraine attacks with typical aura but she never had other prolonged visual disturbances.

Discussion and conclusion

To our knowledge, this is the first case of a “familial” form of persistent aura without infarction. A biological pathway of these phenomena is under investigation and a possible focal alteration of the cortical excitability and/or of the cerebral perfusion have to be carefully investigated. An energetic local neuronal deficit may be hypothesized to explain a so prolonged but potentially reversible disorder.



Headache in Outpatient Neurology Clinics: A snapshot from Liguria

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Background

Headaches are mostly managed in primary care settings and outpatient neurology clinics, with only a minority of patients being treated at specialized Headache Centers. We aimed to assess the impact and clinical characteristics of headache disorders in patients at outpatient neurology clinics in Liguria, Italy.

Methods

In October 2023, a survey was administered to 18 neurologists working in the outpatient neurology clinics in Liguria, part of the National Health System. We initially examined the diagnostic queries for all the consecutive patients to determine the percentage of visits for headache disorders. Headache patients completed a form covering demographic details, medical history, and disease management, including referring physician, prior assessments, emergency room admissions, and use of medications along with their prescribers. Finally, a self-reported questionnaire, based on ICHD-III and HIT-6, characterized headache types and assessed their impact on the quality of life.

Results

Thirteen of 18 neurologists took part in the survey. During the observation, 130 out of 1197 patients (10.8%) were diagnosed with headache disorders. Among the 88 headache patients who completed forms and questionnaires, 78.4% were women; the mean age was 47.9 yrs, and the mean disease duration was 12.1 yrs. Patients were mainly (71.6%) referred by general practitioners. Around a third of the patients (31.8%) saw non-neurology specialists, 17% visited the Emergency Room in the past year, and 64.8% consulted neurologists, including Headache specialists (18.2%). Despite 58.7% of patients reported severe impact on social functioning, the first neurological visit occurred after an average of 6.1 yrs from onset. Migraine prevalence was 56.8%, tension-type headache (TTH) was 22.7%, and 13.6% reported both. Other types of headache accounted for 6.8% of cases. Patients with no treatment were 11.3%, while patients with medication overuse were 17.5%. A significant share of medications (18.6%) was self-prescribed; merely 22% of migraine patients used triptans, and 20.8% had no preventive treatment.

Conclusions

Our findings highlight the persistent need to enhance clinico-diagnostic pathways for headache disorders. Importantly, the role of outpatient neurology clinics emerges as crucial for effective management of headache patients.



A Case of glossopharyngeal Neuralgia Successfully Treated with Amitriptyline and Gabapentin

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Glossopharyngeal neuralgia (GPN) is a rare condition characterized by a brief, intense, unilateral pain with abrupt onset and cessation in regions supplied by the glossopharyngeal nerve. GPN is a very rare condition, accounting for about 1% of all types of cranial neuralgias, with an incidence rate of 0.7/100000 population. There are idiopathic and secondary forms which include demyelinating and autoimmune diseases, tumors, infections and vascular compressions. GPN treatment can be pharmacological or surgical. Common analgesics are not effective, and anticonvulsants are used as first-choice drugs. Nowadays, there are no clear treatment guidelines and GPN diagnosis is challenging. A 64-year-old Italian woman was bothered by a burning sensation during swallowing. Her family doctor decided to start steroid therapy (betamethasone 4 mg/die), without any improvement. She was evaluated by an Otolaryngologist who found a small phlogistic lesion of the left glossopharyngeal fold and recommended antibiotic therapy. In the following days, the patient complained of pain at the base of the tongue, extended to left ear and hypophonia. This pain was described as a short-lasting "electric" sensation of high intensity. Because of the persistence of these episodes, she underwent another otolaryngology evaluation revealing reflex otalgia and odynophagia. In the meantime, the general practitioner recommended her to start carbamazepine (200 mg x 2), with slight benefit. With a suspicion of GPN, she was referred to the Neurology Department. During the hospital stay, she underwent brain MRI with contrast showing left posterior inferior cerebellar artery contiguity with homolateral glossopharyngeal nerve without sure impingement. She was first treated with carbamazepine (400 mg x 2) associated with gabapentin (100 mg x 3). Despite an initial pain improvement, carbamazepine was stopped due to thrombocytopenia. Thus, gabapentin dosage was increased to 300 mg x 3 and it was associated with amitriptyline (25 mg/day) with pain and other symptoms amelioration. Craniofacial pain differential diagnosis and management can prove to be challenging. There is no consensus on the optimal treatment strategy, since current therapies can provoke significant side effects, requiring to switch agents and polytherapy in nonresponsive patients. In conclusion, we report a case of idiopathic GPN that was successfully treated with gabapentin and amitriptyline.



How catastrophizing attitude impacts quality of life in patients with chronic migraine treated with monoclonal anti-CGRP antibodies: a single center real-life experience

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Objectives

Catastrophic thinking plays a vital role in the chronification of pain. Our goal is to assess how pain catastrophizing, evaluated using the Italian version of the Pain Catastrophizing Scale (PCS), impacts the quality of life and contributes to disability in a group of difficult-to-treat individuals. We aim to determine if catastrophizing is a modifiable variable through targeted psychological interview and to assess whether pain catastrophizing, particularly its subdimension related to rumination, affects the response to treatment with subcutaneous monoclonal anti-CGRP antibodies.

Methods

We collected clinical data from 26 consecutive patients attending our headache clinic since July 2021. The patients, diagnosed with chronic migraine with or without MOH according to ICDH-3 criteria, were randomly assigned to receive Galcanezumab, Erenumab, or Fremanezumab treatments. Simultaneously, the patients underwent targeted psychological interview. Evaluations were conducted before treatment initiation (T0), and then after three (T1) and six months (T2). Alongside clinical data and PCS score, we also collected the HIT-6 and the MIDAS scores at each evaluation as outcome measures. Comorbid depression was assessed using the BDI II "Beck Depression Inventory II" scale. Appropriate parametric statistical tests were used based on the data type and sample size.

Results

To date, 26 patients have been included, with 17 completing the T2 assessments. The migraine impact was substantial (HIT-6 ≥ 56) in 95% of the sample. Except for two patients (MIDAS 12), disability was severe across the sample. Initially, 47.6% of patients exhibited a clinically significant level of catastrophizing (PCS ≥ 30). A statistically significant reduction in PCS scores was observed after six months of therapy ($p < 0.001$). PCS showed a mild correlation with HIT-6 (r_s 0.73) but no correlation with BDI-II.

Conclusions

In our cohort catastrophizing thinking was notably present. The combination of monoclonal antibody therapy and psychological intervention focusing on catastrophizing tendencies led to a statistically significant decrease in PCS scores and reduced the impact of migraine on quality of life.



Real-world effectiveness of Anti-CGRP Monoclonal antibodies compared to OnabotulinumtoxinA in Chronic Migraine prevention treatment: the RAMO study

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Objectives

Chronic migraine (CM) is a disabling condition with huge impact on the quality of life.

OnabotulinumtoxinA (BoNT-A) is an effective treatment for CM. Recently, monoclonal antibodies (mAbs) against calcitonin gene related peptide (anti-CGRP) pathways have been approved to. Aim of this study is to compare the effectiveness and safety of anti-CGRP mAbs and BoNT-A after 6 and 12 months of treatment.

Methods

We performed an observational, retrospective, multicenter study in Italy to compare the real-world effectiveness of anti-CGRP mAbs and BoNT-A. Patients with CM having received either treatment according to Italian prescribing regulations were extracted from available clinical databases. Efficacy outcomes included the change from baseline in monthly headache days (MHD), Migraine disability assessment test (MIDAS), and migraine acute medications (MAM) evaluated at 6 and 12 months of follow-up. The primary outcome was MHD change from baseline at 12 months. Safety outcome included serious adverse events (SAE) and treatment discontinuation. Adjusted and unadjusted models were used for the analysis.

Results

216 potentially eligible patients were screened and 183 (86 anti-CGRP mAbs; 97 BoNT-A) were included. 69 patients receiving anti-CGRP mAbs and 85 receiving BoNT-A had a follow-up time up to 12 months. Anti-CGRP mAbs resulted in a significant reduction in MHD compared to BoNT-A at 12 months of follow-up (unadjusted mean difference -4.4 days; 95%CI from -6.8 to -2.0; $p=0.0002$). After adjusting for baseline confounders, marginal mean difference resulted -6.2 days (95%CI from -8.4 to -4.0; $p<0.001$). Similar results were observed at 6 months. Anti-CGRP mAbs showed a significant MIDAS (-31.7 and -19.2 points, $p=0.0001$ and $p=0.269$, respectively) and MAM reduction (-5.1 and -3.1 administrations, $p=0.0023$ and $p=0.0574$, respectively) compared to BoNT-A at 6 and 12 months. No SAE were reported. One patient receiving fremanezumab discontinued treatment due to arthralgia. Treatment discontinuations, mainly for inefficacy, were comparable between the two treatments.

Conclusions

Our results show greater efficacy of mAbs compared with BoNT-A at 6-12-months follow-up. The inefficacy leading to treatment discontinuation was similar. From these data, the sustainability of the two treatments appears adequate, with great efficacy of mAbs treatment.



Intracranial hypotension as a trigger for reversible cerebral vasoconstriction syndrome: a case report and narrative literature review

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Background

Cerebrospinal fluid (CSF) hypotension syndrome is the expression of low CSF pressure, and its prognosis is mainly benign. Reversible cerebral vasoconstriction syndrome (RCVS) is a neurological disorder due to intracranial reversible vasospasm. The association between CSF and RCVS is poorly investigated.

Methods

We describe the case of a 40-year-old woman who developed postural headache following an epidural analgesia. She was initially diagnosed with post-dural puncture headache and a brain CT scan revealed subdural collections compatible with CSF hypotension. She performed an epidural blood patch for headache persistence. Following the procedure, she experienced headache changes, with severe frontal attacks resembling thunderclap headache. Elevated blood pressure was also noted. Brain MRI and MRI angiography confirmed CSF hypotension and revealed multifocal cerebral vasoconstriction consistent with RCVS. Treatment with nimodipine successfully controlled her symptoms, and follow-up imaging demonstrated complete resolution of vasospasm. A narrative review of all the cases of CSF hypotension associated with RCVS was performed.

Results

This case and the literature review of other similar cases suggest a potential association between CSF hypotension and RCVS, supported by clinical and radiological evidence. While the precise pathophysiology of RCVS-CSF hypotension remains unclear, vascular and mechanical factors may be involved.

Conclusions

CSF hypotension can trigger RCVS, and conversely, RCVS can complicate CSF hypotension. RCVS evaluation is necessary when specific red flags occur in the context of CSF hypotension syndrome. Further research is warranted to elucidate the mechanisms connecting these two conditions.

Intracranial hypotension as a trigger for reversible cerebral vasoconstriction syndrome: a case report and narrative literature review



Daridorexant in Cluster Headache: preliminary data

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Background

Cluster headache (CH) is the most common form of TACs. Pain is strictly unilateral and it is associated with ipsilateral autonomic symptoms, has a circadian and circannual presentation^{1,2}, and neuroendocrine hormonal alterations, supporting the involvement of the hypothalamus in the pathogenesis of CH. Pre-clinical studies have shown that neuropeptides such as orexins, somatostatin, GABA, and 5-HT receptors in the paraventricular region of the hypothalamus can modulate nociceptive neurotransmission. Orexins are involved both in nociceptive neurotransmission, and in alteration of sleep-wake rhythm and insomnia³⁻⁶. Daridorexant is a dual receptor antagonist of the orexin, approved for the treatment of chronic insomnia, with a very favorable efficacy and safety profile⁷. There is a lack of data about pathophysiological correlates between CH, trigemino-autonomical symptoms, sleep regulation, hypothalamus and orexin involvement, and nociception. We present a pilot study treating CH patients with Daridorexant to improve quality of sleep to control cluster attacks.

Materials and methods

Daridorexant 50 mg daily was prescribed to eight Chronic and Episodic CH patients afferent to our Headache Center. All patients were in the active period, had nocturnal attacks, were non-responders to traditional preventive and transitional treatments, and had a very poor quality of sleep. Enrollment and 3-6 months follow-up visits: history, clinical indicators, neurological examination, and questionnaires as follow: headache diary (headache frequency, total number of crisis, number of hours, days of CH, nocturnal attacks, MPI), HIT-6, HAM-A/D, MIDAS, Epworth scale for somnolence, Sleep Quality Scale, and subjective evaluation.

Results

N=8 pts (4 female, 4 male), 2 episodic, 6 chronic CH, took Daridorexant for a minimum of 2 months. 6 pts (75.0%) improved all the history and clinical indicators listed above, from 50 to 100%, except in both the HAM, and the Epworth scales, with lower to none improvement. N=2 patient (25.0%) reported slight diurnal somnolence, which did not lead to drug discontinuation.

Discussion and conclusion

Although more information is needed to fully understand the specific role of each hypothalamic nucleus involved in CH, the role of orexin and neurohormones, is becoming more central⁶. Our study suggests the tolerability and the efficacy of daridorexant as an add-on treatment in patients suffering from refractory cluster headache. Indeed, the use of daridorexant in these CH patients is not considerable off-label, due to the co-presence of chronic insomnia that is often related to the CH nocturnal attacks.

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⁷CNS Drugs (2023) 37:267–274 <https://doi.org/10.1007/s40263-023-00987-9> ADIS DRUG Q&A Daridorexant in Insomnia Disorder: A Profile of Its Use. Tina Nie1 · Hannah A. Blair1



Who is the patient accessing to third level headache centre in Campania region: a multicentre survey

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Introduction

Primary headaches such as tension type headache and migraine are prevalent disorders with migraine representing the second most disabling¹. Headache presentation may vary from an episodic and mild form to highly disabling disorders such as cluster headache and chronic migraine. For this reason, a stratified system of care is usually adopted worldwide. In Campania Region a three level organisation has been planned in accordance with the model of European Headache Federation². A primary level would be managed by general practitioners (GPs) that should recognize the most frequent primary headache; a secondary level, directed by territorial neurologists should meet the needs of the great majority of headache patients; finally, a third level is led by Headache Centres in which neurologists provide care to patients with difficult to diagnose or treat headaches.

Methods

We conducted a multicenter study in 4 headache centres in Campania Region (Italy) with different catchment areas. Each centre collected over the period of one month a questionnaire filled out by patients attending the headache clinic as their first visit. The questionnaire was based on 10 simple questions exploring different items: indications to the current visit; timing and booking methods; distance to headache centre; previous consultations for headache; previous diagnoses and treatments; expectation from the visit.

Results

The survey was administered to 108 patients (75% female) with a mean age of 45,1 (SD +/-15,1). The majority of patients report that his GP recommended the visit for headache (50.9%), however, it remains a personal choice for the 24% of the patients. The mean waiting time before the first visit is 127.2 days (SD +/-75.3) with only 30.6% of patients acceding to headache centre within 60 days from booking. Patients living within 20 km from the headache centre are 56.5%, while 6.5% of patients have to journey for more than 50 km. The majority of patients (37.9%) consulted another neurologist before; surprisingly the 33.3% of patients affirm they have never consulted any doctor before and the 24.1% consulted exclusively GPs. Regarding headache treatment history, 87.0% of patients take only NSAIDs as acute medication while only 12.0% refer to use triptans; 72.2% of patients declare they have never used prophylactic drugs for headache, against 18.5% that have already taken (with only 5.5% with 3 or more different drugs). If the patient is asked about his/her main expectation from the visit, the answers were mostly "receive therapy" in 45.4% of cases and "understand the cause of the headache" in 30.5% of cases.

Conclusion

Our data remark that more than half of the patients referring to a headache centre (third level) did not perform a neurologic consultation for their headache before and a first line preventative therapy for headache was performed in only 18,5%. It is crucial to improve knowledge about headache among medical class, enforcing the possibility for patients to be diagnosed and treated at primary and secondary levels, reducing unnecessary demand upon third level centres that could represent the point of care for patients who have already received a diagnosis and need advanced stage therapies.

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The Second Exteroceptive Suppression Period of the Temporalis Muscle in migraine patients with allodynia differs from controls

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The study of the second exteroceptive suppression period (ES2) of the masseter or temporalis muscle could provide information as to the neural circuits involved in migraine pathophysiology. Indeed, the interneurons responsible for ES2 are close to the trigeminal nucleus caudalis and receive afferents from the anti-nociceptive system. Allodynia is known to be related to the sensitization of second and third order neurons in the trigeminal nucleus caudalis and sensory thalamus, respectively.

This observational, retrospective study is aimed at investigating the ES2 of the temporalis muscle in female migraineurs, with and without allodynia, in the interictal period, compared to controls.

Thirty female patients, fulfilling the diagnostic criteria for migraine (13 with aura, 17 without aura, 20 episodic/10 chronic), naive from any pharmacological prophylactic treatment, without relevant psychiatric comorbidities and 20 healthy controls were enrolled.

The exteroceptive suppression of the temporalis muscle activity was registered, according to the standards recommended by the European Headache Federation, in the interictal period (at least 72 hours after the last migraine attack).

Twenty-two migraineurs had allodynia, which was assessed by the Allodynia Symptom Checklist. Their average migraine day frequency was 17 per month.

The ES2 latency and duration between the groups were compared by Student's t-test. There were no differences in the ES2 latency or its duration between the migraine patients or controls, allodynic versus non-allodynic migraineurs. Conversely, the ES2 latency was statistically significantly shorter in allodynic migraineurs than in controls ($p=0.07$).

This study suggests that the reduced latency of ES2 observed in allodynic migraineurs, compared to controls, may reflect an impaired activity of brainstem circuits (second-order neurons in the trigeminal cervical complex and/or inhibitory control from superior antinociceptive systems). Indeed, we suppose that this alteration in ES2 may be a neurophysiological correlate of central sensitization in migraine patients with allodynia.

Further studies are required to confirm these preliminary findings on larger patient samples and such an intriguing hypothesis.



A case of migraine with atypical aura in a patient with pineal gland cyst

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Pineal cysts are a common incidental finding, with a prevalence of 10-54% in the general population¹. These are benign lesions that in rare cases can become symptomatic, mainly causing obstructive hydrocephalus and Parinaud's syndrome. Only a few cases of migraine with aura in patients with midline lesions have been reported in the literature². We present the case of a 22-year-old boy, with specific learning disorder and a family history of migraine, who has suffered from pulsating unilateral headache attacks, with photophobia and nausea, since the age of 10 years. Since 2018 (16 years), migraine attacks with atypical aura appear: the patient has phosphenes always in the right eye, which persist throughout the duration of the crisis. After about 30 minutes, a pulsating right periorbital headache of progressively increasing intensity and refractory to symptomatics also develops, accompanied by mental confusion, disorientation, dysphasia, nausea, projectile vomiting, bilateral visual blurring, auricular fullness, and, in the last attack, paresthesias and hyposthenia in the hands alternately on the right and left. The whole attack lasts 10-12 hours. Between 2018 and 2023, he presented a total of 4 such attacks that always resulted in hospitalization. Brain MRI showed the presence of 12 x 18 mm pineal cyst associated with stenosis of the aqueduct and progressive enlargement of the ventricular system. In October 2023, the patient then underwent endoscopic marsupialization and third ventricle cystostomy surgery under navigation. Intermittent occlusion of Silvio's aqueduct was evident during surgery. Two months after surgery, there were no more episodes of migraine with aura. The mechanism by which a pineal cyst can trigger a migraine aura is not known, but it is conceivable that hydrocephalus results in a compressive effect on subcortical structures such as the thalamus, which can generate spreading depression in animal models².

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When a migraine with an aphasic aura is not only an headache...

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Background

Reversible cerebral vasoconstriction syndrome (RCVS) is a relatively rare disorder characterized by reversible intracerebral vascular spasms and recurrent severe headaches with or without neurologic signs and symptoms. Neuroimaging shows constriction of the Willis'circle arteries. It could be associated to other conditions as postpartum status, exposure to vasoactive substances or immunosuppressants, catecholamine secreting tumors. When it is found to be idiopathic and occurs without any predisposing condition, it is classified as Call–Fleming syndrome (migrainous vasospasm and benign angiopathy of the central nervous system). Misdiagnosis as primary cerebral vasculitis or aneurysmal subarachnoid hemorrhage is common for the overlapping clinical and angiographic features. Therapeutic management is by calcium channel blockers, short course of high-dose glucocorticoid and magnesium sulfate. Due to spontaneous resolution, the prognosis is good.

Clinical case

A 22-year-old female with an history of migraine with visual aura and atrial fibrillation treated by DOACs and antiarrhythmic drugs came to our attention for three episodes (one in 2020 and two in 2023) of aphasia and paresthesia followed by headache. In 2020 a first brain and Angio-MRI was negative. In 2023 she repeated a brain MRI revealing hyperintensity in periventricular and subcortical temporo-parietal area, with restricted diffusion and contrast enhancement on FLAIR sequence and wall contrast enhancement of some insular cortical vessels. Neurological examination was normal, and no episodes occurred during hospitalization. She denied systemic symptoms comprehending oral or genital canker sores, infections or pain. Complete autoimmune and infective profile results were unremarkable. The follow up brain MRI was taken 6 week later and showed complete resolution of the above-mentioned findings. The diagnosis of probable Call-Fleming syndrome was proposed, and calcium channel blocker therapy was introduced.

Conclusions

RCVS is a rare cause of severe headache that can mimic other causes of sudden, severe headache associated to neurological symptoms. The neurologist and neuroradiologist should be aware of these clinical and imaging findings for an appropriate and rapid differential diagnosis.



Use of Galcanezumab for migraine prevention in a patient on concomitant nivolumab for melanoma skin cancer: a case report

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Objectives

Monoclonal antibodies (mAbs) targeting the calcitonin-gene related peptide (CGRP) are currently used for migraine prevention. To date, real-life experience of concomitant use of anti-CGRP mAbs and other mAbs with a different therapeutic indication in multimorbid patients is lacking. Materials. We describe the case of a 56-year-old female migraine patient treated with galcanezumab, a mAb blocking the CGRP, on concomitant treatment with nivolumab, a mAb targeting the anti-programmed death-1 (PD-1), because of melanoma skin cancer.

Clinical case

The patient came to our Headache Center in July 2021 because of a chronic migraine resistant to oral preventives; she had a history of melanoma skin cancer surgically treated in 2016. At that time, galcanezumab was initiated. The patient had 30 monthly migraine days of severe intensity with daily assumption of analgesics before treatment with galcanezumab. After three months of treatment, a mean of 10 monthly migraine days of mild intensity was reported with a reduced related disability. After six months, the same result was observed. In February 2022, after the surgical removal of a locally recurrent melanoma, treatment with nivolumab was introduced. Galcanezumab was continued. The clinical benefit of galcanezumab continued after introduction of nivolumab. No adverse events were reported.

Discussion

Galcanezumab was effective and safe even when combined with nivolumab. Recently, an Italian multicenter observational study evaluated 6-month effectiveness and tolerability of anti-CGRP mAbs when combined with other mAbs for different diseases in 26 patients: preliminary findings confirmed the efficacy and safety of anti-CGRP mAbs even when used in combination with other mAbs.¹ However, patients on nivolumab were not included in the study. To the best of our knowledge, this is the first case of concomitant use of galcanezumab and nivolumab

Conclusion

Galcanezumab proved to be effective and safe even when used in a patient with concomitant nivolumab. A wider real-life experience of use of anti-CGRP mAbs in multimorbid patients on concomitant treatment with other mAbs should be provided in order to be confident in treating these patients.

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