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MEETING ABSTRACTS Open Access

12th European Headache Federation Congress jointly with 32nd National Congress of the Italian Society for the Study of Headaches

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EHF Invited Speakers

S1

KATP channels

Mohammad Al-Mahdi Al-Karagholi (mahdi.alkaragholi@gmail.com)
Danish Headache Center, Department of Neurology, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark
The Journal of Headache and Pain 2018, **19(Suppl 1):**S1

This abstract was not included as it has been previously published [1].

Reference

[1] Al-Karagholi MAM, Hansen JM, Severinsen J, Jansen-Olesen I, Ashina M. The KATP channel in migraine pathophysiology: a novel therapeutic target for migraine. J Headache Pain. 2017; 18(1):90. doi: 10.1186/s10194-017-0800-8.

S2

The secondary headaches: a *cul de sac* for the headache expert ?

Christian Lampl (Christian.Lampl@ordensklinikum.at)
Headache Medical Center, Seilerstätte, Ordensklinikum Linz Barmherzige Schwestern, Austria
The Journal of Headache and Pain 2018, **19(Suppl 1):**S2

Background

According to the new ICHD 3 diagnostic criteria a de novo headache occurring with another disorder recognized to be capable of causing it is always diagnosed as secondary. For example, when a new headache occurs for the first time in close temporal relation to trauma or injury to the head and/or neck, it is coded as a *"secondary headache attributed to the trauma or injury"*. However, it may be possible, that this headache phenomenologically appears to be a primary headache. But, when a pre-existing headache with the characteristics of a primary headache disorder becomes chronic or is made significantly worse in close temporal relation to such trauma or injury, both the initial (primary) headache diagnosis and a diagnosis of *"Headache attributed to trauma or injury to the head and/or neck (or one of its types or subtypes)"* should be given. In other words, since headache is very prevalent, it can occur simultaneously with another disorder with and without a causal relation. Primary or secondary headache or both – clinically/scientifically spoken a dead end? These entities are a challenging diagnostic problem as can be primary or secondary and the etiologies for secondary cases differ depending on the headache type. Secondary headache can be definitely diagnosed only when solid evidence exists from published scientific studies that the disorder is capable of causing headache. Scientific evidence can come from large clinical studies observing close temporal relationships between the disorder and headache outcomes after treatment of the disorder, or from smaller studies using advanced scanning methods, blood tests or other paraclinical tests.

Conclusion

As all secondary headache disorders can be associated with a wide range of underlying etiologies such as infection, anatomical abnormalities, trauma, and immunological disease or sleep disorders, it is possible that these underlying pathophysiological processes generate long-standing activation of nociceptive mechanisms involved in headache. These can lead to chronification and refractoriness of the headache symptomatology.

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1. Headache Classification Committee of the International Headache Society (IHS) (2018) The international classification of headache disorders, 3rd edition. Cephalalgia 38:1–211

S3

Hormonal contraceptives: how they impact on migraine course

Simona Sacco (simona.sacco@univaq.it)
Department of Applied Clinical Sciences and Biotechnology, Section of Neurology, University of L'Aquila, L'Aquila, Italy
The Journal of Headache and Pain 2018, **19(Suppl 1):**S3

The role of female hormones in the pathogenesis of migraine is well-recognized [1,2]. Migraine is more prevalent in women than in men, it usually starts after puberty and in many women improves during pregnancy and after the menopause [1,3,4]. The menstrual phase of the female cycle represents a trigger for migraine attacks in many women [1,4]. Additionally, exogenous hormones may change the course of migraine by inducing de novo migraine, inducing de novo aura, worsening previous migraine but also improving migraine particularly those attacks related to menstruation [5,6]. Several attempts were made to manipulate the female hormonal cycle to try to improve migraine. A working group including headache experts, gynaecologists, stroke experts, and epidemiologists developed a first consensus document about the safety of hormonal contraceptives in female migraineurs of reproductive age [7]. Currently, no formal guidelines specifically address hormonal treatment of migraine. A further consensus document was developed by representatives of the European Headache Federation and the European Society of Hormonal Contraceptives and Reproductive Health. The aim of this consensus document is to provide recommendations on the management of migraine with the use of estrogens and progestogens in women of reproductive age. We systematically reviewed data about the effect of exogenous estrogens and progestogens on the course of migraine during reproductive age. Thereafter a consensus procedure among international experts was undertaken to develop statements

sensitive and specific biomarker, methyl-malonic acid (MMA) status in a group of migraine patients compared to healthy controls.

Methods

Seventy migraine patients (34 chronic and 36 episodic migraineurs) and 70 sex- age matched control subjects were enrolled in this case control study from April to September 2017. Patients were diagnosed based on an expert headache specialist-neurologist examination according to the International Headache Society criteria (ICHD-IIIβ). Migraine characteristics include the number of headache attacks, severity of headaches (from 0 to 10), and duration of each attack in hours were recorded based on a 30-day headache diary. The serum vitamin B12 and MMA levels were measured with ELISA and using commercially available test kits. The study protocol was approved by the ethics committee of the Tehran University of Medical Sciences (ethics board approval code= IR.TUMS.IKHC.REC.1396.2468).

Results

The serum levels of B12 were found to be significantly lower in migraine patients than in control subjects(584.08± 300.20 vs. 750± 350.91pg/ml;P=0.007); whereas migraineurs had higher levels of MMA than control participants(2.171± 1.90 vs. 2.07± 2.05μg/dL;P=0.02). In the fully adjusted regression models, those in the highest vs. the lowest serum B12 quartile had 80% decrease in the odds of having migraine(OR= 0.20, 95% CI= 0.05-0.73;P for trend= 0.008)]; while, patients in the highest quartile of MMA had more than 5 times increased risk of developing migraine(OR= 5.44, 95%CI= 1.49-19.87;P for trend= 0.002). There was no association between serum B12 levels and headache characteristics.

Conclusion

Taken together, these results suggest that increasing level of serum B12 was accompanied by roughly 80% decrease in the odds of developing migraine. In addition, it was shown that participants with higher MMA levels, that considered as lower functional activity of B12, had about 4-to-5 fold higher odds of having migraine.

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

L. Balzano[1], B. Ciccone[2]

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

Correspondence: L. Balzano (neurogino@yahoo.it)

The Journal of Headache and Pain 2018, **19(Suppl 1):**P175

INTRODUCTION

Open-label efficacy study in prophylaxis therapy using Magnesium 225mg, L-Tryptophan 150mg, Boswellia Serrata Casperome® 100mg, Niacin 16mg, Riboflavin 1.4mg, Vitamin D 10mcg (Normorelax® = NRX) to Amitriptyline (AM) in patients with CTE and ESA (1-2-3). Outcomes of th study are: pain modulation (NRS scale), monthly attacks number and monthly analgesic-triptans consumption.

MATERIALS AND METHODS

200 patients with CTE and ESA using ICHD-II were selected: 100 CTE and 100 ESA.

50 CTE assuming NRX (two tablets per day) compared to 50 assuming AM (20 mg evening). 50 ESA assuming NRX, compared to 50 assuming AM. Results were evaluated at T1 (60 days) and T2 (120 days).

The longitudinal variatons of the three outcomes were analyzed through the GEE (Generalized Estimating Equations) modeling in order to check the correlation induced by the repeated measures. In all the Group factor , the time induced by the repeated measures. In all the models the Group factor, the time factor (as a categorical variable) and their interaction were included as predictors.

RESULTS

Both groups show statistically significant changes from T0 to T2 for all the outcomes considered. In CTE patients of NRX and AM group results are, respectively : (Table 1 and Fig. 1)

NRS reduces by 2.4 (p <0.001) and by 3.5 (p <0.001) points, attacks number reduces from 9.5 to 5.7 (p <0.001) and from 9.6 at 4.7 (p <0.001); analgesics frequency is reduced by an average of 3.1 (p <0.001) and 4.9 (p <0.001). Patients percentage showing a reduction in attacks frequency ≥ 50% from baseline is 24% in NRX and 40% in AM group.

In ESA patients in NRX and AM group, results are, respectively: (Table 2 and Fig. 2)

NRS reduces by 3.3 (p <0.001) and by 3.7 (p <0.001) points; attacks number reduces from 9.7 to 5.2 (p <0.001) and from 9.3 to 4.2 (p <0.001); analgesics frequency is reduced by an average of 4.9 (p <0.001) and 7.2 (p <0.001); patients percentage showing a reduction in attacks frequency ≥ 50% from baseline is 40% in NRX and 60% in AM group.

DISCUSSION AND CONCLUSIONS

Results confirm the improvement of all the outcomes in patients treated with NRX.

The greater treatment efficacy with AM compared to NRX is confirmed; there is no statistically significant difference in patients with ESA vs CTE in monthly attacks reduction, with NRX advantage for no side effects and greater patient compliance.

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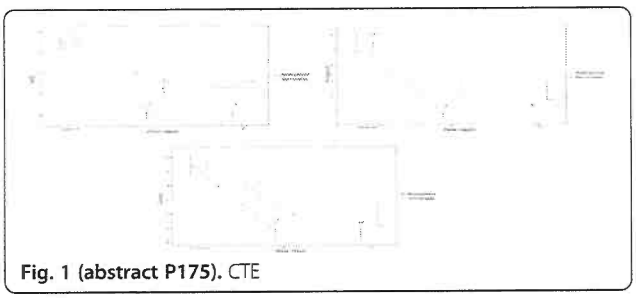


Fig. 1 (abstract P175). CTE

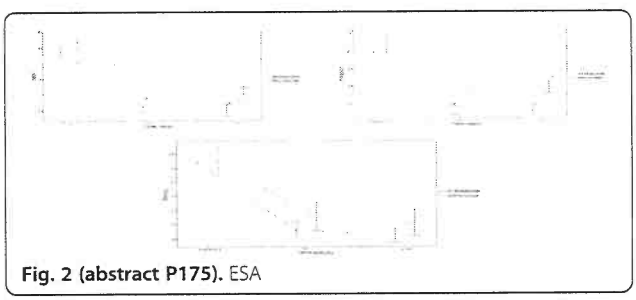


Fig. 2 (abstract P175). ESA

Table 1 (abstract P175). CTE

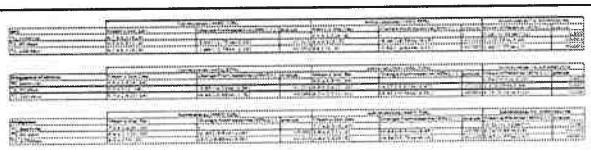
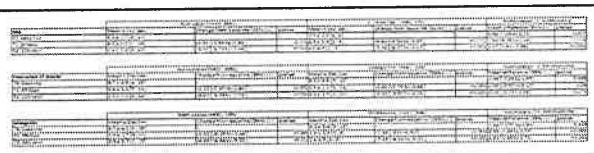


Table 2 (abstract P175). ESA



SISC Poster Presentation

P176

Efficacy in high frequency migraine with aura prevention of a combination of Tanacethum Parthenium, 5 - hydroxy tryptophan and magnesium (Aurastop©)

Giorgio Dalla Volta, Paola Zavarise, Gaelle Ngonga, Danilo Fontana
Headache Center of Neurological Unit of Istituto Clinico Citta' di Brescia, Brescia
Correspondence: Giorgio Dalla Volta (dalla@numerica.it)
The Journal of Headache and Pain 2018, **19(Suppl 1):**P176

Background: Each component of the novel phytotherapic combination of Tanacethum Parthenium (150 mg), 5-hydroxy tryptophan (20 mg) and magnesium (185 mg) (Aurastop©) acts on a different target among the main mechanisms involved in the pathophysiology of migraine and of the aura itself : sensitization of trigeminal vascular system, central sensitization and activation of the "migraine generator" located in the brainstem, through glutammate and kynurenine pathways and the cortical spreading depression [1,2,3]. Aim of this study is to test the effectiveness of Aurastop© in the prophylaxis of migraine with aura with high frequency
Materials and methods: 18 patients (F: n=10, M: n=8, mean age: 28) presenting with an ICHD-3 beta diagnosis of migraine with aura (MWA) with a frequency of more than 5 attacks of migraine with aura per month since at least 6 months, were enrolled in the survey and treated with Aurastop© twice a day for a period of 3 months. Diary cards were filled in during a 3-months period prior the beginning of the survey and during the 3-months duration of the study. The reduction of MWA attacks per month was assessed as the primary end-point; the reduction of the duration and disability of the aura and of the intensity of the headache were considered as secondary end-points.
Results: A statistically significant reduction of MWA attacks /month was observed: more than 95% of the patients referred a reduction >50% of the frquency. Moreover, a sensible reduction of the duration and disability of the aura phenomena was reported by more than 90% of the patients and, in the 60% of the patients also a reduction of the intensity of the headache. No side effects were reported. The efficacy started to appear during the first month of intake and was maintained during the three months of therapy .
Conclusion: In this observational open study, Aurastop© appears to be effective and safe as a preventive treatment of MWA in the patients with a high frequency of attacks.

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P177

Quantitative analysis of perfusion Computed Tomography images increases the evidence of hypoperfusion during migrainous aura

Laura D'Acunto[1], Antonio Granato[1], Miloš Ajčević[1], Giovanni Furlanis[1], Maja Ukmar[2], Irene Zorzenon[2], Mariana Ridolfi[1], Paolo Manganotti[1]
[1]Department of Medical, Technological and Translational Sciences, Headache Centre, University of Trieste, Italy; [2]Department of Radiology, Cattinara Hospital, University of Trieste, Italy
Correspondence: Laura D'Acunto (laura.d.acun@gmail.com)
The Journal of Headache and Pain 2018, **19(Suppl 1):**P177

Background: Perfusion computed tomography (PCT) represents a rapid and practical technique for assessment of salvageable tissue and infarct core in acute stroke imaging [1,2]. Perfusion patterns found during migraine with aura are controversial, in fact normal, hypo- and hyperperfusion were reported, though perfusion measurements were not always performed in the acute phase of the aura [3-6]. Aim of the present study is to demonstrate that an ad hoc quantitative analysis of PTC images may detect perfusion anomalies in migrainous aura that are not highlighted in the routine PCT images analysis.
Patients and Methods: Patients who presented a focal neurological deficit compatible with migraine with aura were enrolled. All the patients performed PTC during migrainous aura and no perfusion abnormality was found at first visual assessment. For each patient, a cerebral region of interest (RoI) was placed by two blinded neuro-radiologists according to the symptoms of the patient. As MTT maps are the most reliable in analysis of hypoperfusion [7], a quantitative analysis of mean transit time (MTT) maps on the RoI, voxel per voxel, by a semi-automatic algorithm was made. Data were compared with the mirrored RoI in the unaffected hemisphere (mRoI) (Fig. 1). Demographic data, characteristics of headache, and asymmetry of MTT between RoI and mRoI [ΔMTT=(MTT RoI – MTT mRoI)/MTT mRoI*100)] were evaluated. Each patient provided a written consent that allowed the analysis of data for research purposes.
Results: Six patients were enrolled (4 F, 2 M, mean age 43±23 y). PTC was performed after 70±15 minutes from symptoms onset. All patients were migraineurs, two of them already suffered with migraine with aura. Characteristics of migrainous aura are shown in Table 1, 50% of patients had headache at the onset of aura. In all patients, MTT values increased in RoI compared to mRoI (mean ΔMTT=19.9% [1.8-60.4%]), without effect of time of PTC performance (Table 1).
Conclusions: An ad hoc quantitative analysis of PTC images during migrainous aura detects an increase of MTT in cerebral RoI that corresponds to hypoperfusion that was not highlighted in the routine PCT images analysis. The use of this quantitative analysis in clinical practice can reduce the percentage of migrainous aura false negatives.

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

L. Balzano[1], B. Ciccone[2],
1 Neurologist – Clinic for the diagnosis and treatment of headaches – Torre del Greco (NA) ASL NA3 SUD
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INTRODUCTION

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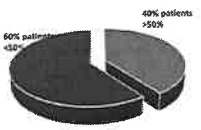
MATERIALS AND METHODS

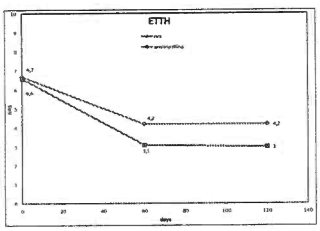
200 patients with ETTH and MWA using ICHD-II were selected: 100 ETTH and 100 MWA. 50 ETTH assuming NRX (two tablets per day) compared to 50 assuming AM (20 mg evening). 50 MWA assuming NRX, compared to 50 assuming AM. Results were evaluated at T1 (60 days) and T2 (120 days).
The longitudinal variatons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

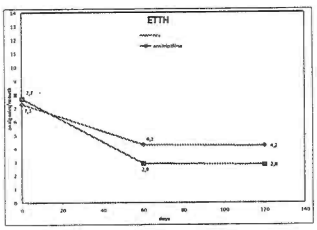
RESULTS

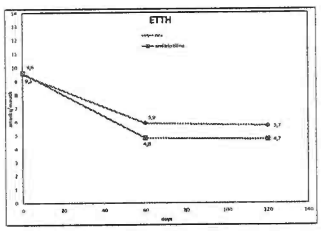
Both groups show statistically significant changes from T0 to T2 for all the outcomes considered.
In ETTH patients of NRX and AM group results are, respectively :
NRS reduces by 2.4 ($p < 0.001$) and by 3.5 ($p < 0.001$) points, attacks number reduces from 9.5 to 5.7 ($p < 0.001$) and from 9.6 at 4.7 ($p < 0.001$); analgesics frequency is reduced by an average of 3.1 ($p < 0.001$) and 4.9 ($p < 0.001$). Patients percentage showing a reduction in attacks frequency ≥ 50% from baseline is 24% in NRX and 40% in AM group.
In MWA patients in NRX and AM group, results are, respectively:
NRS reduces by 3.3 ($p < 0.001$) and by 3.7 ($p < 0.001$) points; attacks number reduces from 9.7 to 5.2 ($p < 0.001$) and from 9.3 to 4.2 ($p < 0.001$); analgesics frequency is reduced by an average of 4.9 ($p < 0.001$) and 7.2 ($p < 0.001$); patients percentage showing a reduction in attacks frequency ≥ 50% from baseline is 40% in NRX and 60% in AM group

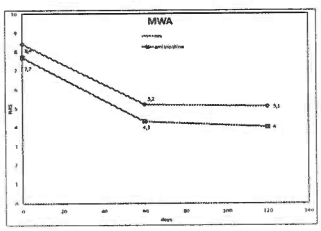


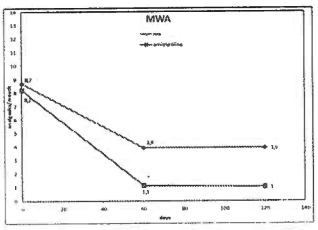
Reduction of attacks to 120 days MWA / NRX

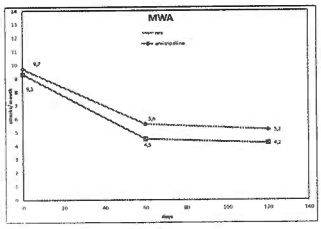












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BIBLIOGRAPHY
1 Ciccone B, D'Otolo G and Balzano L, Efficay of Oral Supplement Compared with Amitriptyline in the Prophylaxis of Episodic Tension Type Headache and Migraine without Aura Current Neurology and Neuroscience An open access journal, Vol 1 (1): 1-2, Feb 2018
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L. Balzano[1], B. Ciccone[2],

1 Neurologist – Clinic for the diagnosis and treatment of headaches – Torre del Greco (NA) ASL NA3 SUD
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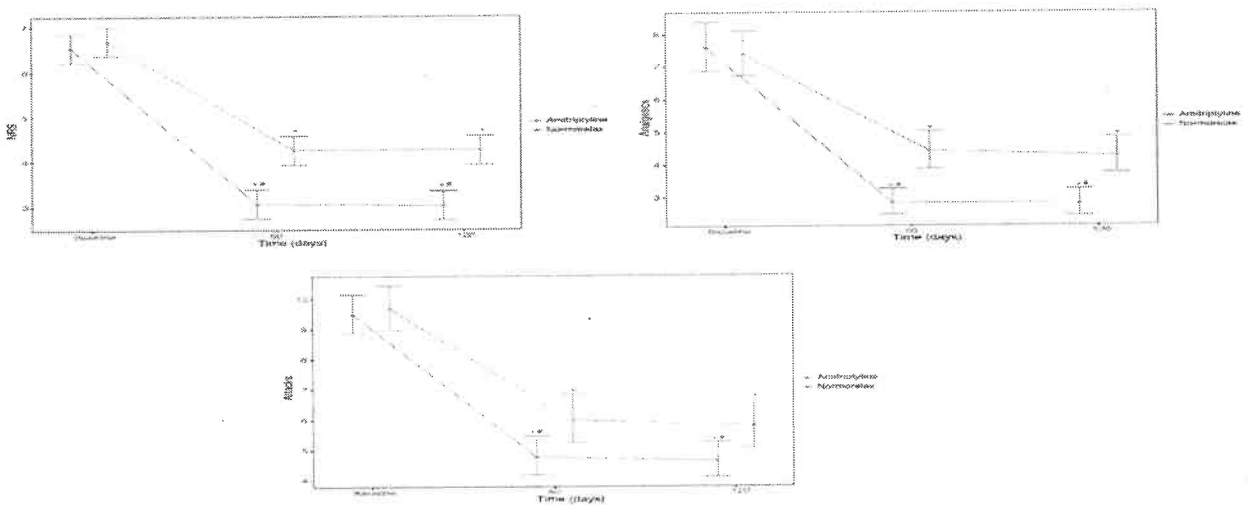
Tab 1 CTE

	Normorelax (n=50; 50%)			Amitriptyline (n=50; 50%)			Normorelax Vs. Amitriptyline	
NRS	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean difference [95% C.I.]	pvalue
T0, baseline	6.7 ± 1.2 [4 ; 9]	-	-	6.6 ± 1.2 [4 ; 8]	-	-	0.16 [-0.31 to 0.62]	0,510
T1, 60 days	4.2 ± 1.2 [2 ; 8]	-2.44 [-2.75 to -2.13]	<0.001	3.1 ± 1 [1 ; 5]	-3.48 [-3.79 to -3.17]	<0.001	1.2 [0.73 to 1.66]	<0.001
T2, 120 days	4.2 ± 1.2 [2 ; 8]	-2.44 [-2.75 to -2.13]	<0.001	3 ± 1 [1 ; 5]	-3.52 [-3.83 to -3.21]	<0.001	1.24 [0.77 to 1.7]	<0.001

	Normorelax (n=50; 50%)			Amitriptyline (n=50; 50%)			Normorelax Vs. Amitriptyline	
Frequence of attacks	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean difference [95% C.I.]	pvalue
T0, baseline	9.5 ± 2.6 [4 ; 14]	-	-	9.6 ± 2.3 [5 ; 14]	-	-	0.08 [-0.9 to 1.05]	0,881
T1, 60 days	5.9 ± 3 [2 ; 14]	-3.65 [-4.72 to -2.58]	<0.001	4.8 ± 2.4 [1 ; 15]	-4.77 [-5.67 to -3.87]	<0.001	1.2 [0.15 to 2.24]	0,025
T2, 120 days	5.7 ± 2.9 [2 ; 14]	-3.83 [-4.89 to -2.78]	<0.001	4.7 ± 2.1 [1 ; 10]	-4.91 [-5.76 to -4.05]	<0.001	1.15 [0.13 to 2.16]	0,026

	Normorelax (n=50; 50%)			Amitriptyline (n=50; 50%)			Normorelax Vs. Amitriptyline	
Analgesics	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean difference [95% C.I.]	pvalue
T0, baseline	7.3 ± 2.4 [0 ; 10]	-	-	7.7 ± 2.9 [3 ; 20]	-	-	-0.31 [-1.32 to 0.7]	0,547
T1, 60 days	4.3 ± 2.1 [0 ; 10]	-2.95 [-3.8 to -2.09]	<0.001	2.9 ± 1.5 [0 ; 6]	-4.84 [-5.71 to -3.97]	<0.001	1.59 [0.88 to 2.3]	<0.001
T2, 120 days	4.2 ± 2 [0 ; 10]	-3.1 [-3.95 to -2.26]	<0.001	2.8 ± 1.5 [0 ; 6]	-4.89 [-5.76 to -4.01]	<0.001	1.47 [0.77 to 2.17]	<0.001

Fig 1 CTE



In ESA patients in NRX and AM group, results are, respectively: (*Tab 2 e Fig 2*)
NRS reduces by 3.3 (p <0.001) and by 3.7 (p <0.001) points; attacks number reduces from 9.7 to 5.2 (p <0.001) and from 9.3 to 4.2 (p <0.001); analgesics frequency is reduced by an average of 4.9 (p <0.001) and 7.2 (p <0.001); patients percentage showing a reduction in attacks frequency ≥ 50% from baseline is 40% in NRX and 60% in AM group.

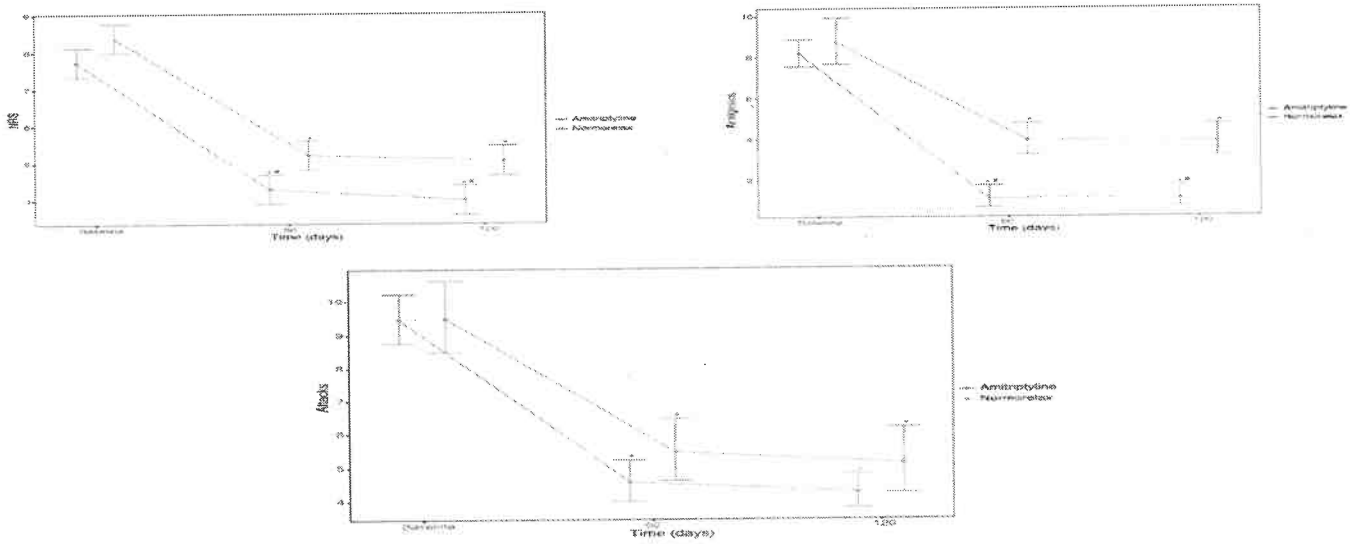
Tab 2 ESA

	Normorelax (n=50; 50%)			Amitriptyline (n=50; 50%)			Normorelax Vs. Amitriptyline	
NRS	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean difference [95% C.I.]	pvalue
T0, baseline	8.4 ± 1.0 [6 ; 10]	-	-	7.7 ± 0.6 [6 ; 8]	-	-	0.64 [0.08 to 1.21]	0,027
T1, 60 days	5.2 ± 2.1 [0 ; 10]	-3.16 [-3.63 to -2.69]	<0.001	4.3 ± 0.9 [2 ; 6]	-3.44 [-3.91 to -2.97]	<0.001	0.92 [0.36 to 1.49]	0,002
T2, 120 days	5.1 ± 2.2 [0 ; 10]	-3.31 [-3.79 to -2.84]	<0.001	4 ± 0.9 [2 ; 5]	-3.74 [-4.21 to -3.27]	<0.001	1.07 [0.5 to 1.64]	<0.001

	Normorelax (n=50; 50%)			Amitriptyline (n=50; 50%)			Normorelax Vs. Amitriptyline	
Frequence of attacks	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean difference [95% C.I.]	pvalue
T0, baseline	9.7 ± 4.0 [4 ; 16]	-	-	9.3 ± 2.6 [3 ; 15]		-	0.36 [-0.95 to 1.67]	0,590
T1, 60 days	5.6 ± 3.4 [0 ; 14]	-4.12 [-5.55 to -2.69]	<0.001	4.5 ± 2.2 [1 ; 11]	-4.82 [-5.76 to -3.88]	<0.001	1.06 [-0.05 to 2.17]	0,06
T2, 120 days	5.2 ± 3.4 [0 ; 14]	-4.49 [-5.95 to -3.02]	<0.001	4.2 ± 1.8 [1 ; 10]	-5.12 [-5.99 to -4.25]	<0.001	0.99 [-0.1 to 2.08]	0,075

	Normorelax (n=50; 50%)			Amitriptyline (n=50; 50%)			Normorelax Vs. Amitriptyline	
Analgesics	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean ± Std. Dev.	Change from baseline [95% C.I.]	pvalue	Mean difference [95% C.I.]	pvalue
T0, baseline	8.7 ± 4.1 [1 ; 20]	-	-	8.2 ± 2.4 [3 ; 12]	-	-	0.52 [-0.77 to 1.81]	0,429
T1, 60 days	3.9 ± 2.7 [0 ; 10]	-4.82 [-6.16 to -3.48]	<0.001	1.1 ± 1.9 [0 ; 6]	-7.16 [-8 to -6.32]	<0.001	2.86 [1.95 to 3.77]	<0.001
T2, 120 days	3.9 ± 2.7 [0 ; 10]	-4.89 [-6.23 to -3.55]	<0.001	1 ± 1.9 [0 ; 6]	-7.18 [-8.01 to -6.35]	<0.001	2.81 [1.89 to 3.73]	<0.001

Fig 2 ESA



DISCUSSION AND CONCLUSIONS

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

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