Letter to the Editor: Medication-Overuse Headache is Common in Portuguese Migraineurs

Carta ao Editor: A Cefaleia por Uso Excessivo de Medicação é Comum em Doentes Portugueses com Enxaqueca

Keywords: Headache Disorders, Secondary; Migraine Disorders; Portugal
Palavras-chave: Portugal; Transtornos da Cefaleia Secundários; Transtornos de Enxaqueca

Dear Editor,

Medication-overuse headache (MOH) is a condition in which the headache treatment becomes the cause. A person with headache starts taking frequent pain medication that will lead to headache worsening and a cycle of increasing medication use and increased pain.[1] The possibility of medication overuse as a headache cause is frequently ignored by patients and health professionals,[1] making it a public health problem.[2]

MOH prevalence is estimated in 1% - 2%,[1,2] but it is present in up to 10% of migraineurs.[3] MOH is associated with lower quality of life[2] and it must be recognized to be effectively treated.[2] To our knowledge, there is no study addressing this problem in Portugal.

Considering a prevalence of 10%[3] (with a precision of 5% and for a confidence level of 95%) a sample size of 139 would be necessary to assess MOH prevalence. We included 146 consecutive patients with a migraine diagnosis according to the International Classification of Headache Disorders-III beta, observed for the first time in a Headache Outpatient Clinic. Demographical, social and headache-related data were collected. Anxiety and depressive symptoms were evaluated using the Hospital Anxiety and Depression scale (HADS), disability was assessed using the Headache-Attributed Lost Time questionnaire (HALT).

MOH was diagnosed in 11/146 migraineurs (7.53%, 95% CI: 4.26 - 12.98). The average number of analgesics used per patient was 1.72, with six patients (54.5%) using only one drug. Non-steroid anti-inflammatory drugs were the most commonly used (6/11), followed by paracetamol (5), metamizole (4), triptans (3) and acetylsalicic acid (1). Migraineurs with a MOH diagnosis were older and reported higher disability than those without MOH. MOH was also associated with chronic migraine. Full comparisons can be found in Table 1.

Although our results could be biased by due to our hospital based-sample, we provide the first estimate of MOH prevalence in Portuguese migraineurs. In line with what was previously described, we found that MOH is more common in the forties[4] and associated with chronic migraine.[1] This information could help clinicians identify headache patients with higher risk of MOH – a condition associated with higher headache-related disability.[1]

Primary care physicians stand in a privileged position to identify and prevent the development of MOH in headache patients. Simultaneously, neurologists and primary care physicians should work together to understand the local and national dimension of this problem and to develop effective public health approaches to minimize this problem. This could include the development of online education tools.[5]

Table 1 - Comparison of migraineurs with and without medication overuse headache

	Migraine + MOH n = 11	Migraine – MOH n = 135	*p*-value
Age, years	45.0 (6.0)	34.0 (17.0)	**0.007**
Age at onset of primary headache, years	28.0 (21.0)	16.5 (8.0)	**0.024**
Duration of disease, years	15.0 (25.0)	14.5 (15.0)	0.829
Female gender, n (%)	11 (100.0%)	121 (89.6%)	0.601
BMI, kg/m^2	25.0 (8.0)	23.5 (5.0)	0.623
Migraine type			**0.029**
Episodic	8 (72.7%)	128 (94.8%)	
Chronic	3 (27.3%)	7 (5.2%)	
Pain intensity, VAS	9.0 (2.0)	8.0 (2.0)	0.101
HALT	47.0 (112.0)	16.0 (24.0)	**0.022**
HADS-A	7.0 (4.0)	8.5 (6.0)	0.603
HADS-D	3.0 (4.0)	4.5 (5.0)	0.376

Comparison of migraineurs with medication overuse headache (migraine + MOH) and without (migraine – MOH). Data expressed as median and interquartile range for continuous variables, and number and percentage for categorical ones. Comparisons were performed using the Fisher's exact test for categorical variables and Mann-Whitney's U test for continuous. Significance level was set at 0.05.
BMI: body mass index; VAS: visual analogue scale; HALT: headache attributed lost-time; HADS: hospital anxiety and depression scale; A: anxiety; D: depression

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Letter to the Editor: Maternally Inherited Diabetes and Deafness is Not Only Biorgan but Multiorgan

Carta ao Editor: A Síndrome Diabetes e Surdez de Transmissão Materna Não é Apenas Bi-Orgânica, mas Multi-Orgânica

Keywords: Child; Deafness/genetics; Diabetes Mellitus/genetics; DNA, Mitochondrial/genetics; Mutation
Palavras-chave: Criança; Diabetes Mellitus/genética; DNA Mitocondrial/genética; Mutação; Surdez/genética

Letter to the Editor,

We read with interest the article by Alves *et al* about a 55-years-old female with maternally-inherited diabetes and deafness (MIDD) due to the mtDNA-variant m.3243A>G.[1] In the index patient's family five other members were also clinically affected (II/5, II/1, II/2, II/3, I/1).[1] In addition to deafness and diabetes some family members also presented with hypertrophy cardiomyopathy (II/3, II/4, II/5), conduction-block (II/2, II/4), myopathy (II/4), depression (II/4), cognitive impairment (II/1, II/4, II/5), basal ganglia calcification (II/5), cerebellar atrophy (II/5), macular dystrophy (II/1, II/4, II/5), proteinuria (II/4, II/5), and muscle weakness (II/4).[1] We have the following comments and concerns.

Phenotypic features in MIDD-patients other than deafness and diabetes are not uncommon.[2] MIDD not only manifests as insulin-deficient diabetes and hearing loss but also as epilepsy, cerebellar ataxia, cognitive impairment, basal ganglia calcification, Parkinson syndrome, cerebral atrophy, stroke, maculopathy, retinopathy, cataract, hyporeninemic hypoaldosteronism, hypothyroidism, short stature, hypoparathyroidism, Addison-disease, dilated cardiomyopathy, WPW-syndrome, intestinal pseudoobstruction, pancreatitis, non-diabetic renal insufficiency, glomerulosclerosis, or myopathy.[2] Thus, MIDD is definitively a multisystem mitochondrial disorder (MIMODS) depending on the stage of the disease. At onset or during the first years only the pancreas and ears may be affected but with progression of the disease MIMODS may develop.

Since MIDs occasionally manifest with unilateral or bilateral basal ganglia calcification and since II/5 also presented with basal ganglia calcification, it would be interesting to know if T2-hypointensitiy in figure 2 of the case report was attributable to basal ganglia calcification or bleeding? Was there any evidence of calcification of the basal ganglia on cerebral CT? Did CT scans in other family members also show basal ganglia calcification?

Since clinical manifestations of the m.3243A>G mutation may strongly depend on the mutation load, it should be explained why cases II/2, II/3, and II/5, who had lower heteroplasmy rates than the clinically unaffected case III/1, nonetheless manifested clinically. Were heteroplasmy rates also determined in tissues other than lymphocytes? Did heteroplasmy rates vary between different tissues?

We do not agree with the statement that there is no curative therapy for MIDs.[1] Patients with MIDs not only profit from symptomatic measures and supplementary therapy but in a few cases also causal measures can be highly effective, such as in MNGIE or primary coenzyme-Q-deficiency.[3]

Overall, this interesting case study may profit from determination of heteroplasmy rates in tissues other than lymphocytes, from prospective investigations of subclinical or mild clinical manifestations of the mutation, and from symptomatic or supplementary therapeutic measures.

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