

Impulsivity prevalence in migraine patients without and with medication overuse

Prevalência de impulsividade em pacientes com enxaqueca sem e com abuso de medicação

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ABSTRACT

Background: Migraine is one of the most common disorders in neurological clinical practice and is part of the group of primary headaches. It often affects individuals in the age group of 25–55 years, when people are at their peak of economic productivity. Many patients ultimately overuse analgesics. Overuse is defined by the use of analgesics for at least 15 times a month — within a minimal three-month period. Impulsivity and migraine cause losses in the lives of individuals suffering from them, as they can compromise these individuals' social, emotional, and professional spheres. Regarding the professional sphere, it results in economic losses compared with the overall population. **Objective:** To investigate the presence of impulsive behavior in patients with migraine and with medication-overuse migraine. **Methods:** Cross-sectional study on 210 female and male patients; 140 were diagnosed with migraine according to criteria of the International Classification of Headache Disorders and were subdivided into two groups (70 patients each). One of these groups was composed of medication-overuse patients; the control group was composed of non-migraine patients (70 patients). All patients were evaluated with the Barratt Impulsivity Scale (BIS-11). **Results:** The group of migraine patients accounted for the highest impulsivity level, followed by the control group and, finally, by the medication-overuse group. However, these differences did not attain statistical significance. **Conclusions:** It was not possible to establish a clear connection between migraine and impulsive behavior. Association was higher among migraineurs without medication overuse.

Keywords: Migraine Disorders; Medication Overuse; Impulsive Behavior; Headache.

RESUMO

Introdução: A enxaqueca é uma das condições mais comuns na prática clínica neurológica, enquadrando-se no grupo das cefaleias primárias. Sua prevalência é maior na faixa etária de 25 a 55 anos, coincidindo com o pico da produtividade econômica. Muitos pacientes recorrem ao uso abusivo de analgésicos. O uso excessivo desses medicamentos é definido pela sua utilização por pelo menos 15 vezes ao mês, por um período de no mínimo três meses. A impulsividade e a enxaqueca causam prejuízos na vida dos indivíduos afetados, podendo comprometer os âmbitos social, emocional e profissional, resultando em um prejuízo monetário a esse grupo, em relação à população em geral. **Objetivo:** Investigar a presença de comportamento impulsivo em pacientes com enxaqueca com abuso de analgésico. **Métodos:** Estudo de corte transversal com 210 pacientes, homens e mulheres, sendo 140 com diagnóstico de enxaqueca segundo os critérios da Classificação Internacional das Cefaleias (IHCD-3), subdivididos em dois grupos de 70 pacientes cada, um composto por pacientes em uso excessivo de medicamentos, e um grupo controle composto por indivíduos sem enxaqueca. Todos os pacientes foram avaliados com a Escala de Impulsividade de Barratt — BIS 11. **Resultados:** O grupo com enxaqueca apresentou maior impulsividade, seguido do grupo controle e, por fim, o grupo com enxaqueca com abuso de medicamentos. No entanto, essas diferenças não atingiram significância estatística. **Conclusão:** Não foi possível encontrar relação direta entre a enxaqueca e comportamentos impulsivos. No entanto, esta relação foi maior entre os pacientes com enxaqueca sem abuso de analgésico.

Palavras-chave: Transtornos de Enxaqueca; Uso Excessivo de Medicamentos Prescritos; Comportamento Impulsivo; Cefaleia.

INTRODUCTION








Migraine is one of the most common complaints in neurological clinical practice¹ and is part of the group of primary headaches, which are simultaneously a symptom and

a disease², in addition to presenting diverse manifestations, among them migraine with aura and without aura.

The prevalence of migraine persists from childhood and early adulthood up to approximately the age of 40, but it starts declining after this age. Overall, it often affects individuals in

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Conflict of interest: There is no conflict of interest to declare.

Received on February 26, 2020; Received in its final form on May 5, 2020; Accepted on May 17, 2020.



the age group of 25–55 years, when they are at their peak of economic productivity³.

Many patients who aim at suppressing the symptoms caused by migraine ultimately overuse medications; however, it is worth highlighting that pain relief only lasts for a short period of time and results in tachyphylaxis. In other words, a primary episodic headache could evolve to a chronic headache due to medication overuse, which is defined by the excessive use of analgesics for at least 15 times a month — this number may vary depending on drug class — within a minimal three-month period of time⁴. Regarding ergotamines, abuse is characterized by a dosage of more than ten days a month, whereas for triptans, the dosage is of one or more triptans, in any formulation, for more than 10 days per month. Regarding acetylsalicylic acid (AAS), paracetamol, and other nonsteroidal anti-inflammatory drugs (NSAIDs), abuse occurs when consumption exceeds 15 days per month. When opioids are overused, the diagnostic criterion for abuse consists of regular intake of one or more opioids, 10 days a month, for more than three months.

Abuse can also occur through unverified overuse of various drug classes. It is confirmed when there is a regular intake of any combination of ergotamine, triptans, simple painkillers, NSAIDs, and/or opioids in a period of 10 days a month for more than three months. Lastly, there is the medication-overuse headache due to other medications, with regular overuse, 10 days a month for at least three months; and overuse of one or more medications other than those aforementioned, taken for acute or symptomatic treatment of headache.

Nowadays, the possible association between migraine patients and their greater likelihood of developing impulsive behaviors, which would be possibly exacerbated in medication-overuse migraine patients, is frequently discussed⁵. In this type of patient, the management of migraine becomes more difficult due to the manifestation of impulsiveness in the precipitated consumption of abortive medications. However, in order to form such association, it is important to adequately define the concept of impulsivity, considering the different understandings about the meaning of impulsivity, which is often associated with the following reactions: (1) changes in the course of action, without previous conscious judgement; (2) occurrence of disruptive or thoughtless behaviors; and (3) tendency to act based on lower planning level compared with individuals presenting the same intellectual level⁶.

Impulsivity is a social emotion that determines a person's propensity to violence. Impulsivity is one of the sources of anger, associated with inhibition difficulties and characterized by the tendency to respond to internal or external stimuli without assessing potential negative consequences⁷.

Impulsivity and migraine cause losses in the lives of individuals suffering from them, as they can compromise these individuals' social, emotional, and professional spheres⁸. The professional sphere is affected by the individuals' absence from work, which results in economic losses compared with

the overall population⁹. Despite their low professional productivity, these patients also increase public health costs due to the high costs generated with medical assistance.

The aim of the present study was to assess the presence of impulsive behavior in migraine and medication-overuse migraine patients by comparing them with the control group.

METHODS

This is a cross-sectional study on the presence of impulsive behavior in migraine patients with and without medication overuse compared with patients in the control group.

Men and women older than 18 years of age were randomly selected, between March and December 2018, from Centro Acadêmico Multiprofissional Dr. Agostinho Paolucci – Faculdade de Medicina de Barbacena (CAM FAME), which is an outpatient clinic that comprises several medical specialties. These patients were not individually scheduled for the research, but were arbitrarily approached by the team while waiting for medical care in the Neurology department and in other medical specialties at this center.

Patients with cognitive deficits were excluded from the study (considering that such deficits would prevent them from answering the questionnaire), as well as individuals who did not agree to participate in the study.

Patients diagnosed with migraine by the neurologist responsible for the study were divided into two groups according to the International Classification of Headache Disorders (ICHD-3)⁴: migraineurs presenting crises four times a month, and migraineurs who, in addition to the crises, also meet the criteria for the diagnosis of medication abuse, regardless of the drug class in question. Patients followed at the CAM FAME outpatient clinic, who were not diagnosed with migraine, were also invited to participate in the research, therefore composing the third research group (control group).

Each group encompassed 70 patients — medication-overuse migraine patients, migraine patients without analgesic overuse, and non-migraine patients — thus totaling 210 patients. This sample size would assure 95% significance level, with sample power of 84.09%.

Initially, patients with headache complains, those who presented migraine due to medication overuse, and control patients signed the informed consent form. Next, all of them answered the questions proposed by the Barratt Impulsivity Scale (BIS-11) – Brazilian Portuguese version. BIS-11 was developed in 1959 as an instrument to assess personality and behavioral constructs related to impulsivity. It was revised in 2009 and is recommended as a reliable tracking instrument. The Brazilian Portuguese version of BIS-11 was already validated, and consists in an instrument of easy and fast application, in addition to being well accepted by patients¹⁰.

The BIS-11 comprises 30 questions, which cover six first-order factors (attention, motor impulsivity, self-control, perseverance,

cognitive instability, and cognitive complexity) followed by three second-order factors (attentional impulsivity, motor impulsivity, and non-planning). Scores are calculated by frequency attributions that range among rarely/never (1), occasionally (2), often (3), and almost always/always (4). The score ranges from 30 to 120 points, and high scores indicate the presence of impulsive behaviors¹¹.

This scale classifies individuals scoring less than 52 points as very controlled; from 52 to 71 points, as under normal impulsivity limits; and those scoring higher than or equal to 72, as highly impulsive⁹. The study was approved by the Ethics Committee of Faculdade de Medicina de Barbacena.

Data analysis

Data in the applied questionnaire were transcribed into an electronic spreadsheet and processed in the STATA statistical software, version 9.2. Relative and absolute distributions in the qualitative variables were calculated as well as the central position and dispersion tendency measurements of quantitative variables. Association among the assessed variables was measured by chi-square and Fisher's exact tests. The relation between qualitative and quantitative variables was measured by Student's t-test, analysis of variance (ANOVA), Mann-Whitney U test, or by the Kruskal-Wallis test, depending on the indications. Differences were statistically significant when $p < 0.05$.

Comparison between groups considered a 5-point difference in the average of the impulsivity scale. Groups (between 65% and 70% in the BIS-11 scale) were compared considering standard deviation of 10.0 in each group, with 95% significance level and sample power of 84.09%.

RESULTS

In total, 210 patients were assessed; they were divided into three groups, which comprised 70 patients each: migraine patients without analgesic overuse (M), medication-overuse migraine patients (MO), and non-migraine patients (NM). Among the evaluated patients, 71 are migraineurs with the presence of aura, with 34 MO and 37 M patients; 139 patients have migraine without aura. Women prevailed in the three groups. These groups were divided into two age groups: 18-39 years and 40-85 years, and the latter group prevailed in the sample (Table 1). The mean and standard deviation of the three groups were MO (41.4 and 12), M (43.5 and 12), and NM (46.6 and 12).

According to the BIS-11, patients' impulsivity level is classified based on three variables: controlled, normal, and impulsive individuals. The group of non-migraine patients (NM) was the one accounting for the largest number of "controlled" individuals, followed by the group with migraine patients without analgesic overuse (M) and, finally, by the group of medication-overuse migraine patients (MO). The MO group comprised the largest number of "normal" individuals, followed by the NM and M groups. Finally, migraine patients without medication overuse (M) prevailed in the "impulsive" variable, followed by individuals in NM and MO groups (Table 2). However, there was no statistically significant difference concerning impulsivity when comparing the three groups ($p > 0.05$).

First-order factors, namely attention, motor impulsivity, self-control, perseverance, cognitive instability, and cognitive

Table 1. Distribution of migraine, medication-overuse migraine, and non-migraine patients according to sex and age.

Characteristics	M		MO		NM		Total		p-value
	n	%	n	%	n	%	n	%	
Sex									
Women	53	75.71	56	70	52	74.29	161	76.67	0.707
Men	17	24.29	14	20	18	25.71	49	23.33	
Total	70	100	70	100	70	100	210	100	
Age group (years)									
18-39	26	37.14	34	48.57	21	30	81	38.57	0.075
40-85	44	62.86	36	51.43	49	70	129	61.43	
Total	70	100	70	100	70	100	210	100	

M: migraine; MO: medication overuse; NM: non-migraine.

Table 2. Impulsivity level among migraine, medication-overuse migraine, and non-migraine patients.

Impulsivity level	M		MO		NM		Total		p-value
	n	%	n	%	n	%	n	%	
Controlled	5	7.14	3	4.29	6	8.57	14	6.67	0.636
Normal	36	51.43	44	62.86	39	55.71	119	56.67	
Impulsive	29	41.43	23	32.86	25	35.71	77	36.67	
Total	70	100	70	100	70	100	210	100	

M: migraine; MO: medication overuse; NM: non-migraine.

complexity consist in other evaluation possibilities provided by BIS-11. Values lower than or equal to 0.05 were the cut-off point set to validate data to be analyzed; thus, attention was the only significant factor ($p=0.058$). The “attention” variable accounted for the same scores in the M and MO groups (median: 13); however, there was greater dispersion in the M group, whose interquartile range was 6, whereas the MO group accounted for an interquartile range of 5. The NM group, whose patients did not have migraine, accounted for the lowest value for this variable (median: 11) (Table 3).

DISCUSSION

Studies focused on assessing the prevalence of migraine between sexes have shown the prevalence of women in this population^{12,13}; the number of women with migraine in the current research confirmed the results in the aforementioned studies. Migraine is more prevalent in individuals in the age group 25–55 years^{14,15,16,17}, but it was not confirmed in the current study, considering that it assessed the migraine prevalence in individuals within the age group of 40–85 years. This result is probably due to the outpatient center where the study was carried out, which mostly assists older patients.

The frequent association between migraine and psychiatric disorders is often addressed in the literature; there are growing evidences about the close relation between these two conditions¹⁸. Disorders frequently associated with migraine are anxiety, high depression levels, and risk of suicide. These psychiatric profiles are more severe in medication-overuse migraine patients¹⁹. Prospective studies have shown that these comorbidities are serious risk factors for migraine development and chronification of pain, which can affect either the course or the consequences of this disease in individuals¹⁸.

Researchers are quite involved in investigating the association between migraine and psychiatric disorders¹⁹. Nevertheless, only few studies in the literature have investigated the possible association between impulsivity and migraine. Medication-overuse migraine is cited

in the literature as a possible impulsive-behavior trigger, although impulsivity is likely the cause of migraine rather than its effect²⁰.

The search for associations between the “impulsivity,” “migraine,” and “drug abuse” variables have made several analyses of the theme to be conducted. Impulsivity, for example, can cause anxious anticipation of pain and, thereby, migraineurs have a tendency to overuse medications and to chronification of pain⁵.

However, one of the few existing studies on the subject evaluated the presence of impulsivity in two groups: patients with chronic migraine and migraineurs with medication abuse. In this study, unlike ours, the Plutchik Impulsivity Scale (PIS) was used to assess impulsive behavior, and no correlation between impulsivity and the two groups in question was found⁵. Another study investigated the presence of impulsivity in migraineurs with and without aura and in non-migraine patients. As in the present study, the BIS-11 was used, and no significant differences were found in the impulsivity scores between the three groups⁷. Most of the studies that investigated the influence of genetics on the occurrence of impulsivity were based on serotonergic polymorphism¹¹, and there are evidences that low levels of serotonin are related to a greater level of impulsivity²¹.

Results in the current study have shown that the migraine group (M) accounted for the highest impulsivity scores, followed by the non-migraine group (NM) and, finally, by the medication-overuse migraine group (MO). Accordingly, there may be a possible association between impulsivity and migraine, regardless of analgesic overuse. Presumably, the profile of medication-overuse migraineurs is close to compulsive behavior.

Studies have analyzed that the prevalence of Attention Deficit Hyperactivity Disorder (ADHD) in children is higher in individuals with high-frequency episodic migraine^{22,23}. However, this pathophysiology is not yet fully understood, but there is consensus on its relation to dopamine level deregulation²⁴, which is associated with the abnormal functioning of the hypothalamic-pituitary-adrenal axis²⁵. On the other hand, the present study showed a different profile regarding the “attention” variable, which was within the selected age group (adult individuals). Migraine patients accounted for the highest attention level in comparison to the control group.

The medical literature lacks studies clarifying the association between impulsivity/attention and migraine; therefore, it is essential to encourage further research aimed at better understanding the pathophysiology capable of proving such association²⁶ and thoroughly investigating it in larger samples.

The present study may have faced a biased selection, considering that the sample available in the units of the outpatient clinic (NM) was mostly composed of older patients. Such fact could be correlated to results different from those

Table 3. Median values and interquartile range found for first-order factors among migraine, medication-overuse migraine, and non-migraine patients.

First-order factors	M	MO	NM	p-value
	Median	Median	Median	
Attention	13 (6)	13 (5)	11 (5)	0.005
Impulsivity motor	14 (8)	13 (6)	14 (6)	0.528
Self-control	13 (5)	14 (5)	14 (6)	0.674
Perseverance	7 (2)	7 (2)	7 (3)	0.268
Cognitive impulsivity	8 (4)	8 (2)	8 (3)	0.796
Cognitive complexity	13 (4)	14 (4)	14 (3)	0.622

M: migraine; MO: medication overuse; NM: non-migraine.

found for the overall population in previous studies, considering that, according to the literature, migraine is prevalent among young people; although it did not have impact on the present results.

Furthermore, a methodological problem is that this is a cross-sectional study, in such a way it may be difficult to establish a causal relationship⁷.

Thus, it is worth highlighting the relevance of analyzing such variable in order to interpret the present study, but without diminishing its importance within the proposed context of the association between migraine/medication overuse and impulsivity.

The current study did not evaluate the hypothesis that medication overuse favors the development of impulsive behaviors; however, this was observed in migraineurs without medication overuse.

In other studies that administered BIS-11, no significant difference was found in the scores of attentional impulsivity and motor impulsivity among patients with migraine with or without aura and control patients⁷.

In conclusion, it was not possible to establish a direct relation between migraine and the development of impulsive behaviors, which would be exacerbated in patients who present medication overuse.

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