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Chronic migraine and comorbidities: prevalence and pharmacological treatment

Migrânea crônica e comorbidades: prevalência e tratamento farmacológico

Migraña crónica y comorbilidades: prevalencia y tratamiento farmacológico

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Abstract: This article aims to evaluate disease and medication load in subjects with chronic migraine-a common and disabling condition that affects the quality of life being associated with reduction in labor and personal aspects.Most cases have several comorbidities and use polypharmacy.The study is a cross-sectional observational study, carried out in a hospital. The population was between 18 and 60 years,both genders,with diagnosis of chronic migraine following the International Classification of Headache Disorders, 2013.To analyze the burden of disease, we applied self-administered questionnaires and the Cumulative Illness Rating Scale(CIRS).Women were majority of the sample, with mean age of 43.9 years; 95.4% had another active disease-specially depressive and anxiety disorders;polypharmacy was observed in 58.6%.The most used drugs were anticonvulsants. Individuals with psychiatric conditions had the highest scores of cumulative illness.The study shows that chronic migraine has an extensive disease and medication load, and that the most relevant relates to the psychiatric domain,responsible for the most prevalent associated medical conditions and concomitant medication.

Keywords: migraine disorders; disease; overuse of prescription drugs.

Resumo: Este artigo tem como objetivo avaliar a carga de doenças e medicamentos em indivíduos com enxaqueca crônica – condição comum e incapacitante que afeta a qualidade de vida estando associada à redução de aspectos laborais e pessoais. A maioria dos casos apresenta diversas comorbidades e faz uso de polifarmácia. A população tinha entre 18 e 60 anos, ambos os sexos, com diagnóstico de enxaqueca crônica seguindo a Classificação Internacional de Cefaleias, 2013. Para analisar a carga da doença, foram aplicados questionários autoaplicáveis e a Escala de Avaliação de Doenças Cumulativas (CIRS). 95,4% apresentavam outra doença ativa, principalmente transtornos depressivos e ansiosos; polifarmácia foi observada em 58,6%.Os medicamentos mais utilizados foram os anticonvulsivantes. Indivíduos com condições psiquiátricas apresentaram os maiores escores de doença cumulativa. O estudo mostra que a enxaqueca crônica tem extensa carga de doença e medicação, e que a mais relevante diz respeito ao domínio psiquiátrico, responsável pelas condições médicas associadas mais prevalentes e medicação concomitante.

Palavras-chave: transtornos de enxaqueca; doenças; uso excessivo de medicamentos prescritos.

Resumen: Este artículo tiene como objetivo proporcionar una carga de enfermedades y medicamentos a individuos con una condición crónica – condición común e incapacitante que afecta la calidad de vida estando asociada a la reducción de aspectos laborales y personales. La mayoría de los casos presentan diversas comorbidades y uso de polifarmácia. Una población de entre 18 y 60 años, ambos sexos, con diagnóstico de enxaqueca crónica siguiendo la Clasificación Internacional de Cefaleias, 2013. Para analizar la carga de la docencia, se aplicaron cuestionarios autoaplicados y la Escala de Avaliação de Doenças Cumulativas (CIRS). 95,4% apresentavam outra doença ativa, principalmente transtornos depresivos e ansiosos; polifarmácia foi observada em 58,6%.Os medicamentos mais utilizados foram os anticonvulsivantes. Individuos con condiciones psiquiátricas presentan las mayores puntuaciones de docencia acumulativa. El estudio muestra que a enxaqueca crônica tem extensa carga de doença e medicação, y que a mais relevante diz respeito ao domínio psiquiátrico, responsável pelas condições médicas associadas mais prevalentes e medicação concomitante.

Palabras clave: transtornos de migraña; enfermedades; uso excesivo de medicamentos recetados.

1 INTRODUCTION

According to the 2016 Global Burden of Diseases (GBD, 2016) migraine is the second leading cause of disability in the world, giving way only to low back pain. Migraine affects about 40 million people in the United States and 1 billion people worldwide (Burch; Buse; Lipton, 2019). Chronic migraine affects up to 2% of the global population and approximately 2.5% of people with episodic migraine progresses to chronic migraine. Such condition is generally associated with other disorders such as psychiatric illnesses, sleep disorders and cardiovascular diseases, causing disability, use of health resources with direct and indirect costs, lower socioeconomic status and lower health-related quality of life. The annual prevalence in the general population is, on average, 11% in The United States of America and Western Europe, 6% in men, and 15 to 18 % in women (Cuciureanu *et al*., 2024).

In Brazil migraine has been found in 15,2% of the population (Peres *et al*., 2019). Chronic daily headache is a condition mostly composed by chronic migraine; its prevalence was 6.1% (Queiroz; Silva Junior, 2015).

The cumulative burden of chronic migraine led it to rank in the top 40 conditions causing worldwide disability according to the World Health Organization's 2012 global burden of disease (Weatherall, 2015)

Chronic migraine subjects require more clinical skills of their doctors, since they are known to present more comorbidities, worse response to treatment, and use of polypharmacy.

Therefore, the objective of the present study was to analyze the number and kind of comorbidities this population present and to list medications used in a sample of chronic migraine patients.

1.2 Aim

Study aimed to evaluate disease load and medication load in subjects with chronic migraine.

1.3 Methods

Study was approved by the local regulatory board under the Presentation Certificate for Ethical Appreciation number 73.130117.40000.0096. Before

selection procedures, all volunteers signed an informed consent term. A cross-sectional observational study was carried out in a Headache Outpatient Clinic of a University Hospital. Study population were individuals previously diagnosed of chronic migraine by headache specialist, in consonance with International Classification of Headache Disorders 2013 criteria, with or without associated medication overuse headache, Data were collected between February, 2018 and August, 2019. Patients who did not meet any of the inclusion criteria, were illiterate (self-administered questionnaires), unable to understand or complete the questionnaires, that refused to participate were not included. Patients who withdrew their consent, who did not complete study procedures were excluded. All participants underwent a standardized and validated survey, conducted by the same trained evaluator. The use of self-report scales intended to avoid investigator bias.

Chronic migraine diagnosis was done through a validated self-applicable migraine questionnaire, based on 2013 International Classification of Headache Disorders criteria (IHS, 2018).

Past and present health conditions were surveyed with the validated modified Cumulative Illness Rating Scale (CIRS) that measures the burden of chronic diseases while simultaneously considers its severity. Thus, the scores for each of the systems are quantified as follows: 0 for no problems affecting any body system; 1 for current mild or significant past disorder; 2 for disability or moderate morbidity that requires daily or first-line treatment; 3 for severe and-or constant disorder and significant disability and-or chronic problems that are difficult to control; 4 for extremely severe disorder, immediate treatment needed, organ failure and-or severe functional disability (Miller; Towers, 1991).

Data regarding pharmacotherapy were surveyed through an inventory filled by the patient.

Results of quantitative variables were described by means, standard deviations, median, minimum and maximum values. For categorical variables, frequencies and percentages were presented. Data analysis was done with the software Stata / SE v.14.1. by StataCorpLP, USA.

1.4 Results

A hundred individuals were evaluated, of which 13 were excluded due to incomplete data in the medical record or during filling out self--administered questionnaires.

About the 87 remaining individuals, 74 (85.1%) were female with a mean age of 43.9 ± 10.5 years of which 63.2 were married.

Considering the characteristics related to the socio-economic profile, 36.8% have a family income between 1 and 2 index, followed by 29.9% with income between 2 and 3 index, 18.4% with an income of up to 1 minimum wage, with 34.5% of the cases 2 people depended on family income and in 29.9% of the cases, 3 people dependent on this income. Most of the sample were graduated on High School and are working.

Is noteworthy that 83 (95.4%) individuals of the sample had some associated medical condition lasting since one to fifty years (Table 1).

Table 1 – Number of medical conditions per subject according to CIRS Systems-Curitiba, 2020

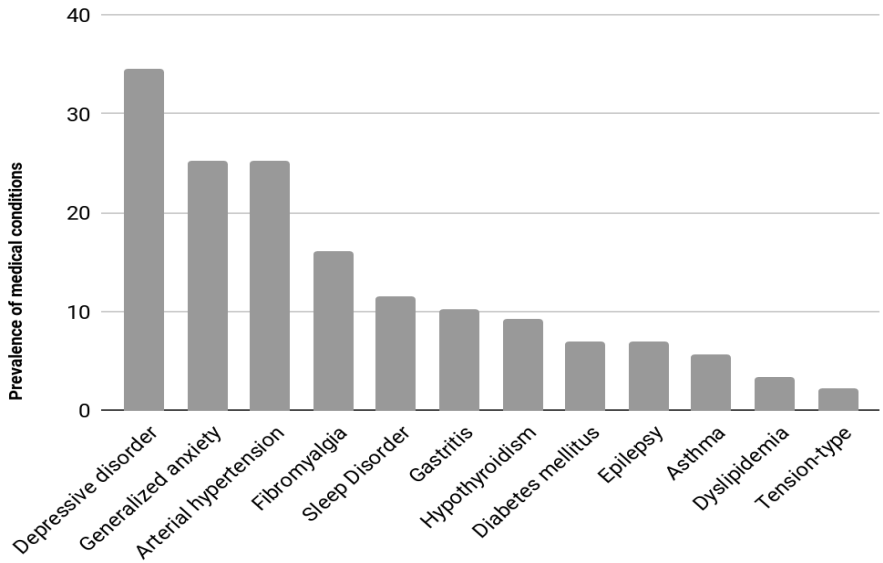
System	Medical conditions/ subject	Subjects (n)	(%)
Psychiatric	0	40	46.0
	1	34	39.1
	2	10	11.5
	3	3	3.4
Endocrinological	0	72	82.8
	1	12	13.8
	2	3	3.4
	3		
Neurological	0	59	67.8
	1	26	29.9
	2	2	2.3
Vascular	0	66	75.9
	1	20	23.0
	2	1	1.1
Bones, joints and muscles	0	59	67.8
	1	19	21.8

System	Medical conditions/ subject	Subjects (n)	(%)
	2	9	10.3
Lungs	0	82	94.3
	1	5	5.7
Liver, gallbladder and pancreas	0	84	96.6
	1	3	3.4
Urinary and Reproductive	0	84	96.6
	1	1	1.1
	2	2	2.3
Upper GI tract	0	77	88.5
	1	10	11.5
Renal	0	84	96.6
	1	3	3.4
Ophthalmological	0	83	95.4
	1	4	4.6
Ear, Nose and Throat	0	80	92.0
	1	7	8.0
Heart	0	85	97.7
	1	2	2.3
Lower GI tract	0	86	98.9
	1	1	1.1
Skin	0	85	97.7
	1	2	2.3
Breast	0	86	98.9
	1	1	1.1

Source: the authors.

The three most prevalent comorbidities associated to Chronic Migraine were Depressive Disorder (34.5%), Anxiety Disorder (25.3%) and Systemic Arterial Hypertension (25.3%) (Figure 1).

Figure 1 – Associated medical conditions in chronic migraine population

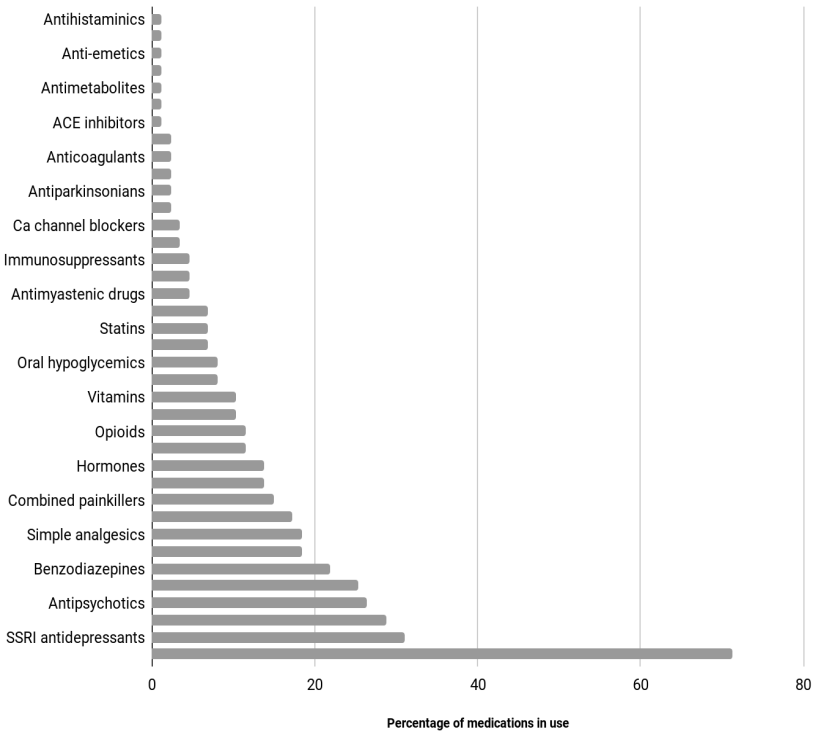


Source: the authors.

Curiously, subjects with psychiatric conditions presented the highest marks at the CIRS (Cumulative Illness Rating Scores), with 40.2% of them, receiving the score 3 brackets (which means: current major depression or more than 2 episodes in the last 10 years; current daily use of anxiolytics, current substance abuse or even by daily need for antipsychotics).

All surveyed subjects used some continuous medication. Twenty-five of them (28.7%) used three different medications; 22 (25.3%) used five medications and 16 (18.4%) used 6 to 13 concomitant medications. The most common medications were psychoactive drugs, such as anti-seizure medication (71.3%), Serotonin Selective Reuptake Inhibitors (SSRI) (31%), Tricyclic Antidepressants (28.7) and Antipsychotics (26.4%). Details of associated medication are summed up in Figure 2.

Figure 2 – Medications taken concomitantly with antimigraine therapy



Source: the authors.

Considering CIRS, regarding to the number of categories (body systems) on which these individuals presented any disease, there was an average of three categories – summarizing, the study population presented an average of 3 body systems affected by any disease.

About the mean total CIRS score, it was 6, ranging from 2 to 20 points. Also, the Severity Index which basically measures the illness load was calculated following the CIRS Criteria and its mean was 2.1 (Table 2).

Table 2 – Cumulative Illness Rating Scale – condensed scores – Curitiba, 2020

CIRS Measures	Mean	Median (range)
Total CIRS scores	6.0	6 (2 – 20)
Number of affected CIRS systems (n/14)	3.0	3 (1 – 9)
Severity Score (total CIRS scores/affected systems "n")	2.1	2 (1 – 3)
Number of CIRS Systems scoring 3	0.6	1 (0 – 2)
Number of CIRS Systems scoring 4	0.1	0 (0 – 2)

CIRS: Cumulative Illness Rating Scale (analyses 14 body systems).
Source: the authors.

2 DISCUSSION

This study evaluated medical and pharmacological complexity in patients with chronic migraine, with the purpose of characterizing the medical profile of this population. The findings of our study show that chronic migraine has an extensive disease and medication load, and that the most relevant of them relates to the psychiatric domain, responsible for most prevalent associated medical conditions and concomitant medication.

The findings of this study show that 85% were women, a result similar to the literature that shows that women are three times more likely to suffer migraines than men (gender ratio 3:1) (Ailani; Burch; Robbins, 2021).

A study on chronic migraine population profile found men in 25.6% of the sample (Scher, 2019). As compared to women, men were slightly older at the onset of their headache (in average 24.1 vs. 22.3 years) and had fewer headaches days / month (4.3 vs. 5.3 days), slightly less severe attacks (according to Migraine Symptom Severity Score, 21.6 vs. 22.6), reduced frequency of grade (according to Migraine Disability Assessment scores (15.7% vs. 24.1%), allodynia (32.6% vs. 49.7%), chronic migraine (6.5% vs. 9.6%, each $p < 0.001$) and common comorbidities. Men were less likely to report seeing a doctor for their headaches and receiving a migraine diagnosis if they did.

The pathophysiology of migraine is complex and not yet fully understood, as well as several neuropeptides, neurotransmitters and different brain

pathways have been implicated. The complexity of its pathophysiology, leads to a variety of multisystemic comorbidities; for example, cardiovascular, psychiatric and other neurological conditions have been found closely associated with migraine (Cámara-Lemarroy *et al*., 2016).

Many authors, consider migraine to be a disabling neurological disorder associated with a wide range of comorbidities (Jeyagurunathan *et al*., 2020). Conversely, such interference in occupational activities was not found in our population study which, in spite of a heavy disease load and multimorbidity, kept active and operative on their jobs.

The findings that 34.5% of the population had depressive disorder, 25.3% present generalized anxiety disorder (GAD), 25,3% systemic arterial hypertension (SAH), 16.1% had fibromyalgia and that 11.5% had sleep disorder echoes other studies, such as the study by D'Amico *et al*. (2018) that carried out a detailed description of chronic migraine subjects morbidities, mainly psychiatric and cardiovascular. Cuciureanu *et al.* reveal similar results: anxiety and depression are two of the most prevalent comorbid conditions associated with migraine (Cuciureanu *et al*., 2024).

The presence of multiple conditions, that is also called multimorbidity, is a risk factor for migraine or chronic migraine persistence. Previous studies have found increased psychiatric comorbidity in chronic migraineurs, Migraine is a prevalent and disabling neurological disorder which is commonly linked with a broad range of psychiatric comorbidities, especially among subjects with migraine with aura or chronic migraine (D'Amico *et al*., 2018). Subjects with migraine and coexisting psychiatric disorders were described to have poorer treatment outcomes and greater disability scores (Jeyagurunathan *et al*., 2020).

Roughly one-fourth of the subjects (26%) reported conditions pertaining to CIRS Neurological System, and in most cases this condition was insomnia which was reported to be the most common sleep complaint among a chronic migraine population (Yang; Wang, 2017). These authors also point out that chronic migraine subjects present more insomnia than those with episodic migraine. Whether insomnia is only associated with chronic migraine, actively contributes to its chronification or is only a symptom of associated psychiatric conditions remains to be answered.

Musculoskeletal pain, the fourth condition most associated with chronic migraine in our population, echoes the early works that found chronic migraine associated with a higher incidence of back pain, fibromyalgia and other musculoskeletal pain conditions (Hovaguimian; Roth, 2022). In addition, as compared to non-migraine subjects and to people with other chronic diseases, chronic migraineurs report more severely impaired physical, mental and social functioning, especially those with a high frequency of headache attacks.

There are evidences showing that in migraine patients, as the number of headache days increase, disease burden such as disability, use of Health Services and direct costs also increase, so it is important to analyze these aspects to guide treatment decisions and management strategies.

Besides knowing the factors that contribute to migraine chronification, the use of new treatment approaches, such as monoclonal antibodies, that spare oral medications and simplify medication schedule, and an organized approach to chronic migraine multimorbidities seem to be important points not only to revert chronic migraine but also to reduce the burden of its associated conditions and its polymedication. Thus, the headache specialist should be able not only to identify multimorbidities, but also to evaluate their severity and the effectiveness of their therapies, being this way able to propose consistent treatments to patients.

3 CONCLUSIONS

Information about the presence of associated conditions in chronic migraine patients, as well as their polypharmacy profile is important to understand and well manage this patient and also avoid the increase of medication load and knowing its risks.

The findings of our study show that chronic migraine has an extensive disease and medication load, and that the most relevant of them relates to the psychiatric domain, responsible for most prevalent associated medical conditions and concomitant medication. Knowledge on the presence of associated condition and the polypharmacy profile is important to better understand, propose specific treatment and avoid the increase of medication load.

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