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Chronic migraine with medication overuse: Association between disability and quality of life measures, and impact of disease on patients' lives

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ABSTRACT

Patients with chronic migraine with medication overuse (CM-MO) have decreased quality of life (QoL) and increased disability: the degree to which these outcomes are connected to disease severity and the pattern of MO towards disease severity are unclear. Patients under withdrawal were administered the Migraine Disability Assessment (MIDAS), the WHO Disability Assessment Schedule (WHODAS), and the Migraine-Specific Quality of Life Questionnaire (MSQ). They overused NSAIDs, triptans, NSAIDs and triptans, and other drugs (ergotamine, caffeine, opioids/barbiturates). We calculated the correlations between MIDAS, WHODAS, and MSQ; compared WHODAS to normative scores; compared MIDAS, WHODAS, and MSQ in patients with different CM-MO severity; and run a logistic regression to predict CM-MO severity based on overused drugs. One hundred ninety-four patients were enrolled: correlations between WHODAS, MSQ, and MIDAS were moderate; wide differences on WHODAS against normative were found; and no trend was found across severity groups. Compared to triptans overusers, patients overusing NSAID and other drugs had higher odds of severe CM-MO. Coupling different disability measures with QoL assessment offered different insights on the lived experience of CM-MO. Future studies are needed to clarify the relationship between overused drugs and CM-MO severity: we added evidence that NSAIDs do not have protective effect in high-frequency CM-MO.

1. Introduction

Chronic migraine (CM) is characterized by headaches occurring 15 or more days per month and can be considered as a negative evolution of the migraine course in a subgroup of subjects [1]. CM prevalence in population studies ranges from 1.4% to 4% and from 2.5% to 3% of migraineurs (14% in clinical samples) progress to CM each year [2–5]. Several factors may play a role in the progression from episodic migraine (EM) to CM, such as lifestyle, comorbid conditions, metabolic dysfunction, mood, genetic terrain, and medication overuse (MO) [1,6,7]. CM is strongly associated with the overuse of non-steroidal analgesic drugs (NSAIDs) as these drugs can widely be accessed as over the counter medications: the fact that frequent use of symptomatic drugs is a risk factor for progression of migraine marks an important difference with other pain-related conditions [8]. Indeed all acute drugs may be associated with chronification, but it is not clear if and how the disease's features are related to the different overused drugs [9] and the mechanisms for chronification are not completely understood yet.

The pattern of overused medication varies across time and countries [10]. A community pharmacy-based study showed that one-fourth of patients overused acute medications and that combination of three or more agents was more frequent in overusers compared to non-overusers: overusers also had higher headache-related, headaches frequency, and higher pain intensity [11]. Findings on chronification process connected to the class of overused medication are however partial and contrasting. Some evidence exists on the increased risk of chronification in patients using triptans, but only in those with a baseline frequency around 10–14 headaches/month, and of the protective effect of NSAIDs in low-frequency migraine sufferers [12,13]. Barbiturates and opioids have also been found to induce migraine progression, with a dose-dependent effect [12].

Recent reviews showed that health-related quality of life (HRQoL) is significantly impaired in persons suffering from chronic forms of headache, compared to non-headache sufferers, as well as compared to those with EM, and that this negative impact is more evident in those suffering from CM, particularly when MO is present [14,15]. CM causes physical health and emotional problems and determines increased disability,

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measured in terms of absenteeism and days with reduced workplace effectiveness; therefore, it has remarkable consequences in terms of increased disease cost, which is three-fold that of EM (3561€/year vs 1222 €/year) [16].

Previous studies addressing disability in chronic migraine with medication overuse (CM-MO) [17–21] generally used the Migraine Disability Assessment (MIDAS) [22]. However, the use of MIDAS in CM patients poses some problems. First, the highest severity grade corresponds to a score > 21, which is intuitively overrepresented among patients reporting more than 45 headaches in the previous three months. In addition, the conceptualization of disability behind MIDAS is highly dependent on headaches frequency and does not account for other features of CM such as reduced mood or obsessive or anxiety disorders but also for the severity of pain, which are likely to impact on functioning in social and workplace roles, particularly as far as interpersonal relationships [17,23,24].

A model that recognizes disability in a multidimensional way is therefore needed. Such disability model should correspond to that endorsed by the World Health Organization (WHO) with the International Classification of Functioning, Disability and Health (ICF) [25]. The understanding of the possible relationships between disability—particularly when viewed as a multidimensional phenomenon—and HRQoL in patients with CM-MO may enhance the understanding of this disorder and help clinicians and researchers in choosing the most appropriate patient-reported outcome measure (PROMs) in specific studies. The WHO also produced an ICF-based disability assessment, the WHO Disability Assessment Schedule second version (WHODAS) [26]: previous studies with neurological patients (namely, EM, myasthenia gravis, epilepsy, stroke and Parkinson's disease) showed that it is suitable to address the increased disability level of patients as well as a moderate association with HRQoL assessments [27–31]. To our knowledge, the relationship between disability, assessed with an instrument like the WHODAS, and HRQoL measures in CM-MO was never addressed.

The primary aim of this study was to assess the relationships between two disability measures, MIDAS and WHODAS, and between them and patients' HRQoL, in order to assess whether these different tools cover similar constructs or offer the possibility to evaluate different facets of CM-related impact: we expect to expand to the sample of CM-MO patients the findings of a previous study on EM patients, i.e., that MIDAS and WHODAS are only partially correlated and that the correlations with HRQoL are mild to moderate. The secondary aim was to address the impact of CM-MO on patients' disability. This was performed with three different procedures: (a) the evaluation of the impact of CM-MO on patients' disability compared to the general population, with the hypothesis that CM-MO patients report worse scores at WHODAS; (b) the evaluation of the extent to which differences in PROMs scores correspond to different severity profiles—based on frequency and intensity of headaches—with the hypothesis that PROMs scores cannot be completely explained by differences in CM-MO severity; and (c) the evaluation of the relative risk of having a more severe disease profile accounting for the type of overused drug, with the hypothesis that those overusing NSAIDs have are more likely to have the most severe profile.

2. Methods

2.1. Patients, procedure, and measures

In this cross-sectional observational study, adult patients with CM-MO according to Silberstein's criteria [32] were consecutively recruited at the Headache Centre of the Neurological Institute C. Besta of Milan between June 2011 and December 2012. Patients were enrolled on occasion of inpatient withdrawal treatment: the questionnaires were provided on the second or third day of hospitalisation. There are two reasons for this: first, to enable physicians to evaluate patients' eligibility; second, to make it more likely that patients were headache-free during administration of the protocol. In any case, they were allowed to postpone it if they had an headache. The study was approved by the institute's ethical committee, and each patient signed an informed consent form prior to data collection. All enrolled patients completed the Migraine-Specific Quality of Life Questionnaire Version 2.1 (MSQ) [33] to evaluate HRQoL, the WHODAS [26,34], and the MIDAS [22,35] to evaluate disability. Headache frequency and average pain intensity were taken from the last two MIDAS items. Mood state was assessed with the Beck Depression Inventory [36].

MSQ is based on 14 items that investigate the impact of headaches on patients HRQoL during the previous 4 weeks. The items are grouped into three subscales: Role Restriction (RR), 7 items assessing how migraines limit one's daily social and work-related activities; Role Prevention (RP), 4 items assessing how migraines prevent social and work-related activities; and Emotional Function (EF), 3 items assessing the emotions associated with headaches. Each item refers on how frequently headaches limits the activity under consideration and is rated on a 6-point scale from none of the time to all of the time. Each subscale has a 0–100 score, with lower scores indicating poor HRQoL. MSQ has been used as an outcome measure in clinical trials, mostly on preventive medications [37–41]: however, its use in research on patients with CM or other types of chronic headaches is limited [37–39]. In its Italian version, it has been used in one observational study in which patients with different type of migraine, of whom 2.5% had CM-MO, were evaluated [42]. Recently, three studies confirmed its validity in CM patients [43–45]: however, the presence of MO was explicitly excluded in the first study, which is based on the *International Classification of Headache Disorders*, 2nd version criteria for CM [46]; in the second study, only 60% of patients had concurrent MO; in the third study, all patients had CM-MO. Therefore, the use of MSQ in patients with CM-MO is restricted to two studies [38,45].

WHODAS is a 36-item ICF-based disability assessment tool that examines the difficulties experienced by an individual due to a given health condition. Six domains are taken into account: understanding and communicating, getting around, self-care, getting along with people, life activities (divided into household and work), and finally participation in society. Patients are required to answer questions regarding how much difficulty, due to their health condition, they experienced during the previous 30 days. Answers are rated on a 5-point scale, from no problems to complete problems/cannot do the activity. Both total and subscale scores are available, ranging from 0 to 100, with higher scores reflecting greater disability. Total score can be calculated also on the basis of 32 items, excluding those related to work activities if the respondent is not currently employed.

MIDAS is composed of 7 questions referred to the preceding 3 months: the first 5 investigate the influence of headaches on paid and school work, household work, and on leisure/family/social duties. MIDAS score is calculated by adding the individual scores of the first 5 questions and indicates the number of days in which migraine interfered with these activities. According to given intervals, 4 disability grades can be calculated: minimal (0–5), mild (6–10), moderate (11–20), and severe (≥21) disability.

BDI-2 is composed of 21 items, each rated on a 0–3 scale, that address cognitive and somatic-affective features of depression. Total score range is 0–63, with higher scores reflecting higher depressive mood.

2.2. Definition of medication overuse categories

The different types of MO were defined as follows: overuse of non-steroidal anti-inflammatory drugs (NSAIDs), when NSAIDS were used for at least 15 days/month; overuse of triptans, when any drug of this class was used for at least 10 days/month; overuse of both NSAIDs and triptans, when NSAIDs were used for at least 15 days/month and triptans for at least 10 days/month; overuse of ergotamine, caffeine,