Portuguese Version of the Medication Adherence Report Scale (MARS-9): Validation in a Population of Chronic Pain Patients

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Abstract

Aim

The aim of present study was to perform the translation, cultural adaptation and validation of the Medication Adherence Report Scale (MARS-P9) for the European Portuguese language in a sample of chronic pain patients.

Methods

A Portuguese version of the 9 items MARS (©Professor Rob Horne) scale (MARS-P9) was constructed through a process of translation, back translation and experts' panel evaluation. A total of 141 chronic pain patients were subsequently evaluated at four time assessments during a one-year pain medication treatment. The protocol interview included the assessment of pain intensity and interference (BPI), clinical outcomes and quality of life (S-TOPS) and MARS-P9.

Results

The internal consistency coefficient was acceptable for the total scale (α = 0.84). Exploratory factor analysis revealed a 2-factor structure (intentional and unintentional non-adherence) that explained 61% of the variance. Convergent and discriminant validity were demonstrated by correlations between MARS scores and Pain interference (r=0.180, $p \leq 0.01$) and S-TOPS (r=0.242, $p \leq 0.05$).

Conclusion

MARS-P9 has been shown to be an adequate instrument for Portuguese researchers and clinicians to assess the pattern of adherence during the management of chronic pain.

Keywords

Medication Adherence; Chronic pain; Longitudinal assessment; Self-report

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Introduction

Chronic pain has been defined, by the International Association for the Study of Pain (IASP), as pain that persists past the normal healing time and hence lacks the acute warning function of physiological nociception; pragmatically, it has been defined as pain lasting or recurring for more than 3 months [1,2]. Chronic pain is generally recognised as an exceedingly common condition [3] and a major public health problem, with very important physical, psychological and familial consequences [4-9]; thus, it should and it has received great attention as a global health priority [9]. As a chronic condition, chronic pain management requires a complex combination of therapeutic methods. Notwithstanding, pharmacological interventions remain the cornerstone of its treatment [10,11], with over 60% of chronic pain patients using medicines as a therapeutic option [11]. In Portugal, a study that included a representative sample of the adult general population revealed a total of 76% of individuals with chronic pain using pharmacological therapy [12].

Non-adherence to prescribed medication remains the major problem faced by health care systems when managing chronic diseases, becoming a missed opportunity for improvement of health outcomes, a waste of resources [13] and a possible explanatory factor for high mortality and morbidity [14]. Medication adherence refers to the patient's compliance with the provider's

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recommendation with respect to timing, dosing and frequency of medication-taking during the prescribed length of time [15].

Despite the effectiveness of pain medicines, they are quite often misused, with almost 50% of medication not taken as prescribed [13]. Moreover, an important recent Portuguese study that analysed the direct and indirect costs associated with chronic pain revealed a total €481.59 million of annual costs for the Portuguese population (95%CI [423.63 to 552.68]) associated with pain medicines [16].

Since the WHO Adherence meeting in 2001, it is well accepted that there is no "gold standard" for measuring adherence behaviour. However, it is recognized that using questionnaires meeting basic psychometric standards, to assess specific behaviours related to specific medical recommendations, allows a better prediction of the adherence behaviour [15]. The Medication Adherence Scale (MARS) (©Professor Rob Horne), developed in England, is a feasible self-reporting scale addressing non-adherence behaviour in a non-threatening and non-judgmental way, which may result in truthful answers, used in a range of long-term conditions. This is a generic tool, which can be used to assess any prescribed drug regardless of the health condition. Adherence is measured as a continuous scale, rather than dichotomous adherent/nonadherent categories, producing an ordinal instead of an interval scale assessment. The MARS (©Professor Rob Horne) has been validated in different languages in different clinical settings and countries and is available in 5, 9 and 10 items[17-23]. All versions contain a common set of 5 items (MARS-5), e.g. *"I forget to take my medicines"*. In other versions condition specific items are added (e.g. *"I only use it when I feel breathless"*). The MARS-P9 uses the extended approach, with additional condition specific items.

Because adherence is a multidimensional phenomenon, biological, psychological and social features must be explored and included. Therefore, to promote a more comprehensive evaluation of adherence, it is crucial to have valuable instruments to guide health care providers in its assessment during the patient care process. Hence, the aim of this study was to provide a translated

and culturally adapted Portuguese version of the 9 item MARS (MARS-P9), to appraise its applicability, reliability, validity and internal consistency and if it is a suitable instrument for measuring pain medication adherence longitudinally, over four-time assessment points along a 12 months' treatment period.

Methods

Translation and cultural adaptation

For the development of the Portuguese version of MARS-9 the guidelines for translation and adaptation of self-report instruments reported by the ISPOR Task Force for Translation and Cultural Adaptation, were followed [24]. The English version of MARS was first translated into Portuguese by two independent professional Portuguese native speakers. The back translation was performed by an outsourced translator, unware of the original instrument and with no connection to the research group. The similarity between versions (the original, the translated and the back translated) were assessed by a panel of three experts from our research group (a methodologist with experience in psychometrics, a clinical psychologist and a professor of pain medicine) and all disparities and ambiguities were examined and resolved by consensus. Finally, the back translation was approved by Professor Rob Horne. The research group removed the first item – *"I only use my [NAME OF MEDICINE] when I need it"*, because of the variability of medicines in use for chronic pain treatment. Also, two other changes were performed to adapt for the study and participants' characteristics, namely: *sick* to *pain* and *inhaler* to *medication*. The revised preliminary Portuguese version of MARS-9 was applied to a small pilot sample of ten chronic pain patients, native in Portuguese language, to assess the comprehension of the language and wording. The final Portuguese version of the MARS-9 was defined and used in the validation sample to assess its validity and reliability.

Participants and Procedure

During a seven-month period, from May to December 2013, 225 consecutive patients, referred to a first consultation in a Chronic Pain Clinic in a tertiary university hospital in Porto, north of

Portugal. Patients followed a standardized protocol that included a first face-to-face interview performed by two trained interviewers and with the attending physician and nurse collaboration, followed by three-time specific telephone interviews - seven days (T7), six months (T6) and twelve months (T12) after baseline interview (T0). A total of 141 patients' respondents in the three follow-up times composed the final sample of the study and were divided in 'adherents' and 'non-adherents' (Figure 1). Non-adherence was defined in terms of the direct response of each patient to the fowling questions: "Is there any medicine that you have decided not to take?" and "Is there any medicine that you have decided not to take as prescribed?" If at least one of the patient's answers was positive, it was considered as being non-adherent. The protocol interview included an assessment of pain intensity and interference, using the Portuguese version of the Brief Pain Inventory (BPI), clinical outcomes and quality of life using the Portuguese version of the Short Form of the Treatment Outcomes in Pain Survey (S-TOPS), and MARS-P9.

The exclusion criteria included the inability to communicate in Portuguese language and the presence of psychiatric and cognitive disorders precluding the interviews. The study protocol was approved by the hospital review boards and ethics committee (FMUP/HSJ 236-13).

Instruments

Medication Adherence Rating Scale (MARS)

The MARS (©Professor Rob Horne) evaluates non-adherence in a non-threating way, where questions are posed as a negative statement to minimize social desirability bias [18]. MARS is available in several versions (with 4, 5, 9 and 10 items), languages (English, German and Arabic) and in a range of long-term conditions (asthma, cardiovascular diseases, chronic obstructive pulmonary disease, diabetes, inflammatory bowel disease, depression and bipolar disease [17,18,20-22,25-29]. The MARS-A-10 contains 9 items assessing intentional aspects of non-adherent (e.g. "*I decide to miss a dose"*) and one assessing unintentional non-adherence *(e.g."I forgot to take it")* behaviours to treatments [18]. Responses are recorded in a 5-point Likert scale, ranging from 1

(always) to 5 (never) and only one item (9) is inverted. Higher scores indicate higher adherence. For the purposes of the present study, and as explained in the translation and cultural adaptation section, item 1 was deleted and two words were suitably changed (*pain* and *medication*). MARS has been shown to have good psychometric properties [25,26] and invariability of intentional non-adherence items in a longitudinal analysis [18].

Brief Pain Inventory (BPI)

BPI is a simple and short questionnaire composed of 15 items aiming to assess two scales: pain intensity and pain interference. The pain intensity scale contains 4 pain intensity items of maximum, minimum, on average, and right now measured with an 11-point numeric rating scale, ranging from 0 (no pain) to 10 (the worst pain possible). The pain interference scale is composed by 7 items of patient's pain-related interference regarding general activities, mood, walking ability, normal work, relations with other people, sleep and enjoyment of life measured also with an 11-point scale, ranging from 0 (no interference) to 10 (extreme interference). BPI is translated in 10 different languages, including a Portuguese version [30] and has been shown to have excellent psychometric properties. Therefore, it is an instrument recommended for clinical and epidemiological research and highly consensual on the guidelines for pain assessment [31].

Shortened and restructured Treatment Outcomes in Pain Survey (S-TOPS)

S-TOPS is an intuitive instrument to assess clinical outcomes and quality of life in pain patients and allowing measurement of the magnitude of change following pain treatment [32]. It contains a total of 29 items divided in 7 scales: 1) Pain symptom; 2) Physical function-lower body; 3) Physical function-upper body; 4) Family and social disability; 5) Role-emotional disability; 6) Patient satisfaction with care; and 7) Patient satisfaction with outcomes. Each scale score is expressed in a range from 0 (no disability/pain) and 100 (maximum disability/pain), except for the 6) and 7) scales which are inverted, ranging from 0 (no satisfaction) and 100 (maximum satisfaction).

It has excellent psychometric properties and sensitivity to change in longitudinal assessment [32].

Statistical analysis and assessment of reliability and validity

Descriptive analyses of the general characteristics of the sample were performed. Categorical variables were described as absolute frequencies (*n*) and relative frequencies (*%*). Summary statistics were presented for each item, subscale and scale, considering also values of missing data and the proportions of scores in the extremes, in order to assess the ceiling and floor effects [33].

Construct validity was assessed by performing factor analysis with principal component and varimax rotation methods [34]. The suitability of factor analysis was confirmed by checking the existence of significant correlations between items and took into account the Keiser-Meyer-Olkin criterion and the Bartlett's sphericity test.

Assessment of convergent and discriminant validity was performed by calculating a set of theoretical hypotheses about interrelations among pain and clinical outcomes and quality of life scales and subscales. It has been assumed a correlation between pain intensity and interference with non-adherence and a correlation between non-adherence and worst clinical outcomes and quality of life domains [11].

Mann-Whitney U tests were performed to compare the total scores of MARS in each assessment moment between the adherents and non-adherents, taking into account the asymmetric distribution of the continuous variable.

For all hypothesis tests a significance level of $\alpha=0.05$ was specified. The statistical analysis was performed using the software program Statistical Package for Social Sciences (SPSS version 24.0).

Results

General Characteristics of the sample

The final sample of participants (n=141) selected for the validation study was composed of 104 females and 37 males, between 23 and 75 years old, with a mean age of 61 years (sd=14.4). They lived predominantly with husband/wife (69%) and completed four or fewer years of education (51%), only 12% having a higher education degree. Most of them were retired (53%), 37% had a full-time job and 10% were unemployed. According to the recent Chronic Pain Syndromes Classification by IASP [35], the distribution of the main pain diagnosis was as follows: musculoskeletal (50%), neuropathic (23%), chronic primary pain (14%), post-surgical or post-traumatic (6%), visceral (4%), oncologic (1%) and headache and orofacial (1%).

Item Descriptive Analysis and Missing Data

Items and subscales of MARS-P9 are presented in Table 1. There are ceiling effects in every items, but no floor effects. Missing data for all items is lower than 1%.

Internal Consistency and Factor Analysis

The analysis of internal consistency of MARS-P9 is presented in Table 2. Cronbach's alpha coefficient of internal consistency was excellent for the total scale (α=0.84). Internal consistency of intentional adherence scale was also excellent (α=0.87).

Construct validity was assessed by performing factor analysis with principal components and varimax rotation methods [34]. The suitability of factor analysis by checking the existence of significant correlations, between the items, was confirmed by Kaiser-Meyer-Olkin (KMO=0.849) and by the Bartlett's sphericity test (QQ=540.996; gl=36; $p<0.001$). Two factors with eigenvalues greater than 1.0 were extracted accounting for 61% of total variance. It yielded eight items with component loadings greater than 0.40 that composed the first factor and explained 49% of the item variance. The second factor, composed by one item loaded greater than 0.40 and accounted for an additional 12% of the variance.

Convergent and Discriminant Validity

A moderate correlation between unintentional non-adherence and pain interference subscale was found (r=0.180, p≤0.01), as shown in Table 3. Only the sub-scale of physical function lower-body was strongly correlated with total adherence (r=0.242, p≤0.05). No other significant correlations were observed.

Differences in Total MARS between Adherents and Non-adherents during one year (T7D, T6M, T12M)

After seven days of treatment, 31% of patients were non-adherent and 67% were adherent. At six months of treatment, an equal distribution in the two groups was observed (49.6% were non-adherent and 50.4% were adherent). Finally, after one-year of treatment, 52.5% of patients were non-adherent and 45.4% adhered to prescribed medication. Significant differences (Graph 1) were observed between adherents and non-adherents concerning the total score of MARS in the three assessment moments: seven days (U=2985.0, p<0.001); six months (U=2897.0, p=0.022); and twelve months (U=2755.5, p=0.002).

Discussion

The importance of non-adherence to treatment regimens is well recognized in research and clinical settings. Moreover, it is well accepted that no single method is considered to be a gold standard to measure adherence, instead it is recommended combining assessment methods [15,36]. To the best of our knowledge, there's no available validated instruments to measure adherence in the field of pain treatments regimens and for the Portuguese language. Accordingly, the aim of present study was the translation, cultural adaptation for Portuguese language and the assessment of the validity of MARS-P9, following international recommended guidelines. The protocol for translation, cultural adaptation and validation was performed as outlined, developing a validated Portuguese version of MARS showing excellent psychometric properties. Internal consistency measured by Cronbach's alpha was excellent (α=0.84) and superior when compared to a sample of asthma patients (α=0.83) [37] and with a sample of rheumatoid arthritis patients (α=0.77) [26].

Concerning the factorial validity of MARS-P9, the 2-factor structure found in the present study fall into two categories, assuming an intentional and an unintentional non-adherence behaviour [18]. Unintentional non-adherence was only assessed with one item as observed in other studies [18,26]. Although the recognition of an overlap between intentional and unintentional adherence behaviour by a growing number of studies [38,39], these two constructs may provide a better understanding of both types of non-adherence behaviour [40-42]. A recent study in older adults showed that intentional non-adherence could vary between 33 to 75% [40].

MARS-P9 may be better detecting non-adherence than using a dichotomous scale with suitable definitions. In this scenario patients have the possibility of expressing their non-adherent behaviour in vary degrees and in a non-judgmental way [18,21]. Interestingly, using more 'objective' methods of asthma medication non-adherence assessments was found to be similar to use the MARS scale [17].

In the present study, the percentage of adherence and non-adherence is similar to the calculated weighted mean of 40% presented in a recent systematic review [11]. In this case, we used two direct and dichotomous questions to place each patient in a particular group of adherence. A strong association between MARS-P9 scores and the categories of adherent or non-adherent was observed. Notwithstanding, no other direct assessment of the criterion validity of MARS-P9 was performed. Indeed, we take into account hypothetic correlations between several interrelated dimensions of clinical outcomes and quality of life in pain patients and pain severity and interference. Only the dimension of physical function lower-body was related to total non-adherence, which is interesting because of the objective impairment created when patients perceive their limitation in physical function lower body, which is pointed as the main change occurring in the population when measuring sensitivity to change [32]. The significant differences observed in each assessment moment may provide some evidence demonstrating that MARS-P9 capture the differences between adherent and non-adherent patients over time. The results of MARS-A-10 for asthma patients provided evidence of its invariance over the time, which may support that the changes in the scores can be attributed to changes in non-adherence behaviour [18].

We believe that identifying patients at risk of non-adherence to pain medicines, using MARS as a self-report measure in clinical practice, is simple, inexpensive and may preclude some previous clinical judgment [36]; and this should be part of a multimethod approach. Assessments with MARS-P9 could be the first step before adherence enhancing interventions can be implemented and a good instrument for longitudinal studies evaluating non-adherence behaviour over time. Although MARS-P9 is an indispensable measure for perceiving non-adherence behaviour, together with questions about objective patterns of treatment use and reasons for non-compliance, it could give reliable information about non-adherence patterns. Therefore, social desirability and recall bias could be controlled or even suppressed.

Limitations

This study must be interpreted taking into account its main limitations. First, this is the first validation of MARS in a population of Chronic Pain patients and prescribed with a heterogeneous set of medications in terms of Pharmacologic-Therapeutic Classification. Second, the socio-demographic characteristics of the sample have to be taken into account, namely the low literacy level and older ages, reflecting the characteristics of the real chronic pain population in Portugal. Although the dichotomous approach (intentional vs unintentional non-adherence) was considered, a small number of studies pointed that there may be an overlap between these two constructs, as was referred before [38,39].

Despite these limitations, MARS-P9 has demonstrate to be adequate and to have excellent psychometric characteristics. Although some questions regarding factor structure and the classification of non-adherence in terms of intentionality and unintentionality, MARS-P9 could be a valuable and available instrument for Portuguese researchers and clinicians to assess the pattern of adherence, during the management of Chronic Pain. We hope to emphasize the need to look at non-adherence from the patient perspective during the treatment of chronic pain.

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