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Development and validation of a multidimensional questionnaire assessing non-adherence to medicines

ABSTRACT

The study aimed to develop and validate an instrument capable of measuring non-adherence to drug treatment in its multiple dimensions. The *Questionário de Adesão a Medicamentos* (Adherence to Medicines Questionnaire) with three questions was applied to 46 people with arterial hypertension in the city of Blumenau, Southern Brazil, in 2006. Non-adherence measures obtained were compared to four other methods (Haynes, Morisky, pill count and clinical outcome). Non-adherence measures varied according to the method. The combined *Questionário de Adesão a Medicamentos* non-adherence measure was 47.8% (95% CI: 32.9;63.1), whereas the gold standard was 69.6% (95% CI: 54.3;82.3). Accuracy measures to detect non-adherence showed a sensitivity of 62.5% and specificity of 85.7%, ROC curve area of 74.1%, and positive predictive value of 90.9%. Results suggest the *Questionário de Adesão a Medicamentos has a good fit.*

DESCRIPTORS: Patient Compliance. Questionnaires. Sensitivity and Specificity. Validity of Tests. Health Evaluation.

INTRODUCTION

Non-adherence to drug treatment is not only related to the act of taking or not taking medication, but also how the patient "manages" his/her treatment: behavior towards the dosage, times, frequency and duration. Conceptually, non-adherence must be viewed as a multiple-dimension construct.

There is no consensus about the measurement method that can be taken as the gold standard.[8] Studies show low or moderate correlation among methods, which can be attributed to the fact that they measure distinct dimensions of a same construct, the establishment of different non-adherence cut-off points, or even the limitations of the methods themselves.[1,3] These questions result in varied non-adherence frequency measures throughout time and among diverse pathologies.[2]

In general, electronic dosage monitoring, which allows for the estimation of dosages taken and respective times, has been used as the gold standard to validate other methods. Manual pill count (a cheaper and easier alternative) is also used to estimate dosages taken.[1,4] Structured questionnaires are widely employed to measure non-adherence due to their operational ease and low cost, even though they have, in their majority, low sensitivity and positive predictive value.[3,4] Thus, the combined use of methods is recommended to improve accuracy.[8]

The present study aimed to develop and validate an instrument capable of measuring drug treatment non-adherence (in its multiple dimensions) among people with arterial hypertension.

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METHODS

Development of the QAM-Q questionnaire

A self-reported adherence questionnaire, entitled *"Questionário de Adesão a Medicamentos - Qualiaids* – QAM-Q (Medication adherence questionnaire), was developed to approach the act of adherence (if the individual takes medication and how much he takes), its process (how he takes this medication in the 7-period day, if he skips dosages, if he takes it irregularly or if he "takes breaks"), and its results (in this case, if his blood pressure was under control).

The following three questions were asked:

1. "In the last seven days, on what days did you not take or take at least one additional pill of medication? (days of the week informed by the interviewee were marked).

2. "On these days, how many pills did you not take or take in addition?" (pills that were not taken or taken additionally were marked in the corresponding times).

3. "What was your blood pressure the last time you had it measured?"

These questions were preceded by an inventory of the interviewee's activities in the previous seven days, followed by an introductory comment that aimed to reduce a feeling of being judged by the interviewer, in case the interviewee mentioned not taking his medication. The QAM-Q was piloted among ten people to correct and adjust questions.

The questionnaire enabled the construction of the following non-adherence measures:

1. Proportion of dosages taken – continuous adherence measure: number of pills taken, multiplied by the number of times, divided by the number of pills prescribed, multiplied by the number of times.

2. Process of taking pills – ordinal measure of the adherence process: frequency of occurrence of neglect (patient did not take any dosages of medications in the previous seven days), "breaks" (patient did not take any medication on that particular day), "taking it irregularly" (patient stops taking medication on different days and at different times), or "partial adherence" (patient takes one medication correctly and the other incorrectly).

3. Reported outcome – dichotomous measure of adherence results: report on the last blood pressure measurement, informing whether it was normal or altered.

A combined measure was constructed, in which the presence of one of these conditions was enough to classify the interviewee as non-adherent: either not taking the correct amount (80%-120% of prescribed dosages), or not taking it in the correct way (without "breaks", "taking it irregularly", "neglect" or "partial adherence"), or reporting that his arterial pressure was altered.

Instrument validation

A total of 46 people with arterial hypertension, who were cared for in one of the ten family health units in the city of Blumenau, southern Brazil, during February of 2006, were studied. These people were randomly selected (sample process is described in another study).[a] Qualified interviewers went to interviewees' homes and applied base questionnaire to collect data on sociodemographic, clinical and therapeutic scheme characteristics.

After seven days, interviewers returned to these homes to apply the QAM-Q. Results obtained by the QAM-Q were compared to those obtained by other non-adherence measurement methods:

1. Questionnaire by Morisky et al,[7] which consists of four questions: 1. "Do you ever forget to take your medication?"; 2. "Are you sometimes careless about taking your medication?"; 3. "When you feel better, do you stop taking your medication at times?"; 4. "If you feel worse when taking the medication, do you occasionally stop taking it?". An affirmative response to any of these questions classifies the individual as non-adherent.

2. Question by Haynes et al:[5] "Many people have some kind of problem to take their medication. In the last 30 days, have you had difficulties to take your blood pressure medication?". An affirmative response classifies the individual as non-adherent.

3. Manual pill count: proportion of pills taken, divided by prescribed pills. Those who took less than 80% or more than 120% of prescribed dosage are considered non-adherent.

4. Clinical outcome: arterial pressure measurement; people whose measurement was equal to or above 140mHg of systolic blood pressure or 90mmHg of diastolic blood pressure are considered non-adherent.

At the end of the interview, manual pill count and arterial pressure measurement with aneroid sphygmomanometer were performed, in accordance with the methodology recommended by the *IV Diretrizes Brasileiras de Hipertensão Arterial* (IV Brazilian Guidelines on Arterial Hypertension).[6] The frequency

[a] Santa Helena ET. Adesão ao tratamento farmacológico de pacientes com hipertensão arterial em unidades de saúde da família em Blumenau, SC [Doctoral thesis]. São Paulo: Faculdade de Medicina da USP; 2007.

values of non-adherence measures obtained by varied methods were calculated with the respective 95% confidence intervals (95% CI).

The association among several non-adherence measures was estimated by Spearman's correlation test, with a p-value<0.05 considered statistically significant.

Criterion validity was established through the calculation of sensitivity, specificity, ROC (receiver operator characteristic) curve area and positive and negative predictive values. A combined measure was used as gold standard, defining as non-adherent an individual who either took less than 80% or more than 120% of the prescribed pills (manual pill count), had a "non-adherent behavior" (according to Morisky et al's questionnaire[7]), or if his arterial pressure was equal to or higher than 140 x 90mmHg.

The study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Commission for Research Project Analysis at the *Hospital das Clínicas da Faculdade de Medicina da USP.*

RESULTS

The sample analyzed was found to be representative of the study population, once statistically significant differences in relation to clinical and sociodemographic characteristics were observed.

The non-adherence values measured varied according to the method used. Non-adherence as estimated by the Haynes question was 8.7% (95% CI: 2.4;20.8). Higher non-adherence values were obtained with the employment of the Morisky questionnaire, 43.4% (95% CI: 28.9;58.9), as well as the manual pill count, 43.4% (95% CI: 28.9;58.9). A total of 21.7% were considered non-adherents through the clinical outcome (95% CI: 10.9;36.4). The result of the combined non-adherence measures using manual pill count, Morisky, and clinical outcome (gold standard) was 69.6% (95% CI: 54.3;82.3).

The measures constructed from the QAM-Q also showed variation. Non-adherence as estimated by the "proportion of dosages taken" was 17.4% (95% CI:

7.8; 31.4), 28.3% by the "process of taking pills" (95% CI: 16.0;43.5), and 30.4% by the "reported outcome" (95% CI: 17.7.;45.8). The combined measure obtained from the QAM-Q resulted in 47.8% of non-adherence (95% CI: 32.9;63.1).

The correlation between the "proportion of dosages taken" measured by QAM-Q and the "manual pill count" was 0.54 (p<0.001), whereas the correlation between the "process of taking pills" measured by the QAM-Q and "Morisky" was 0.32 (p<0.05). In addition, statistically significant correlation was obtained between "Haynes" and "Morisky" (0.41; p<0.01). The correlation between the QAM-Q and the gold standard combined measures was 0.44 (p<0.01).

The Table shows values of sensitivity, specificity, ROC curve area and positive and negative predictive values of QAM-Q non-adherence measures in relation to the gold standard.

DISCUSSION

Different non-adherence results among the methods were observed, once they are measuring distinct dimensions of the same construct (some focus on the "dosage", others on "behavior", and yet others on adherence results), varied time periods (some non-temporal, others referring to 7-day or 30-day periods), or even characteristics or limitations of the methods themselves.[1] The combined measures, from both the QAM-Q and the gold standard, were found to be "stricter" than the other measures, that is, with higher non-adherence values.

The correlation measures were from moderate to low, but they were found to be similar to or higher than those observed in other studies.[1,3,4] The correlation values obtained between the proportion of dosage reported by the QAM-Q and the manual pill count, and between the process of taking pills and Morisky suggest that comparable dimensions are being measured.

As regards criterion validity, the QAM-Q showed good fit, similar to other instruments'.[1,4,5,7,8] The combined measure showed better fit than the isolated measures,

Table. Percent values of sensitivity, specificity, ROC curve area, and positive and negative predictive values of non-adherence measures by the Medication adherence questionnaire (QAM - Q).

Method	Sensitivity	Specificity	ROC curve area	+ PV	- PV
1. Dosage	25.0	100.0	62.5	100.0	36.8
2. Process of taking pills	40.6	100.0	70.3	100.0	42.4
3. Reported outcome	37.5	85.7	61.6	85.7	37.5
4. Combined measure	62.5	85.7	74.1	90.9	50.0

ROC: receiver operator characteristic
PV: predictive value

which could reflect greater conceptual proximity to the gold standard than each isolated measure.

The present study has some limitations. The small number of cases, and the fact that it was performed in a single context and with only one pathology, could limit the generalization of results. Nonetheless, the QAM-Q seems to be capable of obtaining comparable or even better results, when combined with other objective and subjective adherence measurement methods.

There are other ongoing studies to estimate QAM-Q accuracy in varied contexts and including people with different health conditions (people living with HIV/AIDS and those who have undergone liver transplants). In these studies, the questionnaire will be compared to other non-adherence measurement methods (electronic dosage monitoring and biological control), aiming to better estimate their performance in the context of chronic diseases.

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