Journal of the American Society of Hypertension 9 (2015) 420–426

Research Article

Comparison of Morisky Medication Adherence Scale with therapeutic drug monitoring in apparent treatment–resistant hypertension

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Manuscript received December 18, 2014 and accepted April 11, 2015

Abstract

The Morisky Medication Adherence Scale (MMAS–8) is a questionnaire developed for screening of non–adherence in patients with several chronic conditions, including uncomplicated hypertension. However, its accuracy in predicting non–adherence in patients with apparent treatment–resistant hypertension (a–TRH) is not known. Accordingly, we performed a retrospective study in 47 patients with a–TRH who had completed the eight–item MMAS during the initial clinic visit. Non–adherence was defined as presence of undetected serum levels of at least one prescribed antihypertensive drug by therapeutic drug monitoring. We found that 26% of patients were considered to have low adherence score (<6), while the actual prevalence of non–adherence was 51% by therapeutic drug monitoring. Sensitivity of the MMAS–8 was 26% (95% confidence interval, 10.3%–48.4%) with specificity of 75% (95% confidence interval, 53.3%–90.2%). By multivariate analysis, the MMAS–8 score was not an independent predictor of non–adherence, while certain clinical parameters such as heart rate were found to be independent predictors of non–adherence. Our study suggested limited accuracy of the MMAS–8 in detecting medication non–adherence in a–TRH. J Am Soc Hypertens 2015;9(6):420–426.

Keywords: Blood pressure control; self reported adherence; serum drug levels.

Introduction

Adherence to medications is a major challenge that clinicians often face in treatment of chronic medical conditions, including hypertension. This problem is even more pronounced in patients with apparent treatment–resistant hypertension (a–TRH) defined as uncontrolled hypertension with three or more antihypertensive agents or treated hypertension with at least a four–drug regimen regardless of blood pressure (BP).[1] Recent studies from our group and others have reported a high prevalence of non–adherence to antihypertensive medications among patients with a–TRH (50-60%) using the highly sensitive technique of therapeutic drug monitoring.[2–5] Despite the enormous burden of non–adherence to the health care system, practical and reliable methods of adherence detection are not well developed. Adherence can be monitored by several methods such as patient self–report, detailed questionnaire, pill counts, prescription fill rate, or electronic pillboxes.

Among the self-reported measure of adherence, the Morisky Medication Adherence Scale (MMAS) has been used extensively and validated in the primary care setting in the patients with uncomplicated hypertension.[6–8] The

Supported by grants to Dr Vongpatanasin from the University of Texas Southwestern O'Brien Kidney Center P30 DK079328.

Conflict of interest: none.

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1933-1711/$ - see front matter
http://dx.doi.org/10.1016/j.jash.2015.04.004

questionnaire was originally developed as the four–item scale[9] and subsequently revised to an eight–item scale to address additional factors that may influence medication adherence. The questions in the eight–item scale are designed to avoid patients' tendency to overestimate their adherence to healthcare providers and were shown to have higher reliability than the original four–item scale.[10] However, both four–item and eight–item scales have never been validated in patients with a–TRH.

Accordingly, the goal of present investigation is to determine sensitivity and specificity of the MMAS–8 in a cohort of patients referred to a large tertiary care academic medical center specialty hypertension clinic against therapeutic drug monitoring. Furthermore, we also determine accuracy of other independent questionnaire and clinical predictors of medication non–adherence in detecting non–adherence to medications among patients with a-TRH.

Methods

The Institutional Review Board of the University of Texas Southwestern Medical Center approved this study. Medical records of all new patients referred to the hypertension specialty clinic at the University of Texas Southwestern Medical Center for a–TRH and evaluated between January 2009 and October 2014 were reviewed. Patients were included if they met the American Heart Association/Committee of the Council for High Blood Pressure Research definition of a–TRH: (1) failure to achieve office BP <140/90 mm Hg in patients prescribed three or more antihypertensive medications at optimal doses, including if possible a diuretic, or (2) ability to achieve office BP at goal but patient requiring four or more antihypertensive medications.[1] Patients were excluded if they were intolerant to three or more antihypertensive drug classes. Screening for white coat effect with 24–hour ambulatory BP monitoring was conducted for patients who reported normal home BP (<135/85 mm Hg), and patients with demonstrated BP control at home were also excluded. Either private medical insurance or Medicare covered all patients. All patients had reported that they were adherent to prescribed antihypertensive medications prior to therapeutic drug monitoring.

During each clinic visit, after the patient had been resting quietly for 5 minutes, BP was measured by nursing staff using the same validated oscillometric device (Welch Allyn, Vital Signs, Skaneateles Falls, NY) as recommended by guidelines.[11] BP measurement during a single visit was repeated three times separated by 1 minute, and these BP values were averaged. Since January 2009, serum levels of antihypertensive medications were assessed as part of our routine standard of care for new referrals with presumed a–TRH. Since December 2010, all patients were also asked to fill out an eight–item MMAS survey during the initial clinic visit to assess potential non–adherence to antihypertensive medications. Written permission was obtained from Dr Donald Morisky for use of the eight–item MMAS among the study participants. The study participants were also screened with an additional question ''In the past 7 days, how many times did you skip or miss your BP meds for any reason?'' Screening for non–adherence was conducted at Compliance with Clinical Laboratory Improvement Act (CLIA)–certified laboratories as previously described[2] (Supplemental Table 1 and Supplemental Figure 1). This technique has been validated previously for measuring levels of antihypertensive medications.[12,13] Non–adherence was defined as presence of serum levels below detection limit of at least one antihypertensive medication prescribed to the patient by therapeutic drug monitoring.

Predictive value of medication adherence questionnaire was validated against non–adherence by therapeutic drug monitoring. We also determined clinical factors associated with medication non–adherence and assessed incremental predictive value of these factors when used in conjunction with adherence scale.

Statistical Analysis

Statistical analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC). All tests were two–sided, and a P–value $< .05$ was considered statistically significant. Data are presented as mean $\pm$ standard deviation (SD) or mean (95%) as appropriate. Baseline characteristics were compared among the adherent and non–adherent groups using the χ^2 test for categorical variables and t–tests for continuous variables. For non–normally distributed variables, the Kruskal–Wallis test was used. Multivariate analysis to determine predictors of non–adherence was conducted with backward selection technique by first entering all candidate predictors in the model. Then, the least significant variable is deleted. The model is then refitted, and the least significant variable is again deleted. The cycle is repeated until the variables left in the model are all significant. Contribution of clinical predictors over and above that of adherence questionnaire in the prediction of medication adherence was analyzed with the use of discrimination (Harrell's C–statistic).

Results

Between 2009 and 2014, 227 consecutive patients were referred to the University of Texas Southwestern Medical Center Hypertension Clinic for a–TRH. Two patients were found to have white coat effect by 24–hour ambulatory BP monitoring. Therapeutic drug monitoring was performed in 78 patients, while 147 did not undergo measurement of serum drug levels because one of the antihypertensive drugs was not prescribed at or near maximal doses. The MMAS–8 was administered in 50 patients and was completed in 47 patients (Figure 1).