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Non-adherence to cardiovascular pharmacotherapy in Iraq assessed using 8-items Morisky questionnaire and analysis of dried blood spot samples

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SUMMARY

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The study evaluated the non-adherence to selected cardiovascular medications, atenolol, atorvastatin, bisoprolol, diltiazem, lisinopril, simvastatin and valsartan in Iraqi patients by applying a standardized Morisky questionnaire (8-MMAS) and by measuring therapeutic drug concentrations in dried blood spots (DBS) analysed by liquid chromatography - high resolution mass spectrometry (LC-HRMS). Sixty-nine patients on continued use of one or more of the selected drugs were evaluated. The questionnaire showed that 21.7% of participants were non-adherent whereas DBS analysis showed that 49.3% were non-adherent to their medications. No significant correlation between medication non-adherence and gender was detected, but adherence was negatively correlated with the number of medication in the regimen. The 8-items questionnaire was unable to differentiate non-adherence to multi-medications in the prescribed pharmacotherapy regimens. DBS is an alternative to conventional methods to monitor non-adherence objectively. Agreement between the two approaches was weak ($Kappa = 0.269$, p -value 0.05).

INTRODUCTION

Cardiovascular disease (CVD) is a broad term covering disorders of the heart and blood vessels. Examples include hypertension, angina, heart attack, stroke, and heart failure [1]. CVDs accounts for the highest number of deaths worldwide [2]. There is evidence that as many as 50% of prescribed CVD drugs worldwide are not taken by patients as recommended. Medication adherence can be assessed by indirect methods (e.g. questionnaire) or direct methods (concentration of drugs or metabolites in a biological fluid (such as urine or blood). However, no consensus has been reached on a gold standard for routine clinical practice [3]. The 8-item Morisky Medication Adherence Scale (8-MMAS), provides a single qualitative ternary metric

to assess adherence (low, medium, or high) depending on the total score. Conventional direct methods require large blood volumes (0.5 - 10 mL) [1]. Dried blood spot (DBS) sampling is an alternative to conventional methods [4]. It is less invasive, typically involving the collection of just a few drops of blood from a finger or heel prick onto a filter paper [1]. The aim of this research was to assess patients' non-adherence to treatment with atenolol, atorvastatin, bisoprolol, diltiazem, lisinopril, losartan, simvastatin and valsartan by 8-MMAS and determination of the target medications in DBS from the same patients and to compare the results obtained from the two approaches

MATERIALS AND METHODS

69 patients were recruited at the Alsaeder Teaching Hospital in Iraq during routine clinical visits. Following consent, patients were invited to complete an Arabic version of (8-MMAS) questionnaire and to provide a finger-prick blood spots samples on DBS cards. Drugs concentration in DBS was determined by liquid chromatography-high resolution mass spectrometry (LC-HRMS)[5]. Patients were categorized as non-adherent when one or more of their prescribed cardiovascular medications were outside the range of $(0.05) C_{max}$ to C_{max} .

RESULTS AND DISCUSSION

8-MMAS showed that 54 participants (78.3%) were adherent (30 males and 24 females), 15 participants (21.7%) were non-adherent (11 males and 4 females). However, adherence assessment by DBS showed that 35 patients (50.7%) were adherent to medications (21 males and 14 females) and 34 patients (49.3%) were non-adherent (20 males and 14 females). Both approaches showed no significant relationship between medication non-adherence and gender. The negative correlation between adherence and the number of medications was seen in both approaches. DBS analysis showed that adherence to medication was not uniform (Fig 1). 44 participants (63.8%) showed agreement and 25 (36.2%) showed disagreement. 22 patients were classified as adherent according to 8-MMAS but they were non-adherent according to their blood concentration. This difference may be due to prescribing errors, substandard medications, individual pharmacokinetic variability, or drug interactions. The other 3 patients were non-adherent by the 8-MMAS but were defined as adherent according to DBS analysis. The agreement between the two approached was weak ($Kappa = 0.269$, $p\text{-value} < 0.05$).

The answers to the Morisky questions with respect to non-adherence were:

- 75% cited inconvenience with medications
- 70.7% gave no reasons
- 66.7% cited medication side effects
- 58.3% cited poor understanding of treatment
- 58.3% cited travel problem
- 41.7% cited simple forgetfulness

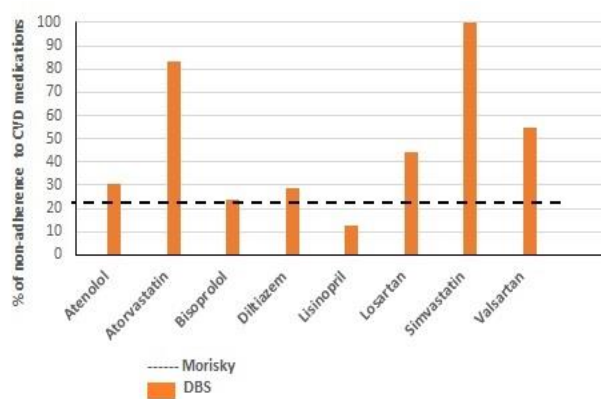


Fig. 1. Comparison of non-adherence among the Iraq patient group for each of the target cardiovascular drugs by DBS analysis and 8-MMAS

CONCLUSIONS

The Morisky 8-MMAS and the DBS sampling approach both indicated levels of non-adherence. Poor agreement between the two approaches was seen. The DBS derived data provided drug specific information about patient medication taking behaviour. The results from the DBS sampling indicated that non-adherence was not uniform towards the different medications in the sample medical regimens tested.

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