How well does self-reported adherence fare compared to therapeutic drug monitoring in HAART?

Awang Bulgiba a,⁎, Umar Y. Mohammed a, Zamri Chik b, Christopher Lee c, Devi Peramalaha

a Julius Centre University of Malaya, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Malaysia
b Department of Pharmacology, Faculty of Medicine, University of Malaya, Malaysia
c Department of Medicine, Sungai Buloh Hospital, Malaysia

A R T I C L E   I N F O
Available online 11 January 2013

Keywords:
Self-reported adherence
HAART
Therapeutic drug monitoring
HIV

A B S T R A C T
Objective. The aim of the study was to determine how well self-reported adherence fares compared to therapeutic drug monitoring in monitoring HAART adherence.

Methods. We administered a validated self-reported adherence (SRA) questionnaire to 925 HIV patients on HAART in a large Malaysian hospital from 2010 to 11. We also performed Therapeutic Drug monitoring (TDM) by concurrently collecting and testing blood samples for Efavirenz, Nevirapine and Lamivudine using Liquid Chromatography/Mass Spectrometry. We compared the SRA against the TDM results. Sensitivity, specificity, positive (PPV) and negative predictive (NPV) and diagnostic accuracy values were computed for each drug.

Results. Self-reported adherence (SRA) over-estimates adherence by between 6 and 10 percentage points compared to therapeutic drug monitoring (TDM). SRA is highly sensitive with sensitivity exceeding 0.90 but is not very specific (0.56–0.63). PPV for SRA ranged between 0.76 (Lamivudine) and 0.84 (Efavirenz) while NPV ranged between 0.78 (Lamivudine) and 0.81 (Efavirenz). Overall diagnostic accuracy ranged between 0.76 (Lamivudine) and 0.84 (Nevirapine).

Conclusion. Self-reported adherence is a surprisingly accurate instrument for measuring HAART adherence compared to TDM and can be reliably used in practice in resource-poor settings.

© 2013 Elsevier Inc. All rights reserved.

Introduction

Measuring adherence to HAART can be difficult, not least because patients may not always tell the truth when asked about adherence. There are many known methods for measuring adherence, but there is no gold standard acceptable to all. Some researchers therefore think that it will be good to use more than one method to measure the adherence level (Abaasa et al., 2008; Chesney, 2006; Malta et al., 2010; Nachega et al., 2010).

An objective and direct method to check adherence is by measuring the plasma concentrations of the antiretroviral drugs using Therapeutic Drug Monitoring (TDM). This is perhaps the best objective method for measuring adherence by detecting the concentration of drugs in the plasma (Fabbiani et al., 2009; Sangsiriwut et al., 2012). Other indirect methods rely on less objective measures (Caswell et al., 2011; Pozniak et al., 2011) like self-reported adherence where-by a patient reports the number of doses he/she had taken or missed during a specified time interval (Muñoz-Moreno et al., 2007; Poeta et al., 2011). Although widely used, self-reported adherence has its advantages and disadvantages (Glass et al., 2010) but remains popular due to its low cost. This study was aimed at determining how well self-reported adherence would fare compared to TDM in measuring adherence to HAART in a resource-poor setting.

Materials and methods

This study was conducted between 2010 and 2011 in a large tertiary level infectious disease-focused hospital in Malaysia. Nine hundred and twenty five adult HIV-positive Malaysian nationals receiving HAART were recruited into a perspective cohort study aimed at studying adherence to HAART. This paper is from the first part of that study.

A validated self-reported adherence questionnaire was adapted from the Adult AIDS Clinical Trials Group (AACTG) adherence questionnaire which was designed and tested by the Centre for AIDS Prevention Studies (CAPS). This instrument is made available free of charge at the following website http://www.caps.ucsf.edu/tools/surveys/. This SRA instrument was adapted for local use and forward and backward translated into another 3 languages other than English (Malay, Chinese and Tamil) and then validated using the test–retest method. The questionnaire was administered and blood samples were collected using venepuncture by a trained phlebotomist. The blood was centrifuged and plasma sent for analysis using a Liquid Chromatography Mass Spectrometry (LC–MS/MS) machine in the university’s laboratory. TDM levels for three medications (Efavirenz, Nevirapine and Lamivudine) were determined based on the detected drugs level in the collected blood sample.

⁎ Corresponding author. Fax: +60 3 7967 4975.
E-mail address: awang@ummc.edu.my (A. Bulgiba).

0091-7435/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ypmed.2013.01.002
Collected data was cleaned and entered into SPSS version 16 for analysis. Sensitivity, specificity, positive and negative predictive values as well as diagnostic accuracy (all with 95% confidence intervals) were computed for each drug. This study was approved by both the ethical committees of University of Malaya Medical Centre and the Ministry of Health Malaysia. Approval was sought for and obtained to study patients in the Sungai Buloh Hospital.

Results

The majority of the respondents were male (76.3%) and Chinese (63.2%) and married (62.3%) with 36.5% in the 31–44 age group and almost half professing to be Buddhists (48.4%). Overall the adherence level as measured by SRA was 0.80, 0.76 and 0.71 for Efavirenz, Nevirapine and Lamivudine, respectively (Table 1). This contrasted with the overall adherence measured using TDM of 0.71, 0.70 and 0.60 for the same drugs respectively.

Table 2 displays the sensitivity, specificity, positive and negative predictive values for the 3 drugs. SRA sensitivity was highest for Efavirenz (0.95; 95% CI 0.92, 0.96) and lowest for Lamivudine (0.89; 95% CI 0.85, 0.93). SRA specificity ranged between 0.56 and 0.63 and was highest for Nevirapine. PPV for SRA ranged between 0.76 (Lamivudine) and 0.84 (Efavirenz). A similar pattern was seen for NPV. Overall diagnostic accuracy ranged between 0.76 (Lamivudine) and 0.84 (Nevirapine).

Discussion

This is the first ever reported study in South East Asia to validate a locally and culturally adapted self-reported adherence (SRA) questionnaire with detected levels of three anti-retroviral medications in human plasma using LC–MS/MS. As expected, SRA adherence levels were slightly higher than those obtained by TDM. Social desirability bias could probably account for some of this difference but it was less than expected.

The levels of sensitivity and PPV of SRA in Malaysia are comparable to levels obtained elsewhere (Godin et al., 2003). We have also determined that SRA is surprisingly sensitive but not very specific and this has been shown by other researchers (Biadgilign et al., 2010). This is to be expected given that high sensitivity is often accompanied by low specificity. The high PPV levels are not actually that surprising given that the actual adherence to medication is high, naturally giving rise to high PPV. The fairly high diagnostic accuracy is probably a result of fairly high discriminative ability of the SRA instrument to decide who has adhered or not adhered to medication. This has been shown elsewhere by other researchers (Duong et al., 2001).

TDM is expensive and requires complex machinery and trained personnel to perform (Rakhmanina et al., 2004). These factors make it rather unsuitable for use in resource-poor environments. With this kind of profile, this begs the question whether SRA could therefore be trusted enough to replace TDM in measuring adherence and the answer is in the affirmative. When high sensitivity and PPV are required, SRA can be relied upon to check adherence. We hope that this piece of research will help answer the question whether SRA could reliably be used to measure adherence in HAART patients in a resource-poor environment.

Limitations of this study include recall bias and social desirability bias (Shi et al., 2010). Recall bias was minimized by ensuring proper definition and articulation of the research question and improving the quality of the questionnaire. Social desirability bias was minimized by engaging a research assistant who was not directly involved in the HIV clinic to collect the data.

Conclusion

Self-reported adherence is a surprisingly accurate instrument for measuring HAART adherence compared to TDM and can be reliably used in practice in a resource-poor setting.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Acknowledgment

This study was supported by University Malaya (UM) Research Grant (UMRG006/09HTM) and SfE/MM Programme UM/MOH High Impact Research Grant (E000010-20001). The authors would like to express their gratitude to the patients who participated in this study and to the staff in Sungai Buloh Hospital and Department of Pharmacology, Faculty of Medicine (UM) for their assistance in the development and validation of the methods used in this study.

References


Table 2

<table>
<thead>
<tr>
<th>Drug</th>
<th>SRA/TDM adherence (%)</th>
<th>TDM adherence (%)</th>
<th>SRA/TDM non-adherence</th>
<th>SRA/TDM adherence (%)</th>
<th>SRA/TDM non-adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>76/252 (80.2)</td>
<td>454/652 (71.2)</td>
<td>241/445</td>
<td>100/180</td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>430/566 (76.0)</td>
<td>394/566 (69.9)</td>
<td>366/394</td>
<td>108/172</td>
<td></td>
</tr>
<tr>
<td>Lamivudine</td>
<td>352/496 (71.0)</td>
<td>299/496 (60.3)</td>
<td>267/299</td>
<td>112/197</td>
<td></td>
</tr>
</tbody>
</table>

Table 1

<table>
<thead>
<tr>
<th>Drug</th>
<th>SRA adherence (%)</th>
<th>TDM adherence (%)</th>
<th>SRA/TDM adherence (%)</th>
<th>SRA/TDM non-adherence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>501/625 (80.2)</td>
<td>445/625 (71.2)</td>
<td>325/625 (52.1)</td>
<td>267/625 (43.0)</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>430/566 (76.0)</td>
<td>394/566 (69.9)</td>
<td>366/394 (56.1)</td>
<td>108/172 (18.0)</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>352/496 (71.0)</td>
<td>299/496 (60.3)</td>
<td>267/299 (55.6)</td>
<td>112/197 (23.0)</td>
</tr>
</tbody>
</table>
Sangsiriwut, K., Anekthananon, T., Ratanasuwan, W., Suwanagool, S., Kolladarungkri, T., 2012. High performance liquid chromatographic assay for the determination of Protease Inhibitors (PIs) and Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) in human plasma.