ARTICLE

Validity of the International HIV Dementia Scale in Brazil

Validade da Escala Internacional de Demência pelo HIV no Brasil

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ABSTRACT

HIV-associated neurocognitive disorders (HAND) remain prevalent in highly active antiretroviral therapy (HAART) era. Tests to detect HAND are needed for early diagnosis and treatment. Validity of International HIV Dementia Scale (IHDS) has been determined in different countries. The aims of this study were validate IHDS in a Brazilian cohort of HIV-patients and verify if IHDS can be reliably administered by a non-clinician health professional. One hundred and eighty-seven (187) patients were submitted to a full neuropsychological assessment. IHDS was administered twice to each patient (by a non-clinician and by a neurologist). HAND was diagnosed in 98 individuals (68 on HAART). IHDS had sensitivity of 55% and specificity of 80%. IHDS had fair agreement with neuropsychological tests (k 0.355) and moderate-to-strong agreement between different evaluators (interclass correlation coefficient (ICC) 0.684). HAND is prevalent nowadays. IHDS is quick and easy to administer, but has marginal sensitivity for the detection of HIV cognitive impairment other than dementia.

Key words: Acquired Immunodeficiency Syndrome, HIV, dementia.

RESUMO

Distúrbios neurocognitivos associados ao HIV (HAND) ainda são comuns em pacientes usando terapia antirretroviral de alta eficácia (HAART). Testes diagnósticos para detecção de HAND são necessários para diagnóstico e terapia precoces. Nossos objetivos foram validar em uma população brasileira a escala internacional de demência pelo HIV (IHDS), já utilizada em outros países, e avaliar se pode ser confiavelmente aplicada por um profissional não médico. Avaliamos 187 pacientes com uma extensa bateria neuropsicológica. IHDS foi ministrada duas vezes (por médico e não médico). HAND foi diagnosticada em 98 indivíduos (68 em uso de HAART). A IHDS teve sensibilidade de 55% e especificidade de 80%, com pouca concordância com os testes neuropsicológicos (k 0,355) e moderada a forte concordância entre observadores (coeficiente de correlação interclasse (ICC) 0,684). HAND ainda é prevalente nos dias atuais. IHDS é um instrumento rápido e fácil de ser aplicado, mas com baixa sensibilidade para detecção de déficit cognitivo outro que não demência.

Palavras-Chave: Síndrome de Imunodeficiência Adquirida, HIV, demência.

The International HIV Dementia Scale (IHDS) is a cross-cultural screening test to detect HIV dementia. It is quick and does not require a neurologist to administer it. It was initially tested on HIV patients from the USA and Uganda, with reported sensitivity and specificity of 80 and 55%, respectively[1]. Subsequently, it was translated into different languages and validated in distinct settings[2,3]. We aimed to validate the IHDS in a Brazilian cohort of HIV patients and determine if non-clinician health professionals can reliably administer the IHDS.

METHODS

We randomly selected 187 of 2,678 HIV patients to undergo a full neurological and neuropsychological assessment. The required number of patients was determined with the statistical program R. Exclusion criteria were age <18 years, current or past opportunistic central nervous system disease, current or past history of drug use or alcohol abuse and severe medical, psychiatric or neurologic disorder believed to

be able to interfere with the study evaluations. Data on antiretroviral therapy use, CD4 counts and HIV viral load were retrieved from medical files. A specific diagnostic form was used for neurological assessment[4].

After translation and back-translation, the IHDS was administered according to the seminal paper[1]. For our Portuguese version, we chose the words *cadeira*, *sapato*, *tijolo* and *biscoito* to replace the original English words. For semantic clues, we used *móvel* (*cadeira*), *calçado* (*sapato*), *material de construção* (*tijolo*) and *alimento* (*biscoito*). The IHDS was administered twice for each patient, first by a physiotherapist (RL) and then by a neurologist (MTTS or RAR). The interval between each assessment was 0–14 days. To avoid word repetition, the physiotherapist provided different words for the patients to recall (*vermelho*, *chapéu*, *cachorro* and *feijão*). The maximum IHDS score is 12, and patients with a score ≤10 are considered at risk for HIV dementia[1].

A neuropsychological test battery was administered to all participants after the IHDS and neurological examination. The battery comprised tests to assess specific domains of neurocognitive function such as verbal memory and learning (Rey Auditory Verbal Learning test), psychomotor performance (Digit Symbol test, Trail Making test), motor speed (Grooved Pegboard test), and frontal systems performance (categorical verbal fluency). Each test was adjusted for age and education using a control group (n=120). Patients were then classified as having normal functioning, asymptomatic neurocognitive impairment (ANI), mild cognitive impairment (MCI) and HIV dementia, according to the proposed criteria for HIV-associated neurocognitive disorders

(HAND)[5]. For statistical analysis, patients with ANI were combined with those with MCI.

SPSS was used for statistical analysis. The following tests were employed: Cronbach's alpha coefficient of reliability, Spearman correlation test, kappa test for inter-rater agreement, Mann-Whitney test, Fisher test, chi-square (χ^2) test, Youden index [Y = sensitivity + specificity - 1], receiver operating characteristic (ROC) curve and interclass correlation coefficient (ICC). IHDS scores measured by different evaluators (physiotherapist *versus* neurologist) were compared for each patient. Similarly, the IHDS performance of each patient was matched with his or her neuropsychological diagnosis from a full neuropsychological evaluation.

RESULTS

The subjects' demographic characteristics are listed in Table. Patients on HAART tended to be older and less educated than HAART-naïve patients (p<0.0001) and less educated than the negative controls (p<0.0001). HAART-naïve patients were younger than the negative controls (p<0.0001).

Using the HAND criteria[5], 98 of 187 individuals (68 on HAART; 30 HAART-naïve) were diagnosed with some cognitive impairment (χ^2 9.888, p=0.002). HIV dementia was diagnosed in 28 patients (χ^2 1.961, p=0.161; 19 on HAART and 9 HAART-naïve) and ANI/MCI in 70 (χ^2 4.84, p=0.028; 49 on HAART and 21 HAART-naïve).

The IHDS had HAND-detection sensitivity and specificity of 55 and 80%, respectively (cut-off ≤10; area under the curve (AUC) 0.731) (Figure). If a cut-off ≤11 was used, the sensitivity

Table. Demographic characteristics and neuropsychological results of HIV-infected patients and HIV-negative controls.

	HAART naïve	HAART	HIV-negative	p-value
Age	32.5 (19–69)	44 (20–73)	41.5 (3077)	<0.001
Education	11 (321)	7 (1–18)	11 (1–25)	<0.001
Female	27 (37.5%)	60 (52.2%)	69 (57.5%)	–
CD4 count	575.5 (34–1610)	392.5 (7–1356)	NA	<0.001
IHDS 1	11 (6.5–12)	10.5 (3–12)	NA	0.002
IHDS 2	11 (5.5–12)	10.5 (3–12)	NA	0.005
DS	35 (0–64)	25 (4–60)	47.5 (14–72)	<0.001
TRAIL A	36 (16–166)	50.5 (12–203)	43 (24–120)	<0.001
TRAIL B	95 (31–220)	112 (34–290)	89 (34–232)	0.041
Verbal fluency	19 (4–40)	16 (7–34)	19 (9–32)	0.012
GPDH	70 (50–290)	77 (10–235)	68 (55–123)	0.006
GPNDH	76 (55–295)	85 (56–305)	76 (62–141)	0.003
RAVLT1	5 (1–8)	4 (1–8)	6 (1–12)	<0.001
RAVLT5	12 (2–15)	10 (4–15)	12 (7–15)	0.005
REV1	9 (2–15)	8 (0–15)	10 (2–15)	0.004
REV2	9 (2–15)	8 (0–15)	10 (4–15)	0.004

NA: not applicable; HAART: highly active antiretroviral therapy; IHDS 1: International HIV dementia scale applied by clinician; IHDS 2: International HIV dementia scale applied by physiotherapist; DS: digit symbol; TRAIL A and TRAIL B: trail making test part A and B; GPDH: grooved pegboard with dominant hand; GPNDH: grooved pegboard with non-dominant hand; RAVLT1: Rey auditory verbal learning test first trial; RAVLT5: Rey auditory verbal learning test last trial; REV 1 and REV 2: Rey auditory verbal learning test first and second evocation, respectively. All results shown are median (range), except Female, which is absolute number (percentage).

Roc Curve
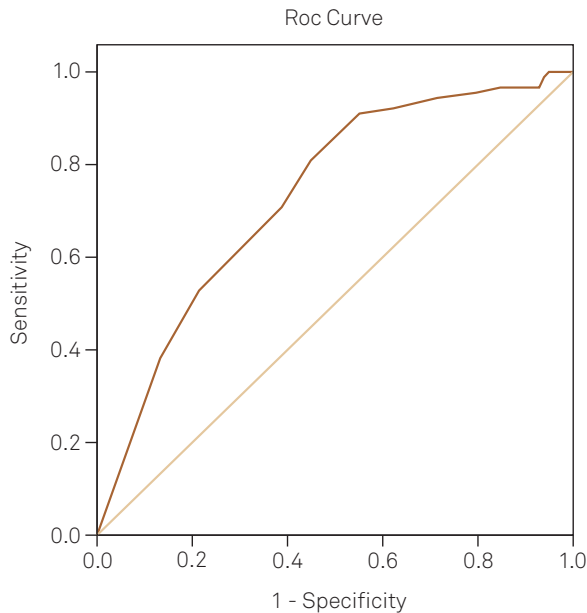
IHDS: International HIV dementia scale; HAND: HIV-associated neurocognitive disorders. AUC=0.731; Standard error (SE)=0.037; 95%CI 0.660–0.803.

Figure. Receiver operating characteristic of the International HIV Dementia Scale (cut-off ≤10) compared to neuropsychological assessment (normal *versus* HIV-associated neurocognitive disorders).

and specificity for diagnosing HAND changed to 78 and 52%, respectively. An additional analysis excluding ANI/MCI cases and using a cut-off ≤10 was performed, and the sensitivity and specificity increased to 78.5 and 80.8%, respectively. If all HIV dementia cases were excluded, the sensitivity of IHDS decreased to 45.7% (cut-off ≤10). However, with a cut-off ≤11, the sensitivity and specificity for detecting ANI/MCI increased to 75.7 and 52.8%, respectively. Considering only ANI/MCI cases, the Youden index for cut-offs of 10 and 11 was 0.265 and 0.285, respectively.

IHDS had fair agreement[6] with neuropsychological tests (kappa=0.355; 95%CI 0.342–0.369), and moderate-to-strong agreement between different evaluators (clinician and non-clinician; ICC 0.684, 95%CI 0.519–0.793).

DISCUSSION

This is the first study to evaluate IHDS performance in a Brazilian cohort of HIV patients. The occurrence and prevalence of HAND is neglected in Brazil, making studies in this field relevant. The prevalence of HAND was 52.4%: 28 patients with HIV dementia (28.5%) and 70 patients with ANI/MCI (71.4%). Patients on HAART were more likely to have HAND than HAART-naïve patients were (χ^2 5.14; p=0.020). This may be because patients on HAART have been infected for a longer period and have lower nadir CD4 counts (data not shown). Our data are in accordance with those of others, demonstrating that a history of a low-nadir CD4 count is a strong predictor of neurocognitive impairment[7].

A screening test for early recognition of HAND has clinical and research relevance. The ideal tool would be quick and easy to use and applicable to different settings. The IHDS is a very brief and easy-to-perform test intended to detect HIV dementia[1]. In our cohort, the IHDS had a sensitivity and specificity for diagnosing HIV dementia of 78.5 and 80.8%, respectively. However, the sensitivity decreased to 45.7% for diagnosing ANI and MCI. IHDS sensitivity could be improved by increasing the IHDS cut-off score to 11. When we used a cut-off ≤11, the sensitivity and specificity for detecting ANI/MCI was 75.7 and 52.8%, respectively. The Youden index was higher when we used the cut-off of ≤11 instead of 10 (0.285 *versus* 0.265). The Youden index is a frequently used summary measure of the ROC curve, measuring the effectiveness of a diagnostic marker and enabling the selection of an optimal threshold value for the marker[8]. The index ranges from -1 to +1. A result closer to +1 suggests an ideal cut-off value. We believe that patients with a score ≤11 should undergo a full neuropsychological assessment. This is important because ANI and MCI are risk factors for developing HIV dementia, and HAND is associated with poor adherence to HAART and higher morbidity and mortality[9]. In addition, early detection of ANI/MCI in HAART-naïve patients could help guide the initiation of HAART.

Finally, we demonstrated that a non-clinician health professional could administer the IHDS with moderate-to-strong agreement between different evaluators (ICC 0.684). IHDS could be useful prior to a clinical appointment and during follow-up for detection of cognitive decline necessitating specialist referral.

In conclusion, HAND remains prevalent (52.4%) in HIV patients, and its early recognition is essential. At a cut-off score of ≤11, the IHDS had sensitivity of 75.7% and specificity of 52.8% for detecting subtle forms of HAND other than HIV dementia. Additionally, we found that the IHDS could be reliably administered by non-clinician medical professionals.

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