Diagnostic test of Brief Peripheral Neuropathy Screen as Distal Sensory Polyneuropathy-HIV Diagnostic Tool

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Abstract

Distal sensory polyneuropathy (DSP) is the most common human immunodeficiency virus (HIV)-associated peripheral neuropathy with a prevalence of 30-67%. Brief peripheral neuropathy screen (BPNS) examination is a non-invasive, fast, cheap, easy-to-do diagnostic method, and one of the clinical tools that can be used to diagnose HIV-DSP. This study to assess the BPNS diagnostic test as a DSP diagnostic tool in HIV patients. The cross-sectional study was conducted on HIV patients that allegedly having DSP. All subjects were examined by BPNS and nerve conduction study (NCS), then the results were analyzed by chi-square test of a 2x2 Table. There were 42 subjects enrolled in this study. The mean patients were 38.88±8.62 years and most of the male patients were 24 subjects (57.14%). Most of the patients had high school education by 20 (47.61%) subjects and did not take anti-retroviral (ARV) by 18 (42.85%) subjects. Most of the research subjects conducted BPNS disturbed examination by 27 (64.28%) subjects and examination of NCS obtained positive DSP by 30 (71.4%) subjects. The obtained sensitivity of 83% BPNS, 83% specificity, 93% positive predictive value, the negative predictive value of 67%, a positive likelihood ratio of 5.00, and a negative likelihood ratio of 0.20. BPNS examination with 83% sensitivity and 83% specificity can be used as a DSP diagnostic tool in HIV patients.

Keywords*: Diagnostic testing, DSP-HIV, Brief peripheral neuropathy screen (BPNS), NCS examination*

Intoduction

Human immunodeficiency virus (HIV) is a retrovirus that can cause immune system failure in humans [1,2]. It is estimated that 35.3 (32.2-38.8) million people are living with HIV in 2012 and annually about 2.3 (1.9-2.7) million with new infections [3]. After the highly active anti retroviral therapy (HAART) era since 1996, the life expectancy of HIV patients has increased. As a consequence, patients and medical personnel will be faced with neurological complications of HIV disease from comorbidities and the drugs used [1,4,5]. Peripheral neuropathy has been documented since early reports of HIV disease and HIV isolation in the human nervous system. The prevalence of peripheral neuropathy in HIV-positive individuals are high and is the most common neurologic complication of HIV infection. Although not life-threatening peripheral neuropathy will affect the quality of life in HIV patients [1,4,6–9].

Distal symmetrical polyneuropathy (DSP) is the most common form of HIV-associated peripheral neuropathy, it also called distal sensory polyneuropathy. Two potential mechanisms for the cause of neurotoxicity plays an important role in the pathogenesis of HIV DSP: viral neurotoxicity and its products and neurotoxic side effects of treatment used in the managements of HIV [1,9]. Where the prevalence ranges from 30%-67% [10]. Until now there is no standard for diagnosing DSP-HIV, but several clinical devices have been developed to assess this condition in both clinical and research practice. One of the most commonly used clinical devices is the brief peripheral neuropathy screen (BPNS) [1].

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Brief Peripheral Neuropathy Screen is one of the clinical tools that can be used to diagnose DSP-HIV [1,11]. Non-neurological clinicians such as general practitioners, trained nurses or therapists may use BPNS to diagnose peripheral neuropathy [11,12]. BPNS has been validated as a screening device to determine the degree of polyneuropathy. This check includes subjective and objective information and takes only <10 minutes for its implementation. The diagnosis of sensory HIV neuropathy can be established if the patient shows ≥1 specific symptoms of BPNS and 1 other sign of decreased ankle/Achilles reflex and/or vibration perception [13].

The availability of electro myo graphy (EMG) tools in peripheral areas in Indonesia is limited, so research is needed to assess the usefulness of BPNS diagnostic tools in establishing the diagnosis of HIV-DSP. Based on the international research, the data showed that BPNS diagnostic tests can be used to help establish a diagnosis of HIV-DSP [11]. Therefore the researchers tried to conduct research on the diagnostic test of BPNS examination compared to the examination of nerve conduction/NCS in HIV patients with DSP suspicion in Dr. Soetomo Teaching Hospital, Surabaya.

Method

The study subjects were HIV patients with allegedly of DSP who visited outpatient of UPIPI at Dr. Soetomo Teaching Hospital Surabaya, Indonesia. The subject inclusion criteria were HIV patients with DSP suspicion and aged 18 to 60 years. While, the subject exclusion criteria were, patients with type 2 Diabetes Mellitus, using neurotoxic drugs (metronidazole, chloramphenicol, vincristine, vinblastine, dapsone, isoniazid, and ethambutol), lower extremity amputations, and lower extremities contracture. The subjects who are willing to participate the research in advance fill out the form informed consent. And then, before this study the researcher conducted a test of ethics at Dr. Soetomo Teaching Hospital Surabaya Indonesia.

This study used a cross-sectional study design that conducted over 5 months. The instruments used in this study were data collecting sheets from interviews and Reflect and Achilles reflex examinations, Riester reflex hammer tool for Reaction Achilles inspection, 128 Hz tuning fork tool for vibration check, NCS tool is EMG/NCV Cadwell, paper of NCS readings. The stages of this study examination of BPNS, subsequent examination of NCS, and all recording results were collected for subsequent data tabulation and statistical analysis.

The data obtained from the data collection sheet then expressed on the scale of the dichotomies, i.e., the nominal scale having 2 positive or negative values. The examination results of HIV patients suspected of having DSP with BPNS examination that was analyzed by the 2x2 table for the dichotomous values, the difference of clinical findings and BPNS positive compared to negative findings. Then, it was compared to NCS, and analyzed by diagnostic test to obtain sensitivity, specificity, positive suspicion value, negative suspicion value, positive possibility ratio, and possible negative ratio. Statistical analysis using SPSS 19 (SPSS, Inc., Chicago, IL) and paint maker program.

Results

The data collection were BPNS examination and NCS examination conducted within 5 months, from December 2014 to April 2015. The basic data of the patient was taken by direct interview with the patient and the BPNS examination was performed by UPIPI whereas the neural conduction examination was done in Electromyography (EMG) room at Department of Neurology Dr. Soetomo Teaching Hospital Surabaya, Indonesia.

The mean patients were 38.88±8.62 years and most of the male patients were 24 (57.14%). Most of the patients had high school education by 20 (47.61%) subjects and did not take anti retro viral (ARV) by 18 (42.85%) subjects. Most of the research subjects conducted by BPNS examination that disturbed of 27 (64.28%) subjects and examination of NCS obtained positive DSP by 30 (71.4%) subjects (Table 1).

Table 1. Characteristics of research subjects

Variables	Research subjects n=42		
	n	%	Mean±SD
Sex			38.88±8.62
Male	24	57.14	
Female	18	42.86	
Education			
Elementary School	9	21.42	
Junior High School	11	26.19	
Senior High School	20	47.61	
College	2	4.78	
The use of ARV			
Non using ARV	18	42.85	
TDF, 3TC, EFV	12	28.57	
TDF, 3TC, NVF	3	7.14	
AZT, 3TC, NVF	9	21.44	
ARV-use duration			
Non using ARV	18	42.85	
<3 months	11	26.19	
>3 months	13	30.96	
BPNS			
Disturbed	27	64.28	
Normal	15	35.72	
NCS			
DSP (+)	30	71.43	
DSP (-)	12	28.57	

Table 2. Tabulation of BPNS and NCS examination results

		NCS		Total
		DSP (+)	DSP (-)	
BPNS	DSP (+)	25 (59.53)	2 (4.75)	27 (64.28)
	DSP (-)	5 (11.90)	10 (23.82)	15 (35.72)
Total		30 (71.43)	12 (28.57)	42 (100.00)

Cross tabulation between BPNS diagnosis and NCS results in the study subjects resulted in a similar diagnosis which 27 patients diagnosed with DSP and BPNS, 25 patients (92.6%) were positively diagnosed with DSP and NCS as well. Out of the 15 patients diagnosed with DSP and BPNS, 10 patients (66.7%) were diagnosed as negative DSP and NCS (Table 2).

Discussion

Brief Peripheral Neuropathy Screen is one of the clinical tools that can be used to diagnose DSP-HIV [1,11]. BPNS cannot distinguish the underlying cause of neuropathy but shows its sensitivity to small nerve fibers/pain fibers, indicating the presence of DSP. This check includes subjective and objective information and takes only <10 minutes for its implementation. The HIV diagnosis of SN can be established if the patient showed ≥1 specific symptoms of BPNS and 1 other sign of decreased ankle/Achilles reflex and/or vibration sensation [13,14].

The data from this study indicated that BPNS examination may be used to establish the diagnosis of HIV DSP, however, did not replace the function of NCS in identifying other conditions similar to DSP such as lumbosacral radiculopathy or another polyradiculoneuropathy. NCS is also more appropriate as a predictor of clinical severity than BPNS.

Diagnostic tests were distinguished by their usefulness as a screening tool, to ascertain and exclude disease, monitor disease course, and determine prognosis. Choosing the right diagnostic check is not easy. The ideal diagnostic test is rare, a test that gives positive results on all sick objects and gives negative results on all not sick subjects. Almost on all types of diagnostic tests it is possible to obtain positive test results on healthy subjects (false positives) and negative results on sick subjects (apparent negative) [15,16].

This diagnostic test study aims to determine the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of BPNS with standard nerve conduction examination/NCS. A diagnostic test can be to diagnose a disease or exclude a disease if it has a high sensitivity and specificity [15]. A high sensitivity diagnostic test is required to detect the presence of a disease, as more cases can be detected by the test. High specificity diagnostic tests are used to confirm the presence of a disease because the greater the specificity of a diagnostic test, the greater the likelihood that patients who do not have a disease are excluded by the test [16].

The results of previous studies showed a more comparison of male patients i.e., 85% and 84% [17,18]. According to the data of HIV patients that undergoing treatment at outpatient UPIPI of Dr. Soetomo Teaching Hospital where the number of male patients 4-7 times more than women [19]. However, in other studies obtained more women 69.8%, 65.3%, and 67.5% [13,20,21]. The results of this study was not much different from previous studies that get an average age of 36.5 ± 9.3 years and mean age was 38.3 ± 10.8 in the HAART group and 35.5 ± 8.7 in the non-HAART group [17,21].

In this study, 18 subjects (42.85%) had not received antiretroviral therapy, as most new subjects were diagnosed, no CD4 results and some research subjects were suspected of having other opportunistic infections. Type of antiretroviral drugs used research subjects using 3 kinds of combinations, namely: a. tenofovir, lamivudine, efavirenz, b. tenofovir, lamivudine, nevirapine, and c. zidovudine, lamivudine, nevirapine. This therapy is according to WHO 2006 first-line therapy for adult patients [19]. Among the antiretrovirals used by the study subjects, there was zidovudine which can cause peripheral neuropathy. The subjects taking antiretrovirals less than 3 months were 26.1% and 31% were taking antiretroviral drugs for more than 3 months. According to a previous study, the peak incidence of DSP HIV occurred on day 90 after the use of antiretrovirals[17].

Sensitivity is the proportion of ailing subjects with positive (absolute positive) diagnostic test results overall sick subjects (false positives and apparent negative) or the possibility that the diagnostic test results are positive when performed on a group of desease subjects. Specificity is the proportion of healthy subjects who give negative (true-negative) diagnostic test results compared to all non-sick subjects (true negative and false positives) or the possibility that the diagnostic test results will be negative when performed on a group of healthy subjects [15].

In previous studies, BPNS showed a sensitivity of 49% and a specificity of 88% for diagnosing HIV-DSP [12]. This estimated value is strongly influenced by the prevalence of disease, where the population in this study is hospital-based so that more suffer than healthy. Positive assumptions are important statistics in the diagnostic test [15].

Another statistic of the diagnostic test is the likelihood ratio (LR), i.e., the likelihood of the sick subjects getting the same test result. The positive likelihood ratio is the proportion of the proportion of sick subjects who test positive with the proportion of healthy subjects who test positive. The negative likelihood ratio is the proportion between the proportion of sick subjects

who tested negative tests and healthy subjects who gave negative test results. In this study, there was a positive likelihood ratio of 5.00 (CI 95%, 1.40-17.90) and a negative likelihood ratio of 0.20 (CI 95%, 0.09-0.46). According to the literature, the ratio of probability ratios varies from 0 to infinity. The results of positive positive diagnostic tests provided a probability ratio value much greater than 1, strong negative test results will give a probability ratio value close to 0 [15].

BPNS examination can be used as a diagnostic tool of DSP HIV and has an advantage if it is compared to the examination of nerve conduction/ NCS. Daily clinical use is faster. easier, cheaper, non-invasive, and can be performed by trained medical and paramedical workers.

Conclusion

In this study, the sensitivity of BPNS examination was 83% and specificity was 83%, positive predictive value 93%, and negative predictive value 67%, positive likelihood ratio 5.00 and negative likelihood ratio 0.20.

Ethical Clearance: This study protocol was approved by ethical clearance Dr.Soetomo teaching hospital, Surabaya, Indonesia

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