

Cardiovascular autonomic dysfunction in Africans infected with human immunodeficiency virus

Divine Nzuobontane MD MPH Blackett Kathleen Ngu MD FRCP¹ Kuaban Christopher MD¹

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SUMMARY

The effects of human immunodeficiency virus (HIV) on cardiovascular autonomic function have been little investigated in African patients. We performed standard heart-rate and blood pressure tests on 75 consecutive consenting patients referred for an HIV test in Yaounde, Cameroon. 54 patients proved to be HIV-infected (30 having progressed to AIDS).

Cardiovascular autonomic dysfunction was present in 8 (28%) patients with AIDS and in 1 (4%) HIV-positive patient without AIDS; no HIV-negative individuals had abnormal results. If borderline results are included, over 80% of HIV-positive patients had cardiovascular autonomic dysfunction.

In HIV-infected patients, simple tests such as blood pressure responses to standing or handgrip can warn of cardiovascular autonomic dysfunction, thus signalling the need for added precautions when invasive procedures are proposed.

INTRODUCTION

28.1 million people are living with HIV infection in Africa today; another 9300 are infected with the virus every day and 2.3 million die from it each year¹. In Cameroon, the prevalence of the infection in the general population rose from 4% in 1996 to 11% in 2001^{2,3}. Although HIV infection is well known to affect the heart, its effects on cardiovascular autonomic function have been little studied in African patients. The issue is important because of the high prevalence of infection and the implications for medical care. In one of the earliest African studies, Rogstad *et al.*⁴ examined autonomic function in patients at various stages of HIV infection and in normal controls. They found evidence of substantial impairment in cardiovascular autonomic function in AIDS patients, with worsening of autonomic function as HIV disease progressed. We investigated the presence of cardiovascular autonomic dysfunction in Cameroonian patients at various stages of HIV infection.

METHODS

We recruited 75 consecutive consenting patients referred for HIV tests (ELISA and western blot) at the University Hospital Centre Yaounde, Cameroon, because of clinical suspicion of HIV infection. Patients with a documented

history of cardiovascular disease before the HIV test were excluded. We also excluded very ill patients who could not satisfactorily perform the autonomic test manoeuvres. 54 (72%) of the patients were HIV infected, of whom 30 had AIDS according to the WHO/Bangui clinical definition for AIDS in Africa⁵.

All patients were clinically assessed for symptoms and signs of heart disease as well as to allow classification of HIV-infected patients into groups with and without AIDS. Cardiovascular autonomic function was tested before the patients' HIV status was known, by a physician who was not aware of the cardiovascular-related clinical findings. Cardiovascular autonomic function was assessed by five standard⁶ blood pressure and heart-rate tests. Blood pressure tests were conducted with an automatic electronic blood pressure machine while heart-rate variations were determined by manually measuring R-R intervals of traces obtained with a semi-automatic electrocardiograph (ECG). Each test was performed only after blood pressure and heart-rate had returned to baseline.

Blood pressure response to standing was measured as the difference in systolic blood pressure with the patient supine and immediately after assumption of the erect posture.

Blood pressure response to sustained handgrip was the difference in diastolic blood pressure before and after maintenance of sustained handgrip with maximum force.

For *heart-rate response to standing from lying position* we calculated the ratio of the longest R-R interval to the shortest R-R interval after the patient moved quickly from supine to upright posture.

Wirral Hospital NHS Trust, St Catherine's Hospital, Birkenhead CH42 0LQ, UK; ¹University Hospital Centre and Faculty of Medicine and Biomedical Sciences, Yaounde, Cameroon

Correspondence to: Dr Divine Nzuobontane

E-mail: divine.nzuobontane@exchange.nwest.wirral-ha.nhs.uk

For *heart-rate response to Valsalva manoeuvre* the patient was asked to blow through a mouthpiece connected to a modified sphygmomanometer and hold the pressure at 40 mmHg for 15 s. The ECG was recorded during and after the manoeuvre. The result was recorded as the ratio of the longest R-R interval during the manoeuvre to the shortest R-R interval after the manoeuvre.

For *heart-rate variation during deep breathing* the patient was asked to breathe deeply at six breaths per minute, an ECG being recorded throughout the procedure. The mean of the difference between minimum and maximum heart-rates obtained from R-R intervals was determined for six breathing cycles.

For grading of cardiovascular autonomic function, results were classified into normal, borderline, and abnormal (scored 0, 1 and 2 respectively) as shown in Table 1. An overall score ≤ 3 was considered to indicate normal autonomic function. Scores > 3 and < 8 were considered borderline and scores ≥ 8 were judged abnormal.

Comparisons were done by chi-square analysis with Yates' continuity correction when necessary. Analysis of variance (anova) was performed for comparison of means of more than two groups and Student's *t*-test for comparison of two different groups. $P < 0.05$ was taken as statistically significant.

RESULTS

Clinical features

Mean age of HIV-infected patients was 34 years and of HIV-negative patients 30 years. Body mass index was 20.55 and 21.85, respectively. None of either group gave a history of diabetes mellitus but we did not undertake any blood glucose tests. None was on antiretroviral medications, since they were recruited before their HIV status was known. Since we excluded individuals with a history of cardiovascular disease including hypertension, no patient was on antihypertensive medications. The possibility of alcoholism was difficult to investigate. Most of the patients had presented with non-cardiovascular symptoms, cough and chest pain being the most prevalent. 23 patients had coexisting pulmonary disease (7 AIDS, 10 HIV-positive non-AIDS, and 6 HIV-negative), ranging from pneumonia to non-specific chest infection. We checked all medical records to exclude pulmonary tuberculosis but we cannot firmly exclude this diagnosis in some patients since we did not undertake any chest X-rays or sputum cultures or conduct clinical follow-up.

Cardiovascular autonomic function

Mean diastolic response to persistent handgrip and systolic response to standing were significantly higher in the AIDS

Table 1 Grading of autonomic function tests

Score	Blood pressure tests		Heart-rate tests			
	BP response standing	BP response handgrip	HR Valsalva	HR deep breathing	HR variation during standing	
Normal	0	≤ 10	≥ 16	> 1.21	≥ 15	≥ 1.04
Borderline	1	11–29	11–15	—	11–14	1.01–1.03
Abnormal	2	≥ 30	≤ 10	≤ 1.21	≤ 10	≤ 1.00

BP=blood pressure; HR=heart-rate

Table 2 Means and standard deviations of autonomic function tests by group

	AIDS (N=30) M±SD	HIV ⁺ ve non-AIDS (N=24) M±SD	HIV ⁻ ve (N=21) M±SD	Anova P
Systolic BP response to standing	10.67±8.28	5.71±4.51	5.24±4.87	<0.01
Diastolic BP response to persistent handgrip	7.50±6.12	12.67±6.87	13.57±4.51	<0.01
HR response to Valsalva	1.05±0.22	1.18±0.23	1.32±0.25	<0.05
HR response to deep breathing	9.220±7.60	11.58±7.97	11.48±3.96	NS
HR response to standing	0.99±0.27	1.07±0.05	1.087±0.05	NS

NS=Not significant; BP=blood pressure; HR=heart-rate

Table 3 Frequency distribution of normal, borderline and abnormal autonomic function

	AIDS (N=30) No. (%)	HIV⁺ve non-AIDS (N=24) No. (%)	HIV⁻ve (N=21) No. (%)
Normal	1 (3.5)	4 (16.7)	10 (52.3) [†]
Borderline	20 (69.0)	19 (79.2)	11 (47.7)
Abnormal	8 (27.6)	1 (4.2) [*]	

^{*}AIDS versus HIV⁺ve non-AIDS χ^2 16.52, $P < 0.01$

[†]AIDS versus HIV⁻ve χ^2 4.78, $P < 0.05$

group than in the HIV-negative group; likewise, the mean heart-rate response to Valsalva manoeuvre was higher in the AIDS group (Table 2). For most autonomic function tests mean values deviated from normal as disease progressed to AIDS.

Cardiovascular autonomic function was abnormal in 8 (28%) AIDS patients but in only 1 HIV-positive patient without AIDS (Table 3). None of the HIV-negative patients had abnormal function.

Only 1 of the 30 AIDS patients had completely normal cardiovascular autonomic function. More than 80% of HIV-infected patients had either abnormal or borderline results—twice the prevalence in seronegative patients.

DISCUSSION

Our results illustrate that cardiovascular autonomic dysfunction is common in African HIV-infected patients and that autonomic function deteriorates with progression to AIDS. Similar findings have been reported by others in previous studies^{4,7-9}.

The findings resemble those reported by Rogstad *et al.*⁴ in their Kenyan study; however, in contrast to their case-control design, we adopted a cross-sectional design because of the difficulty in getting appropriate HIV-seronegative controls in our setting. They used two additional tests—the cold face test and response to mental stress—and their criteria for diagnosis of autonomic dysfunction were slightly different from ours. Like them, we found a significant difference between groups for the Valsalva test. Unlike them, we did not show significant differences for other heart-rate

tests, but we did find clear differences for blood pressure tests. Probably the divergence of results is related to differences in design, sample size, patient selection and grading of autonomic function tests.

Autonomic dysfunction in HIV infection could have far-reaching consequences in the African setting. Because HIV affects various organ systems, invasive procedures are often needed for diagnostic and therapeutic purposes. In the late stages of HIV infection, screening for autonomic dysfunction may be advisable before invasive procedures such as pericardiocentesis, because of the risk of cardiovascular collapse or sudden death. Syncopal reactions have been reported¹⁰ in HIV patients with abnormal autonomic function during such procedures.

Blood pressure tests may be a good option in African clinical practice, where heart-rate tests are often difficult to perform. In addition, our results indicate that, apart from the Valsalva manoeuvre, heart-rate tests may have only a limited role in discriminating autonomic function in HIV-infected patients. This needs to be explored further.

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