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RESEARCH ARTICLE

A PILOT STUDY TO EVALUATE THE EFFECT OF HAART ON GONADAL DYSFUNCTION IN MALE HIV PATIENTS

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Key Words
Highly Active Antiretroviral Therapy (HAART); Human Immunodeficiency Virus (HIV); Endocrine Changes

Background: Derangement of gonadal functions has been reported in association with HIV infection, but data from Indian population are not sufficient.
Aims & Objective: To evaluate the effect of highly active antiretroviral therapy (HAART) on the gonadal dysfunction in male HIV patients.
Materials and Methods: A total of 45 male HIV-positive patients were included and divided in two groups on the basis of CD4 cell count. Patients in groups A and B had CD4 count ≤200 and >200 cell/μL, respectively. Baseline hormone level was measured before the start of HAART, and the patients were followed up for 6 months and the hormone levels were measured again.
Results: In group A (*n* = 29), six (20.69%) patients had testosterone level <200 ng/dL, among them four (66.67%) patients had low luteinizing hormone (LH) and follicle-stimulating hormone (FSH) (secondary hypogonadism) levels. In group B (*n* = 16), none of the patients had low testosterone level whereas two (12.5%) and seven (43.8%) had low LH and FSH level, respectively. Overall of 45 patients, 6 (13.33%) had hypogonadism. Of these six patients, four (66.67%) were having secondary whereas two (33.33%) were primary hypogonadism. After 6 months, condition of five of these six (83.33%) patients improved on HAART.
Conclusion: This study showed the improvement in gonadal dysfunction in HIV patients on administration of HAART. Although the number of patients included in this study was small, but this pilot study provides a basis for further evaluation by a large longitudinal study to substantiate its findings.

INTRODUCTION

A wide spectrum of endocrine abnormalities is observed in HIV-infected patients.[1–3] Derangement of gonadal functions has been reported in association with HIV infection.[4–6] Changes in endocrine function may be related to viral infection of the gland, systemic effects of HIV or an opportunistic infection, infiltration by a neoplasm such as Kaposi's sarcoma, a complication in treatment, or generation of cytokines.[7] Some of these abnormalities are similar to those seen in other systemic illness, whereas others are unique to HIV infection. Low testosterone concentrations are associated with lower CD4 cell count. Gonadal dysfunctions are common among men and women with HIV. Low testosterone concentrations are associated with lower CD4 cell count, advanced stage of illness, and weight loss.[8,9]

The endocrinopathy in the form of gonadal dysfunction may be contributing significantly to the clinical status of the HIV patients, including sexual function, muscle mass, general well-being, and quality of life.[10] There has been no research that has studied the effect of highly active antiretroviral therapy (HAART) on male hypogonadism. All the studies done till now have investigated the effect of injectable/oral testosterone on hypogonadism.[11–15] In view of the variable and incomprehensive data of gonadal dysfunction in patients with HIV, the aim of the present study was (1) to study the incidence of gonadal dysfunctions in male HIV patients and (2) to prospectively investigate the effect of HAART on the gonadal dysfunctions in male HIV patients.

MATERIALS AND METHODS

The study was conducted at Department of General Medicine, Institute of Medical Sciences, Banaras Hindu University (BHU), Varanasi, Uttar Pradesh, India. The cases were selected from the patient attending the ART OPD of Sir Sunderlal Hospital, BHU, Varanasi. A total of 45 male adult patients with HIV infection were enrolled at different stages of diseases and divided

into two groups: group A consisting of HIV-positive patients with CD4 count ≤ 200/μL with or without opportunistic infection, and group B consisting of HIV-positive with CD4 count > 200/μL with stage III/IV disease with or without opportunistic infection. Detailed history and physical examination were carried out to assess gonadal dysfunction and details were recorded on a predesigned format. Baseline blood samples were drawn before the start of HAART and the patients were followed up for 6 months and again the samples redrawn for hormonal assays. In group A (*n* = 29), 20 patients were started on zidovudine-based therapy whereas 9 were started on stavudine-based therapy; in group B (*n* = 16), 12 patients were started on the zidovudine-based therapy and 4 stavudine-based therapy.

Thus, of 45 patients, 32 (71.11%) were started on zidovudine-based therapy and rest were administered stavudine-based therapy. The majority of patients were on zidovudine + lamivudine + nevirapine followed by zidovudine + lamivudine + efavirenz followed by lamivudine + stavudine + efavirenz followed by lamivudine + stavudine + nevirapine therapy. Mean hormonal levels (LH, FSH, and testosterone) for each group were calculated at the start of therapy and also at 6 months on antiretroviral therapy (ART) and were compared.

Statistical Analysis

Data were entered in Excel 2007 and analyzed using SPSS software, version 16.0. The data were presented as mean ± SD for continuous variables and for categorical variables frequency with their respective percentages were given. The data were checked for the assumption of normality before application of statistical test. Wilcoxon signed-rank test was performed to compare the paired observation. A *P*-value of <0.05 was considered as statistically significant.

RESULTS

In this study, the mean age of the cases (*n* = 45) was 36.81 ± 8.85 years and that of the control group (*n* = 45) was 36.84 ± 9.33 years. The mean body mass index (BMI) of the cases was 17.05 ± 2.22 kg/m^2. The BMI has negative correlation with CD4 cell count (Table 3). In group A (*n* = 29), six (20.69%) patients had testosterone level ≤ 200 ng/dL, among these, four (66.67%) patients had low luteinizing hormone (LH) and follicle-stimulating hormone (FSH) (secondary hypogonadism) levels. In group B (*n* = 16), none of the patients had low testosterone level whereas two (12.5%) and seven (43.8%) had low LH and FSH level, respectively. Overall of 45 patients, 6 (13.33%) had hypogonadism. Four of these six (66.67%) patients had secondary whereas two (33.33%) had primary hypogonadism. After 6 months of HAART, the condition of five out of these six patients improved (Tables 2 and 3). One patient remained hypogonad throughout the treatment, although the testosterone level showed a trend toward achieving the normal level.

Table 1: Frequency of patients according to their testosterone level in different CD4 category groups

CD4	Testosterone (ng/dL)		Total
	<200 (%)	>200 (%)	
≤200/μL	6 (20.69)	23 (79.31)	29
>200/μL	0 (0)	16 (100)	16
Total	6 (13.33)	39 (86.67)	45

Table 2: Comparison of variables between baseline and 6 months

Variables	At Baseline†	At 6 Months†	*P*-value
Testosterone	50.8 (18.0–499.0)	54.0 (26.1–602.0)	0.172*
LH	12.10 (4.37–18.0)	13.4 (6.47–18.45)	0.795*
FSH	8.43 (5.62–17.32)	9.56 (5.72–17.90)	0.739*

*† Median (interquartile range); * Not statistically significant by Wilcoxon signed-rank test at 5% level of significance.*

Table 3: Demographic characteristics of patients studied (n = 45 men) at start of therapy

Parameters		Mean ± SD	Minimum	Maximum
Age (years)	CD4 ≤200	38.28 ± 10.76	23	60
	CD4 >200	34.29 ± 8.26	25	50
	Total	37.33 ± 10.44	23	60
BMI (kg/m^2)	CD4 ≤200	15.6 ± 1.98	13.52	21.76
	CD4 >200	18.74 ± 3.16	12.56	24.84
	Total	17.05 ± 2.22	12.56	24.84

Table 4: Biochemical parameters of patients studied (n = 45)

Parameters		Mean ± SD	Minimum	Maximum
Hb (g%)	CD4 ≤200	9.51 ± 2.41	3.7	14
	CD4 >200	9.71 ± 2.00	8.4	12.7
	Total	9.33 ± 2.16	3.7	14
Creatinine (mg/dL)	CD4 ≤200	1.10 ± 0.50	0.5	3.2
	CD4 >200	1.10 ± 0.50	0.4	3.6
	Total	1.07 ± 0.44	0.3	3.6
Urea (mg/dL)	CD4 ≤200	31.02 ± 12.51	30	71
	CD4 >200	29.18 ± 12.48	40	92.4
	Total	30.69 ± 14.15	30	92.4
SGOT (U/L)	CD4 ≤200	58.65 ± 32.75	22	448
	CD4 >200	56.34 ± 31.41	16	194
	Total	57.82±52.75	16	448

DISCUSSION

Many alterations in endocrine function have been reported in association with HIV infection and AIDS.[1–3] Gonadal dysfunction is common among HIV-infected men.[4,5] Our study investigated the gonadal dysfunction in male HIV patients and evaluated the effect of ART on the gonadal function after 6 months of HAART . In this study six (13.33%) patients with hypogonadism showed low testosterone (≤200 ng/dL) levels; among them four had low testosterone

along with low LH and low FSH (secondary hypogonad) levels. Recent studies on hypogonadism report up to 20% prevalence among HIV-infected men. Raffi et al.[16] reported that 29% of the 75 male patients were with hypotestosteronemia. This figure was almost double in our study. Probably, it can be explained by the fact that because all the patients were enrolled on OPD basis, so they were less sick and were having better performance scores.

In a study by Grinspoon and Bilezikian,[1] hypogonadism was found to be secondary (low/normal LH, low testosterone) in 75% (18 of 24) patients. It was found in 66.67% (four of six) patients in our study. Contrary to this, a study carried out by Dobs et al.[17], 20 of 40 men (50%) having AIDS-related complexity were found to also have hypogonadism.[18] In our study, we found that five of six patients showed significant improvements in the testosterone level during the 6 month of HAART, with normalization of LH and testosterone. One patient remained hypogonad throughout the treatment although the testosterone level showed a trend toward achieving normal levels. Two of the six patients reported history of loss of libido. Although the number was small and statistically insignificant, it provided us the different aspect of management of hypogonadism in patients with HIV. Till now, there has been no such study that has reported the effect of HAART on hypogonadism in men. All the studies carried out till now have investigated the effect of injectable testosterone/oral on hypogonadism.[11–13] Evaluation of gonadal function in HIV patients has been performed primarily in men. Although the functional significance of the histological changes in the testes is not clear, symptomatic hypogonadism is common among HIV-infected men. Dobs et al.[17] studied 42 men with AIDS, of whom 67% reported decreased libido and 33% were found to be impotent. Twenty-four of these men had subnormal serum testosterone concentrations; 18 had low or inappropriately normal serum gonadotropin level.[16] But in our study, we found only two patients who had complained of loss of libido.

CONCLUSION

This study has revealed that gonadal dysfunctions are common in HIV patients. Also, we found improvement in gonadal function on administration of HAART in HIV patients with hypogonadism. Although the number of patients included in this study was small and most of the patients were not very sick and had good performance score, this pilot study provides a basis for further evaluation by a large longitudinal study to substantiate its findings. If the observation is a true reflection of gonadal functions in patients with HIV on HAART, it presents a strong case to avoid unnecessary administration of various drugs, thereby decreasing morbidity and financial burden on the poor patients in this part of the country.

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