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GONADAL FUNCTION IN HUMAN IMMUNODEFICIENCY VIRUS (HIV)-INFECTED MEN ASSESSED BY ISOTOPIC DILUTION-LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY (ID-LC-MS/MS) AND CHEMILUMINESCENT ASSAY

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BACKGROUND: HIV infection is associated to premature decline of serum T[1,2]. However, prevalence and biochemical characterization of hypogonadism in HIV-infected men are still to be well defined[1,2].

AIM OF THE STUDY: We evaluated the gonadal status in young to middle aged HIV-infected men in order to characterize hypogonadism by assessing circulating total T (TT) with either Liquid Chromatography tandem Mass Spectrometry (LC-MS/MS) or chemiluminescent immunoassay.

METHODS: Prospective, cross-sectional, observational study on 315 consecutive HIV-infected male patients with ongoing Highly Active Antiretroviral Therapy (HAART), attending the Metabolic Clinic of Infectious Diseases. Serum TT, gonadotropins and sex hormone-binding globulin (SHBG) were measured by chemiluminescent immunoassay. Serum TT was also assessed by the gold standard LC-MS/MS in 233 patients. Free T (FT) was calculated by using Vermeulen equation[3]. Hypogonadism was defined as serum TT levels below 320 ng/dL and/or free T levels below 64 pg/ml[4].

Statistical analysis: Categorical variables were compared using Chi-Square test, while correlations were performed using Spearman's Rho coefficient and linear regression models.

Table 1.	**Total testosterone** *Number of patients (%)*	
	Chemiluminescent immunoassay	**LC-MS/MS**
Eugonadal *(TT ≥ 320 ng/dL and LH ≤ 8.9 mIU/ml)*	274 (87.0)	202 (86.7)
Compensated Hypogonadism *(TT ≥ 320 ng/dL and LH > 9 mIU/ml)*	31 (9.8)	20 (8.6)
Primary Hypogonadism *(TT < 320 ng/dL and LH > 9 mIU/ml)*	3 (1.0)	2 (0.9)
Secondary Hypogonadism *(TT < 320 ng/dL and LH ≤ 8.9 mIU/ml)*	7 (2.2)	9 (3.9)
Total	*315 (100)*	*233 (100)*
	Free testosterone *Number of patients (%)*	
	Chemiluminescent immunoassay	**LC-MS/MS**
Eugonadal *(FT ≥ 64 pg/mL and LH ≤ 8.9 mIU/ml)*	267 (84.8)	199 (85.4)
Compensated Hypogonadism *(FT ≥ 64 pg/mL and LH > 9 mIU/ml)*	26 (8.3)	18 (7.7)
Primary Hypogonadism *(FT < 64 pg/mL and LH > 9 mIU/ml)*	8 (2.5)	4 (1.7)
Secondary Hypogonadism *(FT < 64 pg/mL and LH ≤ 8.9 mIU/ml)*	14 (4.4)	12 (5.2)
Total	*315 (100)*	*233 (100)*

Table 1. Classification of gonadal function, depending on serum TT and calculated FT, using LC-MS/MS and immunoassay for TT measurement.

RESULTS: 315 HIV-infected patients were enrolled (mean age 45.56±5.61 years) with average duration of HIV-infection of 16.57±10.45 years. Considering serum total T levels assessed by LC-MS/MS and immunoassay, 11 patients out of 233 (4.8%) and 10 patients out of 315 (3.2%) had T deficiency, respectively. TT combined with luteinizing hormone (LH) levels was used to classify hypogonadism (Table 1). No difference was found among subgroups comparing the two methodologies used for TT measurement (p=0.914). 56 patients (17.8%) showed SHBG above the normal range (>71.4 nmol/L). Considering calculated FT, the incidence of hypogonadism raised to 6.9% using either immunoassay or LC-MS/MS, respectively (Table 1), with no difference between methodologies (p=0.895). Including compensated form of hypogonadism, the prevalence raised to 13% for TT and to 15% for FT. Patients with low FT were older than eugonadal patients (p=0.005) and showed a significantly longer duration of HIV-infection (p<0.0001) and HAART (p=0.002), while they did not differ for body mass index (p=0.231). FT showed an inverse relation with age (-0.340, p<0.0001, R^2=0.116), years of infection (-0.339, p<0.0001, R^2=0.120) and years of HAART (-0.346, p<0.0001, R^2=0.117), but not with BMI of patients.

CONCLUSIONS: To the best of our knowledge, this is the first, properly-designed prospective study aiming to investigate the gonadal status of HIV-infected men with both LC-MS/MS and chemiluminescent assay. In HIV-infected patients a) the two methodologies have equivalent reliability in TT measurement; b) SHBG for calculated FT is essential for the detection of T deficiency, revealing the real prevalence of hypogonadism in this context; c) duration of HIV-infection and HAART seem to be potent predictive factors for serum FT levels, suggesting a concomitant negative effect of virus *per se* and antiretroviral drugs on gonadal function.

References

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