Article

Clinical and Emotional Factors Related to Erectile Dysfunction in HIV-Infected Men

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Abstract

The prevalence and associated factors of erectile dysfunction (ED) in Human Immunodeficiency Virus (HIV)–infected men remain controversial. The authors evaluated ED, clinical, and emotional variables in a group of 501 HIV-infected men in a cross-sectional 4-month observational study. ED was assessed using the International Index of Erectile Function–5 and emotional status using the Hospital Anxiety and Depression (HAD) questionnaire. Median age (interquartile range) was 42 (35, 48) years. Time since HIV diagnosis was 6.3 (2.6, 17.1) years, 92% were taking antiretroviral treatment and 81.8% had an HIV-RNA viral load <50 copies. The prevalence of ED was 58.5%. ED was mild in 30.1%, mild to moderate in 19.5%, moderate in 6.1%, and severe in 2.5%. ED medications were used by 19% of men. In the univariate analysis, the variables associated with all degrees of ED were older age, longer time since HIV diagnosis, higher scores in HAD, not taking efavirenz, taking etravirine, taking ritonavir, HIV/Hepatitis C Virus coinfection, and taking a protease inhibitor-containing regimen. For mild to moderate, moderate, and severe ED, the same variables were significant, as were lower nadir CD4 cell count, lower social support, taking atazanavir, concomitant conditions, and concomitant treatments. The variables that remained significant in the multivariate analyses, considering all degrees of ED or excluding mild ED were the following: older age and higher scores in HAD total. In summary, ED affected more than half of this cohort of well controlled HIV-infected men. Age and emotional status seemed to play a fundamental role in its presence.

Keywords

HIV infection, sexual dysfunction, mood disorders, quality of life

When understood as a wide concept encompassing physical health and emotional well-being, quality of life is a key aspect of chronic diseases. Sexual health is a state of physical, emotional, mental, and social well-being related to sexuality. Sexual functioning and quality of life are interwoven phenomena (Shamspour, Assari, & Lankarani, 2010). In Human Immunodeficiency Virus (HIV) infection, sexual health has always been an issue of interest. Since the beginning of the epidemic, research has been conducted to determine the presence of sexual dysfunction in people living with HIV infection and to evaluate its prevalence and associated factors.

In the early 1990s, a relationship was established between HIV infection and higher risk of sexual dysfunction in men, especially ejaculatory problems (Jones, Klimes, & Catalan, 1994). Since then, prevalence values have been diverse but high, oscillating between 30% and 74% (Asboe et al., 2007; Cove & Petrak, 2004; Ende, Lo Re, DiNubile, & Mounzer, 2006; Lallemand, Salhi, Linard, Giami, & Rozenbaum, 2002; Moreno-Pérez et al., 2010; Schrooten et al., 2001). There is now general agreement that sexual dysfunction is more present in HIV-infected men than in non-HIV-infected men (Zona et al., 2012).

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Discrepancies also arise with respect to associated factors. The findings of various studies suggested that sexual dysfunction is associated with the use of antiretroviral treatment (ART), specifically, protease inhibitors (PIs; Colson et al., 2002; Moreno-Pérez et al., 2010; Schrooten et al., 2001). However, this relationship remained controversial, since other researchers reported contradictory data (Ende et al., 2006; Lallemand et al., 2002; Wang et al., 2013). Additional factors frequently mentioned include older age (Asboe et al., 2007; Guaraldi et al., 2007; Moreno-Pérez et al., 2010; Pérez, Moreno, Navarro, Santos, & Palacios, 2013), duration of exposure to ART (Asboe et al., 2007; Moreno-Pérez et al., 2010), and emotional disturbances and medications to treat them (Asboe et al., 2007; Guaraldi et al., 2007; Hart et al., 2012; Hart et al., 2015; Pérez et al., 2013). The objectives of this study were to evaluate erectile dysfunction (ED) in a wide sample of men and to explore sociodemographic, clinical, and emotional contributing factors.

Material and Method

The HIV-sex male study aims to evaluate the sexual activity of men living with HIV in Spain. This cross-sectional 4-month observational study was developed in a sample of men attending an HIV Unit in Badalona (Barcelona, Spain). Eligibility criteria included male birth sex, age ≥18 years and documented HIV infection. Concomitant pathologies or treatments were not exclusion criteria. All men who attended the HIV Unit for their regular medical visits were approached in the waiting room. The procedures and objectives of the study were explained verbally and written information was given.

The men who agreed to participate provided their written consent and completed the study questionnaires. The Ethics Committee of Germans Trias i Pujol University Hospital approved the study (PI-13-067). Data were collected from November, 2013 to March, 2014. Participants whose data were incomplete were excluded from the analysis.

Main Outcome Measures

Demographic variables were self-reported and collected with a form developed ad hoc for the study. Data included age, country of birth, marital status, sexual orientation, serologic status of partner (if applicable), use of ED medications in the past 15 days, and adherence to ART in the past 15 days (if applicable). Clinical variables were retrieved from medical records and clinical databases and included time since HIV diagnosis, current CD4 cell count, nadir CD4 cell count, highest HIV-RNA viral load, current HIV-RNA viral load, type of ART if applicable, concomitant conditions, and concomitant treatments.

ED was evaluated using the International Index of Erectile Function (IIEF-5) in its validated Spanish version (Martin-Morales et al., 2001; Rosen, Cappelleri, Smith, Lipsky, & Peña, 1999). The IIEF-5 is a brief, five-item version of the IIEF. Scores are interpreted as follows: severe ED (5-7 points), moderate (8-11 points), mild to moderate (12-16 points), mild (17-21 points), and normal (22-25 points). Two outcome variables were defined: The first one comparing patients without ED and patients with any degree of ED and the second one comparing patients without ED or mild ED and patients with mild to moderate, moderate, and severe ED.

The symptoms of depression and anxiety were measured using the Hospital Anxiety and Depression Scale (HAD) in its validated Spanish version (Herrero et al., 2003; Zigmond & Snaith, 1983). The HAD is a widely used 14-item self-report scale designed to briefly measure current anxiety and depressive symptoms in nonpsychiatric hospital patients. Somatic symptoms are excluded to avoid confounding. Scores on each scale can be interpreted in ranges: normal (0-7), mild (8-10), moderate (11-14), and severe (15-21). The authors consider a score of 11 or higher to indicate probable caseness of mood disorder on the anxiety or depression subscales, and a score of 8-10 as merely suggestive of a disorder (Snaith, 2003).

Finally, the Marlowe–Crowne Social Desirability Scale was included in its validated Spanish version (Ávila Espada & Tomé Rodriguez, 1989; Crowne & Marlowe, 1960). This scale was designed to measure social desirability independently of psychopathology. In other words, it assesses whether patients are responding truthfully or are misrepresenting themselves to manage their self-presentation. Scores are interpreted as follows: Low scorers (0-8) are more willing to respond to the test truthfully, even when their answers might meet with social disapproval; average scorers (9-19) tend to identify an average degree of concern for the social desirability of their responses; and high scorers (20-33) are highly concerned about social approval and respond to test items in such a way as to avoid social disapproval.

Statistical Analyses

Continuous variables were analyzed using the Kolmogorov–Smirnov test to assess for normal distribution. Due to the fact that these variables did not follow a normal distribution, they were expressed as median and interquartile range. Percentages (number of patients) were given for the discrete variables.

To identify covariates that were independently associated with different stages of ED, stepwise logistic regression was used. The multivariate models included all covariates associated with ED at the level of $p \leq .25$ in the univariate analysis, as well as those hypothesized to be associated with ED regardless of statistical significance. Furthermore, the correlation of continuous variables was taken into account to avoid multicollinearity. The statistical analyses were

Table 1. Characteristics of the Study Sample.

	Total (*N* = 501)	Patients without ED (*N* = 208)	Patients with ED (*N* = 293)
Age, years	42 (35, 48)	38 (32, 45)	45 (36, 50)
Country of birth, %			
Spain	73.3	72.6	73.7
Others	26.7	27.4	26.3
Marital status, %			
Single	45.1	46.1	44.4
Married or stable partner	48.1	48.6	47.8
Divorced	6	5.3	6.5
Widow	0.6	—	1.3
Sexual intercourse, %			
Only with men	75.8	76.9	75.1
Only with women	19.2	17.8	20.1
With men and women	5	5.3	4.7
Partner infected with HIV, %	18.6	18.8	18.4
Time since HIV diagnosis, years	6.3 (2.6, 17.1)	4.7 (1.8, 13.3)	7.5 (3, 18.4)
On ART, %	92	91.3	92.5
Type of ART, %			
NNRTI	33.4	40.4	28.5
PI	38.6	33.5	42.1
INSTI	18	18	17.9
INSTI + PI	3.9	4.2	3.6
CCR5 blockers + PI	1.5	0.5	0.7
Other combinations	4.6	3.3	5.4
CD4 cell count, cells/μL	617 (465, 815)	631 (480, 832)	597 (451, 811)
Nadir CD4 cell count, cells/μL	300 (190, 416)	315 (217, 431)	287 (174, 412)
Highest viral load, copies/mL	71.000 (13.000, 240.000)	65.500 (15.000, 220.000)	75.000 (12.235, 248.953)
Undetectable viral load, %[a]	81.7	81.9	81.3
Coinfection with HCV, %	18	12.5	21.8
Concomitant pathologies, %	44.5	39.4	48.1
Use of ED medications, %	19	11.1	24.6
HAD total	11 (6, 16)	8 (4, 12)	12 (8, 17)
HAD anxiety	7 (4, 10)	6 (3, 8)	8 (5, 11)
HAD depression	4 (1, 6)	2 (1, 4)	4 (2, 7)
Adherence to ART, %[b]	97.1	97.1	97.3

Note. HAD = Hospital Anxiety and Depression Scale; HCV = hepatitis C virus; ART = antiretroviral therapy; NNRTI = nonnucleoside reverse transcriptase inhibitors; PI = protease inhibitors; INSTI = integrase strand transfer inhibitors; ED = erectile dysfunction. Data expressed as median (interquartile range), except when indicated otherwise.
[a]Undetectable at ≤50 copies/mL level. [b]Number of patients reporting ≥95% of ART medication intake in the past 15 days.

performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA), assuming a 95% confidence level and two-tailed tests.

Results

The study was proposed to a total of 521 men. Eight men refused to participate and 12 returned the questionnaires uncompleted. Thus, the final sample comprised 501 men. The demographic and clinical characteristics of the study sample are reported in Table 1.

Median age (interquartile range) was 42 (35, 48) years. Two hundred and forty-one (48.1%) of the men were married or had a stable partner (≥6 months), 93 (18.6%) of whom were also infected with HIV. Sexual intercourse was with men only in 380 (75.8%) participants. Median time since HIV diagnosis was 6.3 (2.6, 17.1) years, and 461 (92%) men were taking ART. Of these, 178 (38.6%) took a PI-containing regimen, 154 (33.4%) a nonnucleoside reverse transcriptase inhibitor–containing regimen, and 83 (18%) an integrase strand transfer inhibitor–containing regimen. The most common antiretroviral drugs were tenofovir (275 men, 59.6%), emtricitabine (272, 59%), ritonavir (201, 43.6%), darunavir (149, 32.3%), lamivudine (99, 21.4%), abacavir (95, 20.6%), raltegravir (83, 18%), and efavirenz (65, 14%).

Undetectable HIV-RNA viral load was present in 410 (81.8%) participants, and 429 (93%) adhered to ≥95% of their ART. Ninety (18%) individuals were coinfected

Table 2. Variables Associated With all Degrees of ED.

	Univariate regression			Multivariate regression		
Covariate	*OR*	95% CI	*p*	*OR*	95% CI	*p*
Older age	1.059	[1.038, 1.080]	<.001	1.059	[1.037, 1.08]	<.001
Longer time since HIV diagnosis	1.032	[1.010, 1.054]	.004	—	—	—
HAD total	1.111	[1.077, 1.147]	<.001	1.112	[1.076, 1.148]	<.001
HAD anxiety	1.159	[1.102, 1.221]	<.001	—	—	—
HAD depression	1.234	[1.158, 1.316]	<.001	—	—	—
Not taking efavirenz	2.289	[1.343, 3.904]	.002	—	—	—
Taking etravirine	6.211	[1.421, 27.021]	.015			
Taking ritonavir	1.519	[1.042, 2.221]	.031	—	—	—
HIV/HCV coinfection	1.945	[1.182, 3.195]	.009	—	—	—
Use of a PI-containing regimen	1.473	[1, 2.172]	.050	—	—	—

Note. OR = odds ratio; CI = confidence interval; ED = erectile dysfunction; HIV = human immunodeficiency virus; HAD = Hospital Anxiety and Depression Scale; HCV = hepatitis C virus; PI = protease inhibitor; ART = antiretroviral therapy. The univariate analysis included the following variables: age, country of birth, marital status, sexual orientation, partner with HIV infection, time since HIV diagnosis, being on ARV, type of ARV (families and drugs), current CD4 cell count, nadir CD4 cell count, current HIV-RNA viral load, highest HIV-RNA viral load, HIV/HCV coinfection, presence of concomitant pathologies (and types), presence of concomitant treatments (and types), use of ED medications, HAD total, HAD anxiety, HAD depression, adherence to ARV, social desirability.

with Hepatitis C Virus (HCV) and 223 (44.5%) had one or more concomitant conditions, the most frequent being metabolic disorders (17.2%) and rheumatic and musculoskeletal disorders (13%). Concomitant treatments were taken by 182 (36.3%) men.

According to the IIEF-5, the prevalence of all degrees of ED was 58.5% (293 men). In this group, the degree of ED was mild in 151 men (51.5%), mild to moderate in 98 (33.4%), moderate in 31 (10.5%), and severe in 13 (4.4%). ED medications (mainly tadalafil and sildenafil citrate) had been used in the past 15 days by 95 (19%) men. Among the group of men who had taken ED medications, 24 (25.2%) of them did not report ED, but the rest still reported ED that was mostly mild or mild to moderate.

The HAD total score was 11 (6, 16), with a HAD anxiety subscale of 7 (4, 10) and a HAD depression subscale of 4 (1, 6). These results were within the normal range. The Marlowe–Crowne Social Desirability Scale was 18 (13, 21). Twenty-three (4.6%) men were low scorers, 313 (62.5%) were average scorers, and 162 (32.3%) were high scorers.

Univariate and Multivariate Regression Analyses Considering Any Degree of ED

As seen in Table 2, the variables associated with any degree of ED in the univariate analysis were as follows: older age, longer time since HIV diagnosis (years), higher scores in HAD total, higher scores in HAD anxiety, higher scores in HAD depression, not taking efavirenz, taking etravirine, taking ritonavir, HIV/HCV coinfection, and taking a PI-containing regimen. In the multivariate regression analysis, only older age and higher scores in HAD total remained associated with ED.

Univariate and Multivariate Regression Analyses Considering Mild to Moderate, Moderate, and Severe ED

In the univariate analysis, the associated variables were older age, longer time since HIV diagnosis (years), lower nadir CD4 cell count, higher scores in HAD total, higher scores in HAD anxiety, higher scores in HAD depression, lower social support, not taking efavirenz, taking etravirine, taking atazanavir, taking ritonavir, HIV/HCV coinfection, having concomitant conditions, taking concomitant treatments, and taking a PI-containing regimen. In the multivariate analysis, older age and higher scores in HAD total remained associated with mild to moderate, moderate, and severe ED (Table 3). The findings in both multivariate models were the same when the authors considered all degrees of ED or only mild to moderate, moderate, and severe ED.

Discussion

The current results identify that ED affected more than half of this cohort of well controlled HIV-infected men. Age and emotional status seemed to play a fundamental role in its presence. The term sexual dysfunction encompasses ED, loss of libido, and difficulty achieving orgasm. In HIV infection, several studies have pointed to the existence of difficulties in all three areas (Jones et al., 1994; Lamba, Goldmeier, Mackie, & Scullard, 2004), although ED is the field that has generated most research. Rates of ED in HIV-infected men have oscillated considerably, probably owing to the heterogeneity of the samples evaluated. However, numbers have always been high and have even reached 74% (Ende et al., 2006).

Table 3. Variables Associated With Mild to Moderate, Moderate, and Severe ED.

	Univariate regression			Multivariate regression		
Covariate	*OR*	95% CI	*p*	*OR*	95% CI	*p*
Older age	1.067	[1.043, 1.091]	<.001	0.057	[1.037, 1.081]	<.001
Longer time since HIV diagnosis (years)	1.049	[1.027, 1.073]	<.001	—	—	—
Lower nadir CD4 cell count	1.001	[1, 1.002]	.013			
Higher scores in HAD total	1.087	[1.055, 1.119]	<.001	0.106	[1.076, 1.148]	<.001
Higher scores in HAD anxiety	1.121	[1.066, 1.179]	<.001	—	—	—
Higher scores in HAD depression	1.187	[1.121, 1.257]	<.001	—	—	—
Lower social support	1.167	[1.018, 1.338]	.027			
Not taking efavirenz	2.255	[1.140, 4.461]	.020	—	—	—
Taking etravirine	7.407	[2.611, 20.831]	<.001			
Taking atazanavir	2.618	[1.316, 5.211]	.006			
Taking ritonavir	1.883	[1.251, 2.821]	.002	—	—	—
HIV/HCV coinfection	1.802	[1.121, 2.907]	.016	—	—	—
Having concomitant conditions	1.941	[1.309, 2.873]	.001			
Taking concomitant treatments	2.049	[1.379, 3.051]	<.001			
Use of PI-containing regimen	1.684	[1.112, 2.529]	.012	—	—	—

Note. OR = odds ratio; CI = confidence interval; ED = erectile dysfunction; HIV = human immunodeficiency virus; HAD = Hospital Anxiety and Depression Scale; HCV = hepatitis C virus; PI = protease inhibitor.

In the current study, ED affected more than half of the sample, and although the degree was mild in 51.5% of the men interviewed, mild to moderate ED was present in 33.4%, and moderate and severe ED in 15%. The current results coincide with those of the other Spanish observational study performed to investigate ED in HIV-infected men (Pérez et al., 2013), in which ED was reported by 67% of the participants. The characteristics of the patients assessed in both studies were also similar, namely, the men were young, in their 40s, with good immunological and virological status. Accordingly, the authors believe that the results obtained in the large sample of 501 participants reinforce the data reported by Pérez et al. (2013) and highlight the magnitude of the problem. The current study also provides us with new data about the role of other associated factors.

Several variables were associated with ED in the univariate analyses, although they did not reach significance in the multivariate models. Most of these variables were clinical, namely, longer time since HIV diagnosis, lower nadir CD4 cell count, and existence of concomitant conditions and their treatments. It could be hypothesized that behind this information could be found, the profile of a long-term diagnosed and treated patient in whom ED might be another manifestation of the delicate physical and emotional situation described in previous studies (Coyne et al., 2010; Fumaz et al., 2012; Gonzalez-Garcia et al., 2014).

Although the use of PI-containing regimens were not significant in the multivariate analyses, it is worth mentioning its contribution in the univariate analyses in light of past controversies. Studies that reported a role for PIs in ED were based on drugs not currently used or that were used at higher doses (Colson et al., 2002; Schrooten et al., 2001). In the current study, the PIs taken by the participants were the most recently developed and widely used in the past few years. Therefore, more research is necessary to ascertain whether this new generation of PIs still contributes to ED.

Only two variables remained strongly associated with ED in the multivariate models, namely, older age and HAD total (a summary of anxiety and depression levels). Of note, the authors obtained the same information in the two multivariate models performed, when all degrees of ED were considered and when the authors considered only higher degrees of ED. Other authors included age in their list of relevant variables when discussing ED in HIV infection (Asboe et al., 2007; Moreno-Pérez et al., 2010; Pérez et al., 2013). In the current study, age is particularly relevant, since the patients were relatively young (early 40s). Therefore, the impairment in sexual functioning might affect HIV-infected men both more often (Zona et al., 2012) and earlier, as with other typical manifestations of aging.

Although rates of anxiety and depression were low in the participants, poorer emotional status was another contributing factor for ED. This finding is concordant with those reported elsewhere (Asboe et al., 2007; Guaraldi et al., 2007; Guaraldi et al., 2012; Pérez et al., 2013) and emphasizes the idea that the emotional status of patients who complain about sexual dysfunction should always be contemplated in their assessment. Also, considering that ED medications do not work in absence of sexual stimulation, one could hypothesize that emotional status might partly explain the lack of efficacy of these drugs in the participants who had taken them. Only 25% of the participants referred absence of ED, while the others still had symptoms that were mostly mild or mild to moderate. However,

this low rate of efficacy of ED medications merits further research to ascertain other contributing factors.

The current findings are subject to a series of limitations. All data are self-reported, potentially leading to underreporting of socially undesirable behaviors. Sexual dysfunction is still a delicate topic for some people. Therefore, the authors decided to include a questionnaire that provided information on social desirability. Since no differences were identified between the presence of ED and the degree of social desirability, the authors believe that most of the participants were sincere in their responses.

It should also be taken into account that in the current study, ED was only determined through self-report. It is recommendable to establish ED diagnosis after a complete physical and psychological evaluation to determine vasculogenic or psychogenic factors (Cavallini, 2016; Kellesarian et al., 2016). This study was motivated after the complaints observed in the clinical practice about ED. Thus, the authors were especially interested in knowing patients' perception about it.

Another limitation is that the current study lacks a control group formed by HIV-noninfected participants with similar sociodemographic characteristics. The presence of a control group always provides more robust value to the findings. Also, the IIEF was used to asses ED. This questionnaire was constructed and validated in heterosexual men and a modified IIEF for men who have sex with men exists (Coyne et al., 2010). The IIEF was used because all men who attended the HIV unit, regardless of their sexual preference were included. One of the researchers was always available to answer any doubts when patients answered the questionnaires. Previous studies have successfully evaluated ED with the IIEF in groups formed by heterosexual men and men who have sex with men (Romero-Velez et al., 2014). For all these reasons, the authors believe that the current data are reliable.

The analysis of additional clinical parameters such as serum testosterone or estradiol levels were not included. Although some studies reported a relationship between these parameters and ED in HIV-infected men (Lamba et al., 2004), others did not (Ende et al., 2006, Rochira et al., 2011). Therefore, further research should be performed to clarify this discrepancy. The current study did not include the assessment of smoking either. Cigarette smoking is associated with ED in the general population (Kovac, Labbate, Ramasamy, Tang, & Lipshultz, 2015) and prevalence of smoking continues to be very high among HIV-infected people (Parks, Hernandez-Ramirez, Silverberg, Crothers, & Dubrow, 2016). Nevertheless, in a previous study smoking duration was related to ED only in HIV-negative men (Hart et al., 2015). More studies should be developed to evaluate better this variable in men with HIV infection. Finally, almost all the study patients had met the objectives of HIV treatment, namely, they were on ART and virologically suppressed. However, in patients with ED, this prevents us from distinguishing between the role of ART and the impact of the chronic inflammation caused by the virus itself.

One of the strengths of this study is its large and varied sample (501 participants). It assessed an extensive list of sociodemographic, clinical, and emotional variables as well. These also included parameters that have been considered controversial in the past, such as antiretroviral drugs.

Conclusions

The current study identifies that many men living with HIV infection experience mild to moderate ED and that this is related to older age and emotional disturbances. Considering the negative impact of sexual dysfunctions on quality of life, sexual health should be included in the regular assessment of men living with HIV infection. The health professional should try to facilitate an environment of trust, free of judgment.

Declaration of Conflicting Interests

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