Infect Dis Trop Med 2015; 1 (2): e104

Self-reported sexual dysfunction in HIV-positive subjects: a cross-sectional study

M.R. Pinzone[1], M. Gussio[1], F. Bellissimo[1], C. Coco[1], F. Bisicchia[1], G. Pellicanò[2], F. Palermo[1], M.T. Mughini[1], B. Cacopardo[1], G. Nunnari[1], B.M. Celesia[1]

[1]Department of Clinical and Experimental Medicine, Division of Infectious Diseases, University of Catania, Catania, Italy
[2]Unit of Infectious Diseases, A.O.U. "G. Martino" Policlinico, University of Messina, Messina, Italy

ABSTRACT:

— ***Background:*** Sexual dysfunction (SD) has been reported to be more prevalent among HIV-positive patients in comparison with age-matched HIV-negative individuals. The aetiology of SD is multifactorial and includes endocrine alterations, peripheral and autonomic neuropathy, psychological aspects and vascular diseases.

— ***Patients and Methods:*** In this cross-sectional study, we evaluated the prevalence of and risk factors for self-reported SD in a cohort of HIV-infected HAART-treated patients. SD evaluation was performed using the Female Sexual Function Index (FSFI) for women and the International Index of Erectile Function (IIEF) for men. All subjects were screened for anxiety by administering the Self Rating Anxiety State SAS 054.

— ***Results****:* 152 patients were enrolled, 71.7% male, median age 45 (IQR 39-49) years. Median CD4+ T-cell count was 577 (IQR 373-842) cells/μl, HIV-1 RNA viral load was <50 copies/ml in 78.9% of patients. The median duration of HAART was 8.5 (IQR 4-13) years, 61.8% were taking a PI-based antiretroviral regimen, 36.2% a NNRTI-based one. 7% of women denied any sexual activity and were excluded from analysis. 58% of the remaining 141 subjects reported SD. SD was more frequent in men (65% vs 34%, p =0.0024, OR 3.5, 95% CI 1.6 to 8.2) and elderly subjects (≥50 years) (54% vs 28%, p =0.0029, OR 3.8, 95% CI 1.5 to 9.6). Of 71 men with erectile dysfunction (ED), 26.7% reported severe ED, 73.3% mild/moderate ED. 74 subjects (52.5%) had a z score ≥45 that was suggestive of anxiety. Logistic regression analysis confirmed that age (p =0.008) and male sex (p =0.0087) but not anxiety (p =0.068) were associated with SD.

— ***Conclusions****:* SD was highly prevalent among HIV-positive patients and was associated with male sex and increasing age. A greater understanding of factors associated with SD may help developing focused intervention strategies to improve the quality of life of HIV-infected subjects.

— ***Key words:*** Anxiety, Erectile dysfunction, HAART, HIV, Sexual dysfunction.

INTRODUCTION

Sexual satisfaction represents an important quality-of-life issue. This topic has received little attention in the setting of HIV infection, with most research focusing on understanding the factors associated with unprotected sex and evaluating the efficacy of interventions aimed at modifying these behaviours. However, several reports have shown that sexual dysfunction (SD) is more prevalent among HIV-positive patients in comparison with age-matched HIV-negative individuals[1-4]. Erectile dysfunction (ED), defined as the inability to achieve or maintain an erection for sexual intercourse, is common among elderly men and subjects with chronic diseases.

Corresponding Author: Benedetto Maurizio Celesia, MD, PhD; e-mail: bmcelesia@tin.it

The aetiology of ED is multifactorial and includes endocrine alterations, peripheral and autonomic neuropathy, psychological aspects and vascular diseases[1]. In the pre-HAART era, hypogonadism occurred in up to 50% of patients with AIDS and was therefore a significant risk factor for ED[5]. In the HAART era, ED is still highly prevalent among HIV-infected patients, though the prevalence rate varies widely from 9% to 74%, probably because of different study design and lack of standardized methods for its assessment[6-12]. Many risk factors for ED, including hypogonadism, dyslipidemia, diabetes, central obesity and drug abuse, are overrepresented among subjects with HIV infection[1]. Anxiety and depression are common among patients living with HIV infection and may contribute to ED[13,14]. The association between ED and antiretroviral drugs, especially protease inhibitors (PI), is unclear as published studies have reported conflicting results[6-12].

Few studies have evaluated SD in women with HIV infection. HIV-positive women are more likely to experience lower levels of sexual interest, desire and satisfaction in comparison with uninfected ones[15-17]. Female SD (FSD) is affected by medical and psychological issues. On the one hand, medical problems, including diabetes, advanced HIV infection, endocrinopathies may reduce sexual desire and pleasure; on the other hand, psychological problems, related to anxiety, depression, changes in body image, may contribute to sexual distress and reduce sexual satisfaction[15-17].

The aim of our cross-sectional study was to evaluate the prevalence of and risk factors for SD in a cohort of HIV-infected subjects.

PATIENTS AND METHODS

Study participants

We enrolled 152 consecutive patients on HAART for at least six months followed at two AIDS outpatient clinics in Catania and Messina, Sicily (Italy). All patients gave their written informed consent prior to enrolment. Social, demographic and clinical parameters (HIV viral load, CD4+ T-cell count, CDC stage, time from infection and length of antiretroviral exposure, number of therapeutic lines, type of antiretroviral treatment (PI- or non-nucleoside reverse-transcriptase inhibitor (NNRTI)-based or other regimen) were collected from medical records at the time of test administration.

SD evaluation was performed by self-administered validated questionnaires:

- Female Sexual Function Index (FSFI)[18,19] for women: a 19-item self-report survey exploring six domains of female sexual functioning over the last four weeks, including sexual arousal and desire, lubrication, orgasm, satisfaction and pain during intercourse. For each domain, questions assess the subjective frequency and severity of problems and overall satisfaction within sexual relationships. FSFI maximum score is 36, with higher scores indicating better sexual functioning. A score ≤23 was considered diagnostic of SD.
- International Index of Erectile Function (IIEF) for men: a cut off value of 25 in the erectile domain was considered diagnostic of ED. EF was classified into four diagnostic categories: (1) no ED (EF score = 26-30); (2) mild-moderate ED (EF score = 17-25); (3) moderate ED (EF score = 11-16); (4) severe ED (EF = 6-10)[20,21]. Information regarding EF was restricted to the four weeks before study entry.

All subjects were screened for anxiety by administering the Self Rating Anxiety State SAS 054[22], a self-administered test exploring symptoms and signs of anxiety over the last week.

The Self Rating Anxiety State SAS 054 consists of:

- 15 items exploring sympathetic symptoms (palpitations, accelerated heart rate, sweating, nausea, shortness of breath, paresthesias) and symptoms of post-traumatic stress disorders (PTSD), such as panic attacks, sleep disorders, nightmares;
- 5 items exploring the well-being status.

A score from 1 to 4 was assigned to each answer (never, sometimes, frequently and always). The total raw scores ranged from 20 to 80. The crude score was then converted into a standard score (n + n/4 = z score). The clinical interpretation of anxiety index score is reported below: 20-44: normal range; 45-59: moderate anxiety; 60-74: severe anxiety; ≥75: extreme anxiety. Patients with a z score ≥45 points were considered anxious.

STATISTICS

Categorical variables are presented as number of cases (percentage) and were compared by the χ^2 test or Fisher's exact test, when appropriate. Continuous variables are expressed as median (interquartile range, IQR) and were compared by Mann-Whitney test. Identified variables in the univariate analyses with a *p*-value less than 0.05 were included in a logistic regression model to determine the relationship between the dependent variable (SD) and independent variables such as demographic, clinical and social factors.

RESULTS

Demographic and viro-immunological characteristics of the study population

Of the 152 patients included in this analysis, 109 (71.7%) were male. The median age was 45 (IQR 39-49) years; 24.3% were older than 50 years. As for risk factors for HIV infection, 58 (38.2%) were heterosexual, 60 (39.5%) were men having sex with men (MSM), 32 (21.1%) were intravenous drug users (IDU); 42.8% were single, 8% had diabetes, 46% were smokers. Median time from HIV diagnosis was 11 (IQR 5-15) years. 36 (23.7%) subjects had a previous AIDS diagnosis (CDC stage C), 80 (52.6%) were asymptomatic (CDC A). Median CD4+ T-cell count was 577 (IQR 373-842) cells/µl, HIV-1 viral load was <50 copies/ml in 120 (78.9%) patients. The median duration of HAART was 8.5 (IQR 4-13) years. 22.4% were on first-line HAART, 19.1% were on second-line therapy,

28.3% were on third/fourth-line, 30.2% were on fifth-line therapy or more. 94 (61.8%) were taking a PI-based antiretroviral regimen, 55 (36.2%) a NNRTI-based one.

Please refer to Table 1 and Table 2 for additional data.

Prevalence of and risk factors for SD in the study population

11 (7%) women denied any sexual activity and were excluded from analysis. 82 (58%) out of the remaining 141 subjects reported SD. SD was more frequent in men (65% vs 34%, p =0.0024, OR 3.5, 95% CI 1.6 to 8.2) and elderly subjects (≥50 years) (54% vs 28%, p =0.0029, OR 3.8, 95% CI 1.5 to 9.6). 74 subjects (52.5%) had a z score ≥45 that was suggestive of anxiety.

After stratifying by sex, we found that 71 males (65%) reported ED (26.7% severe ED, 73.3% mild/moderate ED), while 47.7% showed symptoms of anxiety. ED was more frequent in elderly subjects (78% vs 60%, p =0.048, OR 2.7, 95% CI 1.01-2.26) and in anxious patients (77% vs 54%, p =0.05, OR 3.04, 95% CI 1.3-7.12). No significant association was found with current HAART treatment (PI- or NNRTI-based), CDC clinical stage, diabetes, smoking and HIV viral load.

Among women, 11 (34.4%) reported SD and 53.1% reported symptoms of anxiety. FSD was more frequent in elderly subjects (100% vs 28%, p =0.033) but was not related with anxiety, current HAART treatment, CDC clinical stage, diabetes, smoking and HIV viral load.

Logistic regression analysis showed that age (p =0.008) and male sex (p =0.0087) but not anxiety (p =0.068) were still associated with SD.

Table 1. Characteristics of study participants.

	N=152
Age (years)**	45 (39-49)
Sex (Male/Female)*	109 (71.7)/43 (28.3)
Time since HIV diagnosis (years)**	11 (5-15)
Risk factors for HIV infection	
Homosexual*	60 (39.5)
IDU*	32 (21.1)
Heterosexual*	58 (38.2)
Other*	2 (1.2)
HIV stage (1993 CDC criteria)	
A*	80 (52.6)
B*	36 (23.7)
C*	36 (23.7)
CD4+ T-cell count (cells/µl)**	577 (373-842)
HIV RNA viral load <50 copies/ml*	120 (78.9)
Time on HAART (years)**	8.5 (4-13)
HAART	
I line*	34 (22.4)
II line*	29 (19.1)
III/IV line *	43 (28.3)
V line or more*	46 (30.2)
PI-based HAART*	94 (61.8)
NNRTI-based HAART*	55 (36.2)

*Data presented as N (%) **Data presented as median (IQR)
HAART: highly active antiretroviral therapy; PI: protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; IDU: intravenous drug use.

DISCUSSION

In our study, 58% of patients reported altered sexual functioning. SD was associated with male sex and increasing age. The association between SD and age has been observed in both HIV-infected and uninfected subjects[6,7,12]. The pathophysiology of SD is complex and includes vascular, psychosocial, neurological and endocrinological aspects[1]. Many of these factors have an increased prevalence among older subjects. Moreover, considering that HIV infection has been associated with chronic inflammation and increased atherosclerosis[10], it is not surprising to find that the prevalence of ED among HIV-infected men is higher when compared to the general population. Furthermore, considering that HIV infection has become a chronic disease, the prevalence of aging-associated diseases, including SD, is expected to increase.

In univariate analysis, men with anxiety were more likely to report ED in comparison with non-anxious subjects. This observation highlights the importance of psychological factors in sexual health. Psychological problems, including depression and anxiety, are very common among HIV-positive subjects and often represent a neglected issue in HIV healthcare[13,14]. In addition, some authors have reported that body image may have a significant impact on SD[8,11]. Lipodystrophy may reduce sex appeal perception and contribute to psychological distress, leading to impaired sexual functioning. It has also been suggested that adipose tissue alterations may cause an increased peripheral aromatization of androgens

Table 2. Characteristics of male and female study participants.

	Men N=109	Women N=32
Age (years)**	47 (40-52)	42 (38-47)
Time since HIV diagnosis (years)**	11 (5-15)	14 (6-16)
Risk factors for HIV infection		
Homosexual*	59 (54.1)	0 (0)
IDU*	22 (20.2)	7 (22)
Heterosexual*	27 (24.8)	25 (78)
Other*	1 (0.9)	0 (0)
HIV stage (1993 CDC criteria)		
A*	124 (50.5)	23 (71.8)
B*	50 (20.2)	8 (25)
C*	77 (29.3)	1 (3.2)
CD4+ T-cell count (cells/µl)**	587 (383-861)	579 (337-740)
HIV RNA viral load <50 copies/ml*	88 (80)	26 (81.2)
Time on HAART (years)**	8 (4-13)	9 (4-12)
HAART		
I line*	24 (22.1)	8 (25)
II line*	25 (22.9)	3 (9.3)
III/IV line *	31 (28.4)	10 (31.3)
V line or more*	29 (26.6)	11 (34.4)
PI-based HAART*	59 (54.1)	21 (65.6)
NNRTI-based HAART *	42 (38.5)	9 (28.1)

*Data presented as N (%) **Data presented as median (IQR)
HAART: highly active antiretroviral therapy; PI: protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; IDU: intravenous drug use.

to estrogens with subsequent raised estrogen levels, which may contribute to low sexual desire among patients with HIV-related lipodystrophy[23].

SD has been associated with decreased quality of life, unsafe sex practices and reduced adherence to HAART. Non-adherent patients are more likely to have a suboptimal control of HIV viral load and increased viral concentrations in semen or vaginal secretions, leading to an increased risk of HIV transmission[11]. Moreover, men with SD may take drugs to treat ED outside of medical prescription, raising the likelihood of pharmacokinetic interaction with antiretroviral drugs.

The association between SD and HAART is controversial. Consistent with previous studies[6,8,12], we did not find any association between exposure to antiretroviral drugs and SD. However, other authors have reported an increased risk of SD among patients receiving PI[7,9]. Differences in study populations as well as the lack of standardized methods to evaluate SD are likely to contribute to conflicting results.

Of interest, the frequency of sexual inactivity was higher among women in comparison with men. This observation is consistent with previous studies, showing a high prevalence of sexual abstinence following diagnosis with HIV among both young and old women[15,24,25]. Anxiety related to the possibility of infecting sexual partners, even when participating in safe sex, may reduce the pleasure of sexual intimacy and cause a decline in sexual interest. Many women may prefer avoiding sexual activity rather than seeking any medical support. Issues related with sexual changes after HIV diagnosis in women have received little attention so far, with most research focusing on factors associated with unsafe sexual practices and evaluating the efficacy of educational interventions aimed at modifying these behaviours.

Our study has several limitations: firstly, it has a small sample size; secondly, we could not evaluate the hormonal profile of our patients and the association between SD and adherence to HAART. Thirdly, assessment of depressive symptoms using a specific scale was not available. Finally, because of the cross-sectional design of the study, causal relationships could not be established.

CONCLUSIONS

We found that SD is highly prevalent among HIV-positive patients and may have a significant impact on their quality of life. A greater understanding of factors associated with SD may help developing focused intervention strategies in the setting of HIV infection.

Conflict of interest:
None declared

References

1. Santi D, Brigante G, Zona S, Guaraldi G, Rochira V. Male sexual dysfunction and HIV—a clinical perspective. Nat Rev Urol 2014; 11: 99-109.
2. Shindel AW, Horberg MA, Smith JF, Breyer BN. Sexual dysfunction, HIV, and AIDS in men who have sex with men. AIDS Patient Care STDS 2011; 25: 341-349.
3. Trotta MP, Ammassari A, Murri R, Monforte Ad, Antinori A. Sexual dysfunction in HIV infection. Lancet 2007; 369: 905-906.
4. Zona S, Guaraldi G, Luzi K, Beggi M, Santi D, Stentarelli C, Madeo B, Rochira V. Erectile dysfunction is more common in young to middle-aged HIV-infected men than in HIV uninfected men. J Sex Med 2012; 9: 1923-1930.
5. Dobs AS, Dempsey MA, Ladenson PW, Polk BF. Endocrine disorders in men infected with human immunodeficiency virus. Am J Med 1988; 84: 611-616.
6. Crum-Cianflone NF, Bavaro M, Hale B, Amling C, Truett A, Brandt C, Pope B, Furtek K, Medina S, Wallace MR. Erectile dysfunction and hypogonadism among men with HIV. AIDS Patient Care STDS 2007; 21: 9-19.
7. Schrooten W, Colebunders R, Youle M, Molenberghs G, Dedes N, Koitz G, Finazzi R, de Mey I, Florence E, Dreezen C; Eurosupport Study Group. Sexual dysfunction associated with protease inhibitor containing highly active antiretroviral treatment. AIDS 2001; 15: 1019-1023.
8. Guaraldi G, Luzi K, Murri R, Granata A, De Paola M, Orlando G, Squillace N, Malmusi D, Carani C, Comelli D, Esposito R, Martinez E. Sexual dysfunction in HIV-infected men: role of antiretroviral therapy, hypogonadism and lipodystrophy. Antivir Ther 2007; 12: 1059-1065.
9. Collazos J, Mayo J, Martínez E, Ibarra S. Association between sexual disturbances and sexual hormones with specific antiretroviral drugs. AIDS 2002; 16: 1294-1295.
10. De Ryck I, Van Laeken D, Apers L, Colebunders R. Erectile Dysfunction, Testosterone Deficiency, and Risk of Coronary Heart Disease in a Cohort of Men Living with HIV in Belgium. J Sex Med 2013; 10: 1816-1822.
11. Trotta MP, Ammassari A, Murri R, Marconi P, Zaccarelli M, Cozzi-Lepri A, Acinapura R, Abrescia N, De Longis P, Tozzi V, Scalzini A, Vullo V, Boumis E, Nasta P, Monforte Ad, Antinori A; AdICoNA and AdeSpall Study Group. Self-reported sexual dysfunction is frequent among HIV infected persons and is associated with suboptimal adherence to antiretrovirals. AIDS Patient Care STDS 2008; 22: 291-299.
12. Wang Q, Young J, Bernasconi E Cavassini M, Vernazza P, Hirschel B, Weber R, Furrer H, Stoeckle M, Bucher HC, Fux C; Swiss HIV Cohort Study. The prevalence of erectile dysfunction and its association with antiretroviral therapy in HIV-infected men: the Swiss HIV Cohort Study. Antivir Ther 2013; 18: 337-344.
13. Lowther K, Selman L, Harding R, Higginson IJ. Experience of persistent psychological symptoms and perceived stigma among people with HIV on antiretroviral therapy (ART): A systematic review. Int J Nurs Stud 2014; pii S0020-7489: (14) 00022-4.
14. Celesia BM, Nigro L, Pinzone MR, Coco C, La Rosa R, Bisicchia F, Mavilla S, Gussio M, Pellicanò G, Milioni V, Palermo F, Russo R, Mughini MT, Martellotta F, Taibi R, Cacopardo B, Nunnari G. High prevalence of undiagnosed anxiety symptoms among HIV-positive individuals on cART: a cross-sectional study. Eur Rev Med Pharmacol Sci 2013; 17: 2040-2046.
15. Wilson TE, Jean-Louis G, Schwartz R Golub ET, Cohen MH, Maki P, Greenblatt R, Massad LS, Robison E, Goparaju L, Lindau S. HIV Infection and Women's Sexual Functioning. J Acquir Immune Defic Syndr 2010; 54: 360-367.
16. Siegel K, Schrimshaw EW, Lekas HM. Diminished sexual activity, interest, and feelings of attractiveness among HIV-infected women in two eras of the AIDS epidemic. Arch Sex Behav 2006; 35: 437-449.
17. Florence E, Schrooten W, Dreezen C, Gordillo V, Nilsson Schönnesson L, Asboe D, Koitz G, Colebunders R; Eurosupport Study Group. Prevalence and factors associated with sexual dysfunction among HIV-positive women in Europe. AIDS Care 2004; 16: 550-557.

18. Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, Ferguson D, D'Agostino R Jr. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther 2000; 26: 191-208.
19. Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cut-off scores. J Sex Marital Ther 2005; 31: 1-20.
20. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 1997; 49: 822-830.
21. Cappelleri JC, Rosen RC, Smith MD, Mishra A, Osterloh IH. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. Urology 1999; 54: 346-351.
22. Chiesi F, Primi C, Carmona J. Measuring statistics anxiety: cross country validity of the statistic anxiety scale (SAS). J Psychoeduc Assess 2011; 29: 559-569.
23. Goldmeier D, Scullard G, Kapembwa M, Lamba H, Frize G. Does increased aromatase activity in adipose fibroblasts cause low sexual desire in patients with HIV lipodystrophy? Sex Transm Infect 2002; 78: 64-66.
24. Siegel K, Schrimshaw EW. Reasons for adoption of celibacy among older men and women living with HIV/AIDS. J Sex Res 2003; 40: 189-200.
25. Hankins C, Gendron S, Tran T, Lamping D, Lapointe N. Sexuality in Montreal women living with HIV. AIDS Care 1997; 9: 261-271.