Antiretroviral therapy as a factor protective against anal dysplasia in HIV-infected males who have sex with males

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Background: Studies show higher incidences of anal carcinoma and faster progression in HIV-infected MSM patients. Chronic infection with oncogenic HPV is associated with the development of anal dysplasia. Antiretroviral therapy (ARV) has been shown to decrease the incidence of cervical carcinoma in women living with HIV; however, so far in the majority of publications ARV has not proven to have a beneficial effect on the appearance of anal dysplastic lesions, except in the Swiss cohort.Antiretroviral therapy (ARV) has been shown to decrease the incidence of cervical carcinoma in women with HIV.

Objectives: 1-Analyze the role of ARVs in the prevalence of high-grade anal intraepithelial neoplasia (HGAIN) and/or anal cancer in our cohort of HIV positive MSM.2-Describe the prevalence and grade of anal dysplasia and HVP infection in our study subjects. 3-Evaluate the risk factors associated with the appearance of HGAIN and/or anal cancer.

Material and Methods: A cross-sectional study of an HIV-positive MSM cohort. Epidemiological (condylomas, sexual habits, use of condom, smoking, alcohol consumption, other infections, etc), clinical (months since HIV diagnosis, HIV stage according to CDC criteria, ARV, virological failure), and analytical (Cd4 lymphocyte, Viral Load (VL), Cd4 nadir) data were collected. Two anal mucosa samples were taken and sent for HR-HPV PCR testing and cytology. . The genotypes 16, 18, 26, 31, 33, 35, 39, 45, 51–53, 56, 58, 59, 66, 68, 73 and 82 were considered high risk (HR-HPV). Genotypes 6, 11, 34, 40, 42–44, 54, 55, 57, 61, 70–72, 81, 83, 84 and 89 were considered low risk (LR-HPV) [18].Anoscopy was then performed for histological samples. The cytology classification was that of Bethesda [19] which classifies the lesions into 2 types: atypical squamous cells (ASC), low squamous intraepithelial lesions (LSIL) and high squamous intraepithelial lesions (HSIL).
The histology classification employed divides the lesions into LSIL (AIN1/condyloma), HSIL (AIN2, AIN3), Carcinoma *in situ,* and invasive carcinoma (20). We considered lesions ≥ AIN2 those that proceeded beyond AIN2 to Carcinoma *in situ.*

Results

Table 1. General description of the patient cohort

Characteristics of Patients MSM-HIV	n=140
Mean age; years (± SD)	37.27 (± 8.9)
Median number of partners over previous 12 months (IQR)	1 (1 - 6.75)
Habitually using condoms; n (%), 95%CI	109 (77.9) (71-81)
Perianal/genital condylomatosis; n (%), (95%CI)	42 (30), (20 - 36)
History of condylomas; n(%), (95%CI)	50 (35.7), (28-44)
Median duration of HIV months, (IQR)	33 (11 - 84)
Mean VL of HIV (log), (±SD)	3.83 (± 4.33)
CD4 (cells/µL), (± SD)	652.87 (± 261.71)
CD8 (cells/µL), (± SD)	1431.07 (± 4366.35)
CD4 nadir (cells/µL), (± SD)	356.29 (± 246.92)
AIDS stage (A3, B3, C); n (%), 95%CI	46 (32.9), (27 - 43)
Receiving ARV; n (%), 95%CI	108 (77), (70 - 84)
Number of months of ARV; mean (IQR)	23.5 (8 - 80.3)
Virological treatment failure; n (%), 95%CI	7 (6), (2 - 10)
History of syphilis treated; n (%), 95%CI	26 (18.6), (12 – 26)
Other STD; n (%), 95%CI	56 (40), (32-50)
Latent tuberculosis treated; n (%)	17 (12.5)
Chronic HCV infection; n (%)	6 (4.3)
Chronic HBV infection; n (%)	3 (2.1)
Smoking habit; n (%), 95%CI	67 (47.9), (41 - 58)
Ex-IVDA, n (%)	2 (1.5)
Median daily alcohol consumption; (SAU), (IQR)	0 (0 - 1)

Table2. Results of the PCR of HPV, cytology and anoscopy

Outcomes	MSM-HIV patients; n=140
PCR of HPV-positive, n (%), 95%CI	124 (88.6)
High-risk HPV	74 (59.7), (51 - 70)
Low-risk HPV	92 (74.2), (69 - 85)
Low and High-risk HPV	58 (46.8), (39 - 58)
Genotypes most frequents, n (%)	
VPH6	20 (16.1)
VPH11	16 (12.9)
VPH16	38 (30.6)
VPH18	15 (12.1)
VPH51	19 (15.3)
VPH 61	16 (12.1)
VPH 84	17 (13.7)
Anal cytology; n (%),95%CI	120 (85.7)
LSIL	59 (49.2), (38 - 57)
HSIL	3 (2.5), (0 - 6)
ASC	3 (2.5), (0 - 6)
Normal	55 (45.8), (39 - 57)
Anoscopy; Histology, n (%), 95%CI	
Normal	46 (32.8), (28-44)
AIN1	66 (4.1), (38 - 56)
AIN2	12 (8.5), (4 - 13)
AIN3	4 (2.9), (0 - 6)
Carcinoma *in situ*	12 (8.6), (4 - 13)

Table 3. Results of multivariate analyses of risk factors associated with the appearance of ≥AIN2 lesions

Variables	P*	OR	95%CI
ARV	0.0028	0.21	0.054-0.84
Current perianal condylomas	0.019	4.26	1.27-14.3
Clinical history of syphilis	0.025	0.078	0.008-0.721
HPV 68	0.032	10.6	1.23-91.47
AIDS stage	0.26	0.15	0.006-3.98
Duration of HIV	0.15	0.98	0.955-1.007
Duration of ARV	0.35	1	0.98-1.04
Number of HR-HPV genotypes in anal mucosa	0.38	1.17	0.82-1.68
CD4 nadir; cells/ uL	0.15	0.997	0.99-1
Cd4 nadir < 200 cells/ uL	0.97	0.94	0.032-28.3

Notes: MSM: males who have sex with males; VL: viral load; HCV: hepatitis C virus infection; HBV: hepatitis B virus infection; SAU: standard alcohol units; ex-IVDA: ex-intravenous drug abuser; SD: standard deviation; STD: sexually transmitted diseases; HPV: human papilloma virus; HR-HPV: high-risk human papilloma virus, LR-HPV: low-risk human papilloma virus; LSIL: low grade squamous intraepithelial cell lesion; HSIL: high squamous intraepithelial lesion; ASC, abnormalities of uncertain significance; AIN: anal intraepithelial neoplasia . IQR (inter-quartile range)

Conclusions

In our cohort of HIV patients MSM, the antiretroviral therapy has a protective effect against the development of dysplastic anal lesions. 1/6 patients from our cohort has HGAIN, 1/11 has Carcimoma in situ, and 3/4 of them are infected with HR-HPV genotypes.
The finding of anal or genital warts and HPV-68 genotype in anal mucosa are two predictors of HGAIN and/or carcinoma in our cohort of HIV-MSM.
This result requires further testing for confirmation of the finding.