ANAL MOLECULAR HPV & CYTOLOGICAL FINDINGS FROM HIV POSITIVE AND NEGATIVE MSM IN IRELAND

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Introduction

HPV is the most common sexually transmitted infection in the world. 88% of anal cancers are caused by HPV infection, with HPV 16 and HPV 18 being responsible for the vast majority of these cancers and associated precancerous anal lesions. Anal cancer is an uncommon cancer in the general population with rates of between 1 and 2 cases per 100,000 per year. Certain populations are more affected than others, however. Men who have sex with men (MSM) have an estimated rate of anal cancer of about 40 per 100,000 per year. HIV positive MSM are at an even higher risk with incidence rates of up to 131 per 100,000 person years, higher than the rate of cervical cancer in the general female population before the advent of widespread cervical pap screening (40-50/100,000). This research aims to describe the anal cytology and molecular findings among a HIV positive and negative MSM population in Ireland.

Methods

Participants were recruited from HIV and STI outpatient clinics. Participants were excluded if they were partially vaccinated with the HPV vaccine or if they had a previous history of anal cancer. 148 participants underwent repeat testing at 1 year. Samples were collected from the anal canal using a dacron swab and placed into PreservCyt (ThinPrep vial) transport medium. HPV DNA testing was performed using the Cobas HPV test on the Cobas 4800 Platform (Roche diagnostics). This assay allows for specific genotyping of HPV16 and HPV18, with the remaining 12 high-risk HPV (hrHPV) types (HPV 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) classed together as "Other hrHPV DNA". HPV mRNA testing was performed using the Aptima HPV assay and Panther platform (Hologic). This is an in vitro acid amplification test used for the qualitative detection of E6/E7 viral transcripts from all abovementioned 14 hrHPV. Samples also underwent anal pap staining and cytological analysis. Samples that tested positive for the presence of hrHPV DNA underwent further analysis using P16/Ki67 dual staining.

Results

Demographics: 252 participants were recruited to this study between January 2019 and November 2019. 202 (80%) of participants were seropositive for HIV. The median age of participants was 35 years (IQR 30 – 40 years). 122 (48%) participants were of Irish origin, with a further 41 (16%) being of European origin. 63 (25%) participants were originally from Central and South America, with 16 (6%), 6 (2%) and 4 (2%) being of Asian, African and North American origin respectively. Prior to recruitment, 40 participants (16%) had already completed HPV vaccination, with the remainder not having received any HPV vaccine in the past. Of those who received the vaccine, 29 were HIV positive (14% of all HIV positive participants) and 11 were HIV negative (22% of all HIV negative patients). 202 (80%) of participants reported drinking alcohol regularly. 99 participants (39%) were smokers. 52 (21%) were ex-smokers, and 101 (40%) reported being never-smokers. 62 participants (25%) reported a previous history of perianal HPV/warts. 42 (17%) of participants reported never or rarely practicing receptive anal intercourse during sex and 75 (33%) reported often or always practicing receptive anal intercourse during sex. 125 (50%) reported sometimes practicing receptive anal intercourse during sex. The median number of lifetime partners reported by study participants was 90 (IQR 25 – 200). The median number of sexual partners in the 12 months leading up to recruitment was 5 (IQR 2 -15). Of the 202 HIV positive participants, 201 were in receipt of antiretroviral therapy and 197 participants (98%) had a viral load of less than 40 HIV viral copies per ml. The median most recent CD4 count of HIV positive participants was 715 (IQR 527 – 874). 181 participants had reliable nadir CD4 counts available. The median nadir CD4 count was 356 (IQR 260 – 481). 13 participants (5%) had evidence of external perianal HPV on examination. 21 participants (8%) were found to have a palpable abnormality on digital rectal examination.

hrHPV DNA: 234 participants had valid baseline samples for HPV16 DNA analysis. 52 (22%) tested positive for HPV16 DNA. 232 had valid baseline samples for HPV18 DNA analysis, of which 22 (9%) tested positive. 238 participants had valid baseline samples for other hrHPV DNA analysis, of which 139 (58%) tested positive. HIV positivity was significantly associated with the presence of other hrHPV DNA on multivariate logistic regression analysis (OR 2.87, 95%CI 1.34-6.14, p=0.007). Overall, 240 participants had valid baseline samples for any hrHPV DNA analysis, of which 153 (64%) tested positive for at least one hrHPV type. HIV positivity was statistically significantly associated with the presence of any hrHPV DNA on multivariate analysis (OR 2.71, 95%CI 1.29-5.70, p=0.008).

hrHPV mRNA: 252 participants had valid baseline samples for hrHPV mRNA analysis, of which 101 (40%) tested positive. Current smoking was significantly associated with hrHPV mRNA positivity on multivariate logistic regression analysis (OR 2.02, 95%CI 1.11-3.68, p=0.022).

Anal Cytology: 245 valid samples underwent cytological analysis. 110 (45%) were reported as normal, 81 (33%) were reported as anal intraepithelial neoplasia 1 (AIN1) (low-grade squamous intraepithelial lesion (LSIL)), 46 (19%) were reported as AIN2 (high-grade squamous intraepithelial lesion (HSIL)) and 8 (3%) were reported as AIN3 (HSIL). Receptive anal intercourse was significantly associated with the presence of HSIL (OR 8.81, 95%CI 1.91-40.65, p=0.005) on multivariate analysis.

P16/Ki-67: 145 participants had valid P16-Ki67 dual staining results. 50 (34%) of these samples were positive for P16/Ki-67 dual staining. Being originally from Ireland was significantly associated with lower rates of dual staining positivity on multivariate analysis (OR 0.25, 95%CI 0.10-0.60, p=0.002).

1 year follow-up: HPV16 DNA persistence was seen in 77% (17/22). HPV18 DNA persistence was seen in 44% (4/9), & other hrHPV DNA in 77% (58/75). Persistence of any hrHPV DNA was seen in 79% (63/80). hr HPV mRNA persistence was seen in 60% of participants (29/48). HSIL persistence was present in 22% (7/32), with AIN3 persistence seen in 17% (1/6). Persistent dual staining positivity at 1 year was seen in 57% (8/14).

Conclusion

This study demonstrates the molecular burden of hrHPV infection and persistence among this high risk group in an Irish context for the first time. It also demonstrates the burden of cytological HPV changes in this population. More research is required to correlated these molecular and cytological findings with histological findings among this population. In light of recent data showing the benefit of treating anal cancer precursor lesions in HIV positive MSM (the ANCHOR study), this research supports calls for the consideration of the currently unmet need in Ireland for anal cancer screening.