

PROSPECTIVE STUDY OF THE EFFICACY OF 5% IMIQUIMOD VS EXCISION OF ANAL HSIL IN PATIENTS INFECTED BY HIV (2010-2018)

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BACKGROUND

Anal canal carcinoma (ASCC) is one of the most frequent non-AIDS defining tumours in HIV patients, especially in women and men who have sex with men (MSM). There are different recommendations on the therapeutic management of these lesions and they are often based on small observational studies. One of the recommendations is surgical excision. However, several side effects have been notified such as incontinence, narrowing of the anal canal and a high percentage of recurrence. Imiquimod is an antiviral and anti-tumour drug with activity against HPV and is indicated to treat external condylomas. There are two previously published studies in HIV patients with a response rate to imiquimod of 45-61% (1,2). The main objectives of this study were to analyze the real-life efficacy and safety of the surgery and 5% imiquimod for the treatment of HSIL lesions in HIV+ patients, as well as to evaluate the clearance rate of oncogenic HPV genotypes, the prevalence and incidence of anal HSIL in our cohort, the spontaneous regression of the lesions and the progression rate towards AC.

METHODS

Prospective study (May 2010- May 2018) in HIV+ patients diagnosed with HSIL, included in a cohort of 486 HIV+ patients in a screening, diagnosis, treatment and follow up of anal dysplasia program. At the baseline (V1) and follow up visits, a cytology, HPV PCR and high resolution anoscopy (HRA) were performed and data regarding their HIV and sexual behaviours was recorded. If the HRA was classified as normal or LSIL, the patients were followed up annually as at V1. Those diagnosed with HSIL were offered a surgical treatment, excision (electrocoagulation) since 2010 or topical 5% imiquimod since 2012 (this was self-applied in the anal canal 3 times/week for 16 weeks). Response to treatment was analyzed at 3-6 months after finalizing treatment by carrying out a cytology, HPV PCR (GeneAmp PCR System 9700, Applied Biosystems) and HRA (Zeiss 150 fo©). If HRA was normal or LSIL, the patients were followed up annually. If the HSIL lesion persisted, repetition of the surgical excision or another cycle of Imiquimod was considered. The cytological and histological classification used was that of Bethesda and the LASTS Project for HPV-Associated Lesion. We defined cure as the absence of lesion after treatment, clean borders and no need for further therapy. Recurrence was defined as the reappearance of the lesion after a previously normal HRA.

RESULTS

Of the 486 HIV+ patients included in the cohort during the follow up period, 84 were diagnosed with anal HSIL. The prevalence of anal HSIL was 17.2% and the incidence was 8.457x1000 patients-year. 6 (7.4%) cases of HSIL regressed spontaneously, 1 (1.2%) progressed to ASCC having received treatment with imiquimod and two surgical interventions and 1(1.2%) presented ASCC 5 years after surgical intervention of HSIL. 2 (2.3%) died before receiving treatment (1 lung cancer, 1 non Hodgkin Linfoma). 75 (90.5%) were treated, 41 (3.9%) with surgery as a first option and 35 (46.1%) with imiquimod (3 haven't completed follow up yet).

Table 1. Baseline characteristics of patients with anal HSIL

Patients with HSIL	n= 84
Age, mean +/- DS (year).	36 +/-10.95
Gender,	
Female, n (%)	11 (13.1)
MSM, n (%)	76 (86.9)
Prior history of AIDS	25 (29.8%)
CD4 Nadir, mean +/- DS (cel/uL)	346.5 +/-233.8
ART, n(%)	70 (83.3%)
Viral load < 50 cop/uL	71 (84.2%)
CD4, mean +/- DS (cel/uL)	652.04 +/- 295.7
CD8, mean +/- DS (cel/uL)	1534.4 +/-5456.01
PCR of HPV, n(%)	n= 83
High-Risk(HR) HPV	67 (79.8)
Low-Rsik(LR) HPV	63 (75)
LR and HR-HPV	52 (61.9)
Genotypes of HPV, n(%)	
HPV 6	30 (35.7)
HPV 11	14 (16.7)
HPV 16	29 (34.5)
HPV 18	16 (19)
HPV 42	12 (14.3)
HPV 51	12 (14.3)
HPV 53	12 (14.3)
HPV 59	11 (13.1)
HPV 61	12 (14.3)
HPV 62	11 (13.1)
HPV 68	11 (13.1)
Nº of HPV, median, (IQR)	
HR-HPV	2 (1-3)
LR-HPV	1 (1-2)

Table 2. Results of response to treatment.

	Surgery N= 41	5% Imiquimod N =32	p
Cure rate, n(%)	31 (75.6)	28 (87.9)	0.2
1 only surgical intervention	31 (75.4)		
≥ 2 interventions	10 (24.5)		
Recurrence rate	6 (14.6)	2 (6.3)	0.27
Adverse events (AE)	39 (95.1)	2 (4.3)	0.046
	[pain(85.4%)>Rectal bleeding(68.3%) > others]	(Abandonment to treatment due to severe AE)	
Clearance rate of HR-HPV genotypes	26 (64.5)	11 (35.5)	0.09

CONCLUSIONS

In our cohort of MSM HIV patients, the incidence of HSIL was high and was mostly in Young adult MSM receiving ART and with a good virological and immunological state. Self-administration of 5% imiquimod was as effective as surgery but more comfortable and with less side effects.

1- Van der Snoeck EM, Den Hollander JC, van der Ende ME. Imiquimod 5% cream for five consecutive days a week in an HIV-infected observational cohort up to 32 weeks in the treatment of high-grade squamous intraepithelial lesions. Sex Transm Infect 2015; 91: 245-7.
 2- Fox PA, Nathan M, Francis N, Singh N, Weir J, Dixon G, Barton SE, Bower M. A double-blind, randomized controlled trial of the use of imiquimod cream for the treatment of anal canal high-grade anal intraepithelial neoplasia in HIV-positive MSM on HAART, with long-term follow-up data including the use of open-label imiquimod. AIDS 2010; 24: 2331-5.