Visual Inspection With Acetic Acid (VIA) Agrees Reasonably Well With Pap Smear and HR HPV Typing for Follow-up AfterVIA/Cryotherapy in HIV-infected Women

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Background

As See and Treat programs using VIA and cryotherapy gain popularity, knowing the appropriate follow-up is critical. Few studies have addressed the optimal follow-up for HIV-infected women after VIA and immediate cryotherapy. This study seeks to identify the optimal follow-up test to accurately detect persistent moderate/severe cervical dysplasia and cancer in HIV-infected women who participated in a See and Treat program consisting of VIA, digital cervicography and immediate cryotherapy.

Introduction

- Cervical cancer is the most common cancer among women in the developing world, with an incidence of over 500,000 per year.
- Greater than 80% of the world's new cases and deaths due to cervical cancer occur in the developing world and fewer than 5% are screened for cervical cancer
- The UN World Health Organization estimates that approximately 2,635 Kenyan women are diagnosed with cervical cancer every year, with 2,111 dying from the disease, making it the most prevalent (and preventable) gynecologic cancer among women in the country.
- About 38.8% of Kenyan women in the general population are estimated to harbor cervical human papilloma virus (HPV) infection.
- Few studies have addressed the optimal follow up for HIV infected women after VIA and immediate cryotherapy
- We assessed the prevalence of cervical neoplasia among HIV infected women who have undergone VIA and cryotherapy for cervical dysplasia using repeat VIA, conventional Pap smear and high risk HPV typing

Methods

- This is a cross sectional study involving 517 HIV-infected women attending 4 AMPATH-CCSPP (Cervical cancer Screening and Prevention Program) sites who have undergone VIA and cryotherapy >6 months for cervical dysplasia.

Eligibility Criteria

- Female, age-18-55 years, documented HIV infection, has undergone VIA and cryotherapy > 6 months.

Exclusion Criteria

- Not pregnant, no history of pregnancy or D&C within the last 3 months, no current mucopurulent discharge or active vaginal bleeding, no history of STI or cervical infection in the last 2 weeks, generally healthy and no debilitating disease, able to give informed consent and agrees to procedures and follow-up visits. Women with suspected frank cervical cancer will not be enrolled.
- All women underwent VIA, conventional Pap smear, endocervical cytobrush for HPV typing
- Women with any abnormal result for VIA, Pap smear, or HR HPV underwent colposcopy and biopsy
- Treatment for cervical neoplasia/cancer followed the standard of care in the AMPATH cervical cancer screening program

Results

Table 1: Demographic and Clinical Characteristics

	N=517	
Age (mean/range)		
	No.	**%**
Marital status		
Single	103	20
Married	281	54
Divorced	8	2
Widowed	99	19
Separated	26	5
Educational Level		
None	22	4
Primary	264	51
Secondary	185	36
College	40	8
University	6	1
Most recent CD4		
<250	67	13
250 to 350	130	25
350 to 500	138	27
>500	181	35
NA	1	<1
First sexual activity <18 y.o.	185	36
Currently using contraception	168	33
Currently on HAART	450	87

Table 2: Results of VIA, PAP and HPV Testing After VIA/Cryotherapy

TEST	No.	%
VIA		
Negative	417	80.7
Positive	100	19.3
Pap Smear		
Normal	398	77
LGSIL	26	5
HGSIL	45	8.7
HR HPV		
Negative	242	46.8
Positive	275	53.2

Table 3: Logistic Regression Analysis Among Those Having at Least One Positive VIA, PAP and/or HPV Typing Tests

		Odds ratio	p	95% CI lower	95% CI upper
Age	18-30 yrs (REF)				
	30-35 yrs	0.62	0.29	0.25	1.52
	35-40 yrs	1.64	0.26	0.70	3.82
	> 40 yrs	1.30	0.56	0.54	3.16
CD4	< 250 (REF)				
	200-350	0.61	0.33	0.23	1.63
	350-500	0.38	0.06	0.14	1.06
	> 500	0.71	0.47	0.28	1.78
WHO Stage	1 (REF)				
	2	0.88	0.75	0.41	1.89
	3~4	1.44	0.30	0.72	2.85
ART	No (REF)				
	Yes	0.76	0.56	0.31	1.87
Age at first sex	younger than 18 (REF)				
	18 or older	0.46	0.05	0.21	1.00
	N/A	0.65	0.21	0.33	1.27
Contraception	No (REF)				
	Yes	2.39	0.01	1.26	4.51

Table 4:Concordance of VIA, PAP and HR HPV Testing After VIA/Cryotherapy

VIA/PAP/HPV	No.	%
--/--/--	174	36.4
--/--/+	163	34.1
--/+/--	20	4.2
--/+/+	32	6.7
+/--/--	26	5.4
+/--/+	42	8.8
+/+/--	4	0.8
+/+/+	17	3.6
Total	**478**	**100.0%**

Table 5: Cervical Biopsy Results

	No.	%
Biopsy Result		
Inadequate	4	1.2%
Normal	126	38.2%
CIN I	50	15.2%
CIN II	25	7.6%
CIN III	41	12.4%
CIS	4	1.2%
Carcinoma	2	0.6%
Not available	78	23.6%
Total	**330**	**100.0%**

- We found that the disease negative rate after VIA and cryotherapy (negative VIA, normal Pap smear, negative HR HPV) at ≥ 6 months was 37% (CI=29-46%).
- Only 4% (CI=1-9%) had persistently abnormal testing on all 3 tests.
- A significant proportion (63%) continued to have at least one abnormal test.
- VIA has comparable sensitivity as Pap smear (p=0.16) but lower sensitivity than HR HPV testing (P<0.01)*
- VIA has lower specificity than Pap smear (p<0.01) but higher specificity than HR HPV testing (p<0.001)*

* Based on CIN II or greater by histology.

Conclusions

- The disease negative rate after VIA and immediate cryotherapy (37%) among HIV-infected women in our study is less than previously reported for HIV-uninfected women(85-88%).
- Follow-up with VIA agrees reasonably well with Pap and HR HPV tests
- Further studies need to address the efficacy of cryotherapy for treatment of cervical neoplasia among HIV infected women

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