Oral lesions in HIV-infected patients, before and after antiretroviral treatment

A Masiiwa, S Naidoo

Oral lesions cause considerable morbidity in HIV-infected patients. Antiretroviral therapy (ART) reconstitutes the immune system and reduces the incidence of opportunistic infections and malignancies. The aim of the present study was to determine the prevalence and range of oral lesions in patients before and after starting ART in Harare, Zimbabwe. A longitudinal, prospective study of oral lesions presenting in HIV-infected patients at baseline and three and six months after the initiation of ART was conducted. The study was undertaken at three hospitals in Harare. Two hundred and ten patients were enrolled; 96 (46%) and 49 (23%) patients presented for follow-up at three and six months, respectively. Two-thirds of the patients who completed follow-up were female; median age was 36 years. At six months of ART, the overall prevalence of oral lesions declined significantly (p<0.05). Oral candidiasis was the most common finding and showed the most significant reduction on ART. In contrast, the incidence of facial warts increased from baseline to three and six months. ART was effective in reducing the overall prevalence of oral lesions in HIV-infected patients, although incidence was variable depending on the type of lesion. Unmasking immune reconstitution inflammatory syndrome to human papillomavirus (HPV) is the likely cause for the increase in facial warts.

Introduction

Oral manifestations associated with HIV infection include fungal, viral and bacterial infections, as well as neoplasms, periodontal disease and salivary gland disease, and may be the presenting features of HIV. Oral lesions may cause pain, discomfort and restrict food intake, leading to malnutrition. Hence early detection of oral lesions is a vital component of managing HIV patients; it may reduce morbidity and may indicate the need for antiretroviral therapy (ART). Recent studies from developed countries show that ART reduces the prevalence of oral lesions in infected adults and children, but there remains a paucity of data from the African continent.

Studies from Zimbabwe have previously documented the prevalence of oral lesions prior to starting ART. The Zimbabwean ART rollout programme started in April 2004, and in Harare hospitals in 2006. The aim of the present study was to determine the effect of ART on the prevalence oral lesions in Zimbabwean HIV patients starting treatment.

Methods

ART-naïve, HIV-infected outpatients attending Beatrice Road Infectious Disease Hospital (BRIDH), Wilkins Infectious Disease Hospital (WIDH) and Parirenyatwa Paediatric Opportunistic Infection Clinic (PPOIC) in Harare were prospectively enrolled following informed consent, between November 2007 and July 2008.

A systematic intraoral assessment and an extraoral examination (salivary gland swellings, lymphadenopathy and other facial swellings) were performed by a trained dental surgeon. Classification of oral lesions was done using Roed-Peterson and Renstrup (1969) and EC-Clearinghouse (1993) criteria. The Roed-Peterson and Renstrup classification was used to localise the lesions and to diagnose the oral lesions, and the EC-Clearinghouse (1993) criteria for detailed criteria related to diagnosis and their degree of association with HIV infection.

The following information was recorded at baseline on a structured data capture sheet: age, gender, previous medical history, mode of HIV transmission, CD4-cell counts, WHO stage, drug therapy and cotrimoxazole prophylaxis. All the patients started first-line ART as per national policy: stavudine (or zidovudine) plus lamivudine and nevirapine or efavirenz. Patients were clinically examined at three and six months, with a CD4 count at six months. Statistical analysis was carried out on the patients that completed the six-month follow-up. The study was approved by the Senate Research Ethics Committee of the University of the Western Cape and the Medical Research Council of Zimbabwe. Permission and approval from the Director of Health Services for Harare City.
and Clinical Director of Parirenyatwa Group of Hospitals were obtained.

Results

Two hundred and ten patients were enrolled in the study, but only 96 (46%) and 49 (23%) patients presented for follow-up at three and six months, respectively. Thirty-one of 49 (63%) were female and the median age was 36 years. The median and interquartile ranges for CD4 count at baseline were 112 cells/µl, (IQR 75.5-166.5) and at six months 182 cells/µl, (IQR 126-251.5). Orofacial lesions for the sample of 49 participants at the three time-points are detailed in Table I. Oral candidiasis was the most common oral lesion of which the occurrence significantly decreased on ART. The prevalence of herpes zoster also significantly decreased, and the trend in all lesions, except for facial warts, was a reduction in lesions on ART. Interestingly, there was a significant increase in facial warts in patients starting ART from the low level at baseline. At six months, 20% of patients presented with facial warts.

Discussion

The present study confirms previous findings, from both developed countries and the limited number of studies in Africa, that ART reduces the prevalence of oral lesions in persons with HIV-2,7,14-16,19 and that oral candidiasis is the most common oral lesion. An unusual finding was the higher prevalence of erythematous candidiasis (EC) compared to the pseudomembranous (PC) type. Few studies have recorded such results.14,20 Results at baseline (n=210) showed that the prevalence of PC was higher than EC. The finding at six months could have been due to the reduced sample size (n=49).

Unusual findings in the present study relate to mucosal hyperpigmentation and orofacial warts. There was a high number of patients presenting with mucosal hyperpigmentation, a condition not reported in previous Zimbabwean studies. Mucosal hyperpigmentation has been linked to the administration of zidovudine and ketoconazole, and to Addison’s disease. It is thought to be due to the disregulation of cytokines in HIV-infected persons promoting an increased release of alpha melanocyte-stimulating hormone.4,6,17,21,23,28 It is unclear why this cohort manifested an increase in mucosal hyperpigmentation, but it could be due to the fact that they manifested advanced immunosuppression and that some of these lesions were due to Kaposis sarcoma. Unfortunately, lack of funding for histological investigations precluded a definitive diagnosis.

The study cohort had a surprisingly low prevalence of intraoral warts: only two patients at baseline. Previous Zimbabwean studies4,5 did not report on the presence of warts. The suggested association of oral warts and development of squamous cell carcinoma17,24 requires careful monitoring when intraoral warts are found. Interestingly, there was a significant increase in the presence of extroral warts affecting the face, with 20% manifesting facial planar warts at six months. Immune reconstitution inflammatory syndrome, involving unmasking of de novo warts or paradoxical expansion of existing warts, has been well described15,29-31 and we postulate that this is the mechanism by which patients developed warts. These lesions can result in poor aesthetics26 for patients on ART and need to be treated timeously.

The present study was limited by a number of factors, not least of which was the high rate of loss to follow-up. Unfortunately, the data collection phases of study coincided with the political violence surrounding a contested presidential election. The recruitment of children was difficult, due to the shortage of paediatricians able to initiate ART. The high cost of laboratory investigations meant that clinical findings and a presumptive diagnosis had to be used for the majority of lesions.

Acknowledgements

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References


Table I: Orofacial lesions at baseline, three months and six months for patients completing follow up (n=49)

<table>
<thead>
<tr>
<th>Oral lesion</th>
<th>Baseline n (%)</th>
<th>3 months n (%)</th>
<th>6 months n (%)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Any lesion</td>
<td>42 (86)</td>
<td>28 (57)</td>
<td>28 (57)</td>
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<tr>
<td>Oral candidiasis</td>
<td>35 (71)</td>
<td>10 (20)</td>
<td>1 (2)</td>
<td>&lt;0.0001</td>
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<td>Pseudomembranous</td>
<td>11 (22)</td>
<td>2 (4)</td>
<td>1 (2)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Erythematous</td>
<td>15 (31)</td>
<td>3 (6)</td>
<td>0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hairy leukoplakia</td>
<td>8 (16)</td>
<td>6 (12)</td>
<td>6 (12)</td>
<td>0.6879</td>
</tr>
<tr>
<td>Mucosal hyperpigmentation</td>
<td>7 (14)</td>
<td>9 (18)</td>
<td>6 (12)</td>
<td>0.8833</td>
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<tr>
<td>Herpes zoster</td>
<td>6 (12)</td>
<td>0</td>
<td>0</td>
<td>0.0019</td>
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<tr>
<td>Angular cheilitis</td>
<td>5 (10)</td>
<td>4 (8)</td>
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<td>0.0833</td>
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<td>Salivary gland disease</td>
<td>9 (18)</td>
<td>2 (4)</td>
<td>5 (10)</td>
<td>0.4419</td>
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<td>Aphthous ulceration</td>
<td>3 (6)</td>
<td>1 (2)</td>
<td>0</td>
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<td>Periodontal diseases</td>
<td>2 (4)</td>
<td>1 (2)</td>
<td>0</td>
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<td>Warts</td>
<td>2 (4)</td>
<td>9 (18)</td>
<td>10 (20)</td>
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Protease inhibitors: A New Face of oral AIDS? AIDS Care STDs 2000; 14: 627-635