ORIGINAL ARTICLE

EFFECT OF ANTIRETROVIRAL THERAPY ON ORAL LESIONS IN HIV/AIDS

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ABSTRACT

Antiretroviral therapy (ART) is given to the HIV/AIDS patients and the frequency of the oral lesions especially oral candidiasis, necrotizing periodontal conditions, Kaposi sarcoma, oral hairy leukoplakia and recurrent oral ulcers has been reported to be decreased after this treatment due to reconstitution of the immune system. This study was designed to determine the effect of antiretroviral therapy on the oral mucosa of HIV/AIDS patients clinically and cytologicaly. A total of 25 patients not taking ART (Non-ART group) and 35 patients taking ART (ART group) were included in this study. Oral lesions were identified according to criteria established by Oral HIV/AIDS Research Alliance. For observing cytological changes oral smears were prepared by scrapping the buccal mucosa. Slides were stained with Haematoxylin and Eosin, Papanicolaou, Periodic Acid Schiff's and Gomori's methenamine silver stains. Increased frequency of mucositis, oral ulcers, oral hairy leukoplakia (OHL), chronic periodontitis and oral wart was seen in ART group as compared to Non-ART group while oral mucosal pigmentation was significantly higher in ART group (p=0.00). Oral candidiasis was more frequent in Non-ART group as compared to ART group. Increased frequency of fungi, micronuclei and nuclear atypia were seen in Non-ART group as compared to ART group but the results were insignificant. This study highlights that oral lesions especially oral candidiasis are decreased after antiretroviral therapy while some lesions especially oral pigmentation has been significantly increased which may be due to the side effects of this therapy.

Key Words: *HIV/AIDS, immunosuppression, Pakistan, ART effect, oral lesions.*

INTRODUCTION

Oral lesions especially oral candidiasis, necrotizing periodontal conditions, Kaposi sarcoma, oral hairy leukoplakia, oral warts and recurrent oral ulcers are essentially related to HIV/AIDS disease progression.[1] These oral lesions are strongly associated to low CD4+ count and high viral load.[2] Antiretroviral therapy is given to HIV/AIDS patients that usually consists of two nucleoside reverse transcriptase inhibitors (NRTI) alongwith non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor (PI).[3] Antiretroviral therapy reduces the viral load by inhibiting the viral replication and results in the reconstitution of the immune system alongwith the increase in CD4+ lymphocyte count.[4] Frequency of oral lesions has been reported to be decreased after antiretroviral therapy (ART) especially in case of oral candidiasis, oral hairy leukoplakia, necrotizing periodontal conditions and various AIDS related malignancies like Kaposi sarcoma.[5] But some lesions especially oral warts related to human papilloma virus (HPV) and oral ulcers, xerostomia, mucositis, hyperpigmentation, erythema multiforme and lichenoid reactions have been reported to be increased after ART attributed to the immune reconstitution, adverse effects of ART or drug resistance.[6]

No study has been reported from Pakistan that describes effect of ART on the frequency of oral lesions in HIV/AIDS patients. So this study was designed to study whether the oral lesions were less frequent in the patients taking ART or not as compared to the patients not taking ART in the local population.

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METHODOLOGY

The study was approved from the ethical review board of University of Health Sciences Lahore. Patients were divided into two groups. Group1 comprised of 25 patients not taking ART and it was named as Non-ART group while in Group two 35 patients were included taking ART and it was named as ART group. It was ensured that all the patients were on the same regimen of antiretroviral therapy. After taking written informed consent and relevant clinical history the patients were clinically staged according to WHO clinical staging system.7 Detailed clinical examination was performed and oral lesions were identified according to criteria established by Oral HIV/AIDS Research Alliance (OHARA).8 Oral smears were prepared by scrapping the buccal mucosa and four slides were prepared from each subject. All the slides were fixed with 95% ethanol and stained with Haematoxylin and Eosin, Papanicolaou, Periodic Acid Schiff's and Gomori's methenamine silver stains. CD4+ lymphocyte count was determined using flow cytometer. Frequencies with the percentages of all the clinical and cytological variables for ART and Non-ART group were uploaded and analyzed using SPSS 18. The Chi- square tests were used to find the associations between the variables. A p value ≤ 0.05 was considered significant.

RESULTS

Increased frequency of mucositis (2%), oral ulcers (6%), oral hairy leukoplakia (OHL) (3%), chronic periodontitis (26%) and oral wart (3%) were seen in ART group as compared to Non-ART group while oral mucosal pigmentation was significantly higher (63%) in ART group (p=0.00). The results obtained are summarized in Table 1. Oral candidiasis (Fig 1) was more frequent (12%) in Non-ART group as compared to ART group (6%). These trends are summarized in Graph 1. Cytological changes in the oral mucosa including fungi, micronuclei and nuclear atypia (Fig 2, Fig 3) were frequent in Non-ART group as compared to ART group.

DISCUSSION

Antiretroviral therapy provides effective treatment options for the patients affected with HIV/AIDS. The initial goal of antiretroviral therapy (ART) is to improve survival without progressing to AIDS and try to alleviate the adverse effects of treatment. Immune reconstitutions via the recovery of CD4+ count serve as marker for monitoring the response to therapy because of its predictive ability for AIDS related events and death.[8] After the use of ART, oral manifestations related to HIV have been decreased in patients.[5] Oral lesion can be used to predict the efficacy of ART as these lesions are the mirrors of immune status due to their strong association with low CD4+ count. Recurrent oral lesions especially oral candidiasis, oral hairy leukoplakia, necrotizing periodontal conditions and oral ulcers in a HIV/AIDS infected patient already on ART warrants the ART failure and need to change the regimen in such patient alongwith the reassessment of immune status.[9]

Due to the limitations of the study time and difficult approach to the patients not taking ART alongwith their least motivation to give samples equal number of patients could not be included in both groups of the study.

In this study oral lesions were more frequent in ART group (63%) as compared to Non-ART group (36%) which is in contrary to the results of Patton et al. (2002)[10] who had reported a decrease from 47.6% during the pre-antiretroviral era to 37.5% after the

TABLE 1: ASSOCIATION OF ART AND NON-ART GROUPS IN N=60 PATIENTS

Variables	ART 35 N (%)	NON-ART 25 N (%)	Total 60 N (%)	P value
Mucositis	1 (2%)	0 (0%)	1 (1.7%)	1
Oral ulcers	2 (6%)	1 (4%)	3 (5%)	1
Oral candidiasis	2 (6%)	3 (12%)	5 (8%)	0.64
OHL	1 (3%)	0 (0%)	1 (1.7%)	1
Chronic periodontitis	9 (26%)	5 (20%)	14 (23%)	0.60
Oral wart	1 (3%)	0 (0%)	1 (1.7%)	1
Oral pigmentation	22 (63%)	2 (8%)	24 (40%)	0.00
Inflammation	23 (66%)	15(60%)	38 (63.3%)	0.65
Dysplasia	6 (17%)	4 (16%)	10 (16.6%)	1
Fungi	17 (48.5%)	14 (56%)	31 (51.6%)	0.8
Micronuclei	19 (54%)	18 (72%)	37 (62%)	0.19
Nuclear atypia	13 (37%)	11 (44%)	24 (40%)	0.59

Fig 1: Pseudomembranous candidiasis on the tongue of a27 year old female

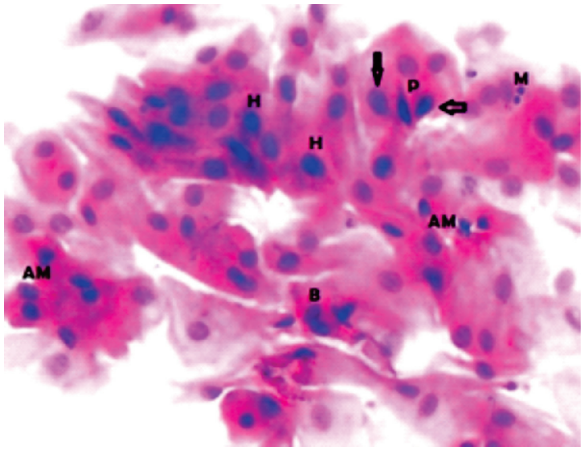

Fig 2: Oral squamous cells showing moderate nuclear pleomorphism (P), hyperchromasia (H), atypical mitosis (AM) with binucleation (B) and micronuclei (M) in oral squamous cells (H&E, 400X)

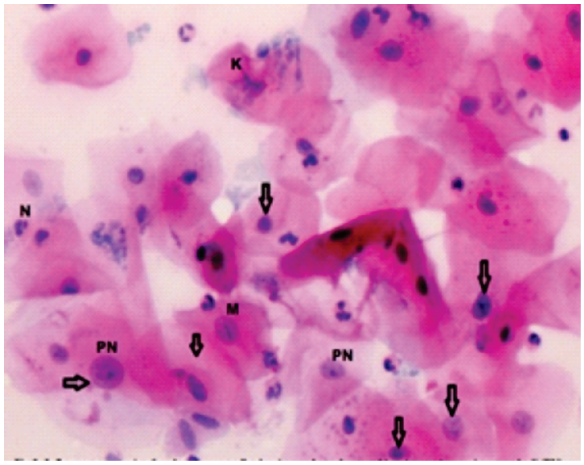

Fig 3: Inflammatory atypia of oral squamous cells showing nuclear pleomorphism (arrows), prominent nucleoli (PN), typical mitosis (M) and neutrophils (N) karyolysis (K)(H& E, 400X)

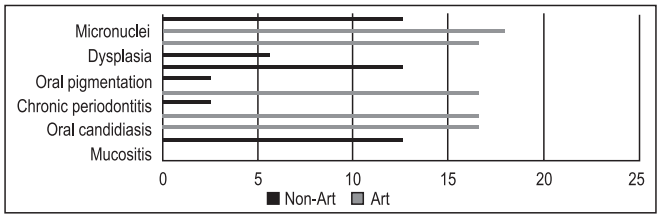

Fig 1: Comparison of various oral lesions in ART and Non-ART group. Note that oral pigmentation is significantly increased (p=0.00) in ART group

inception of ART. It may be due to short sample size or it may be due to the fact that most patients in ART group (n=22) had CD4+lymphocyte count <350 cells/mm^3 which is considered as the state of advanced immunosuppression according to WHO immunological classification system.[11]

Frequency of the oral candidiasis was decreased in the ART group as compared to Non-ART group which is concordant with the results of Umadevi et al. (2007).[6] Increased frequency of mucositis, oral ulcers, oral hairy leukoplakia (OHL), and chronic periodontitis was seen in ART group as compared to Non-ART group. These results are in contrary to the results of the Ramírez-Amador et al. (2007)[9] and Lourenço et al. (2011)[12] who reported a decrease in the frequency of above mentioned oral lesions after ART. Oral mucosal pigmentation was significantly higher (p=0.00) in ART group patients as compared to Non-ART group. This is in accordance with the results of Umadevi et al. (2007).[6] Higher frequency of oral pigmentation in patients taking ART is attributed to the adverse effects of antiretroviral therapy.[13] Increased frequency of mild to moderate inflammation and dysplasia were seen in ART group while fungi, micronuclei and nuclear atypia were more frequent in Non-ART group as compared to ART group. No study has been reported that describes the frequency of these cytological changes in the oral squamous cells of HIV/AIDS patients taking or not taking ART.

CONCLUSION

Increased frequency of mucositis, oral ulcers, oral hairy leukoplakia (OHL), chronic periodontitis and oral wart was seen in ART group as compared to Non-ART group while oral mucosal pigmentation was significantly higher in ART group (p=0.00). Oral candidiasis was more frequent in Non-ART group as compared to ART group. Regarding the cytological changes, increased frequency of fungi, micronuclei and nuclear atypia were seen in Non-ART group as compared to ART group but the results were insignificant.

More studies should be carried out with the larger sample size as these studies can be helpful in improving the oral health status of the HIV/AIDS patients in Pakistan. Immune status of these patients and ART

efficacy can be predicted in them by using oral lesions as a clinical and cytological markers of the immunosuppression.

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4 AH Nagi:	Support in study design/data collection/supervision