

Comparison of Oral Manifestations in HIV Positive Children with and without HAART

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ABSTRACT

Introduction: The advent of HAART had reduced the incidence and type of oral lesions as found in many studies. However, these studies are mostly conducted among adults and studies related to the incidence of oral lesions in children are few till date, particularly in India. Thus, the present study was carried out find differences in the incidence of oral lesions among the HIV positive children receiving HAART and not receiving HAART.

Material and Methods: The present study comprised a total 60 HIV positive pediatric patients divided into two groups. Group I comprised of 30 HIV positive children receiving HAART for a minimum of 3 months. Group II comprised of 30 HIV positive children without HAART and who came to the ART centre for first time without previous history of anti – retroviral therapy. The oral lesions associated with HIV infection were diagnosed based on their clinical presentation. Fisher's chi-square test was used to compare the lesions. Significance will be obtained using P-value. For all the tests, a P-value of 0.05 or less was considered for statistical significance and a P-value of 0.02 or less was considered for statistical highly significance.

Results: The manifestations that were observed in Group I were taken into consideration for comparing the incidence of oral manifestations. Candidiasis were more in HIV +ve children without HAART with statistically highly significant value.

Conclusion: The present study found that HIV infected patients receiving HAART predominantly combination of stavudine, lamivudine, nevirapine, zidovudine and effiviranez for a period of less than a year, had a significantly lower prevalence of oral lesion particularly oral candidiasis, oral hairy leukoplakia, parotid gland enlargement and cervical lymphadenopathy.

KEYWORDS: Anti-retroviral therapy, HAART, HIV.

INTRODUCTION

Human immunodeficiency virus (HIV) infection is considered a pandemic by the World Health Organization (WHO). From its discovery in 1981 to 2006, acquired immunodeficiency syndrome (AIDS) has killed more than 25 million people. HIV infects about 0.6% of the world's population. In 2005, AIDS claimed an estimated 2.4 – 3.3 million lives, of which more than 570,000 children. Most of the cases are seen in sub-Saharan countries and developing nation.¹ Globally, the number of children living with HIV increased from 1.5 million in 2001 to 2.5 million in 2007. However, estimated new infections among children declined from

460,000 in 2001 to 420,000 in 2007. Deaths due to AIDS among children have increased.²

In India the trends indicate that shift from one group to the next. The trends indicate that HIV infection is spreading in two ways; from urban to rural areas and from individuals practicing high risk behavior to the general population. Data from antenatal clinics indicate rising HIV prevalence among women, which in turn contribute to increasing HIV infections in children.²

The relatively few studies of oral lesions in patients on HAART have been conducted elsewhere and do indicate significant differences in the influence of HAART on

types of oral lesion for example, oral candidiasis, oral hairy leukoplakia, Kaposi sarcoma, and HIV associated periodontal disease have been reported to decrease. On the other hand, HIV Salivary gland diseases, human papilloma virus (HPV) associated oral lesion including papilloma, condylomas and focal epithelial hyperplasia (oral warts), xerostomia and recurrent oral ulceration appear to have increased. There are also reports indicating no change in the occurrence of HIV associated oral lesion in children receiving HAART.³

The reasons for these differences are not entirely clear. Some authors have associated these variations with differences in access to oral health care, demographic and social factors, mode of HIV transmission, types of co-infections, disease stage and immune reconstitution.⁴

The advent of HAART had reduced the incidence and type of oral lesions as found in many studies. However, these studies are mostly done in adults and studies related to the incidence of oral lesions in children are few till date, particularly in India. In this context, oral lesions in HIV positive children receiving HAART are studied. Differences in the incidence of oral lesions among the HIV positive children receiving HAART and not receiving HAART were also studied.

MATERIALS AND METHODS

The present study comprised a total 60 HIV positive pediatric patients randomly selected from the ART centre in Government General Hospital, Ranchi, India. Patients were divided into two groups. Group I comprised of 30 HIV positive children receiving HAART for a minimum of 3 months. Group II comprised of 30 HIV positive children without HAART and who came to the ART centre for first time without previous history of anti – retroviral therapy. The study protocol was approved by the ethical committee of the institute as well as permission was taken from medical incharge in the ART Centre, Ranchi. Written consent was obtained from the parents of these children in a consent form before recording the cases. Address and contact number was not to be taken to maintain confidentiality. These children were selected from same age group (2 years- 13 years) and same socioeconomic status. The details to be taken from these children for subsequent analysis include age, oral lesions and

therapeutic drug usage. Patients were interviewed using a standard structured case sheet performa to obtain information regarding social and demographic details, past medical history, family history and history of previous medication if any. Previous and current episodes of oral manifestations present, previous use of HAART and any other medicine and current treatment all were recorded. Current and previous oral manifestations were categorized and were recorded. An oral examination was carried out by a qualified dental surgeon. The extra-oral and peri-oral tissues were examined first, followed by the intra-oral tissues, for changes in size, colour and shape of anatomical areas as well as for clinical signs and lesions. The oral lesions associated with HIV infection were diagnosed based on their clinical presentation and where multiple sites were involved, all sites were documented.

HAART regimens

Four types of regimens of HAART were included in this study namely:

- 1) STV+LMV+NVP
- 2) STV+LMV+EFV
- 3) ZDV+LMV+NVP
- 4) ZDV+LMV+EFV

(STV-Stavudine, LMV- Lamivudine, NVP-Nevirapine, EFZ- Effavirenz)

Out of the regimens any of the regime was given to the patients and was sometimes substituted or stopped because of any of the reasons such as toxicity/side effects, pregnancy, newly drug available, clinical treatment failure, immunological failure, virologic failure, treatment failure, poor adherence, illness hospitalization, patient lack of finance, patient decision. Fisher’s chi- square test was used to compare the lesions. Significance will be obtained using P- value. For all the tests, a P-value of 0.05 or less was considered for statistical significance and a P-value of 0.02 or less was considered for statistical highly significance.

RESULTS

The current study involves 30 children each in two groups. The antiretroviral drugs that was given to these patients were recorded, which include, (Zidovudine, Lamivudine, Stavudine, Nevirapine and Effiviranez and where divided into four regimen (I-IV) (Table 1).

Table 1: Highly Active Antiretroviral Therapy (HAART) Drugs Used For Treatment

REGIMEN (GROUPS)	DRUGS USED
REGIMEN I	*STV+LMV+NVP
REGIMEN II	*STV+LMV+EFV
REGIMEN III	*ZDV+LMV+NVP
REGIMEN IV	*ZDV+LMV+EFV

*NOTE: STV- Stavudine, LMV- Lamivudine, NVP- Nevirapine, ZDV- Zidovudine, EFV- effiviranez

Table 2: Comparing incidence of oral lesion with HAART (group1) and without HAART (group-2) with chi square value, P value and inference

Name of disease	HIV +ve WITH HAART n=30	HIV +ve WITH OUT HAART n=30	Chi Sqr Value	'P' value	Significance
Candidiasis	7	17	6.94	0.0083	Highly Significant
Gingivitis/periodontitis	6	13	3.77	0.0522	NS
Angular chelitis	7	14	3.59	0.0581	NS
Ulcerative stomatitis	3	8	2.78	0.09	NS
Oral hairy leukoplakia	1	3	1.07	0.30	NS
Hyperpigmentation	6	1	4.04	0.04	Significant
Viral infection	1	4	1.96	0.16	NS
Kaposi's sarcoma	0	1	1.02	0.31	NS
Cervical lymphadenopathy	7	12	1.92	0.17	NS
Parotid gland enlargement	4	10	3.35	0.07	NS
Mucocele	0	0	–	–	–
Dental caries	24	27	1.18	0.28	NS

P>0.05 Not Significant P<0.05 Significant

P<0.02 HS

The oral manifestations of children in Group I (HIV +ve with HAART) were compared to that of Group II (without HAART). The manifestations that were observed in Group I was taken into consideration for comparing the incidence of oral manifestations. The statistical analysis using Fishers Chi-square test showed that the statistical analysis using Fishers Chi-square test showed that hyperpigmentation was significantly more in children receiving HAART. Candidiasis were more in HIV +ve children without HAART with statistically highly significant value was obtained. However the prevalence of other lesions where statistically not significant in both the groups (Table 2).

DISCUSSION

The advent of Highly Active AntiRetroviral Therapy has reduced the mortality and morbidity rates in HIV positive individuals. This is due to reduction of HIV viral load and consequent recovery of immune system.¹ Patients receiving HAART are protected to some extent against candidiasis, salivary gland disease, Kaposi sarcoma and oral hairy leukoplakia.^{1,5}

In the present study the diagnosis of initial infection in children is established by Polymerase Chain Reaction. However, the antiretroviral drugs are not given to children below the age of 5 years. The CD4+Tcells are monitored and necessary instructions are given to the parents of these children. However, antiretroviral drugs in the form of syrups are given to infants with low CD4+Tcell count.

Previous studies have shown that mother to child transmission was the dominant mode of transmission of the virus to infected children the present study also showed similar finding.⁶

In case of oral lesions with limited cross sectional reports indicates that oral candidiasis is one of the

common and serious complication of HIV infection in young children which is in accordance with the present study in which the prevalence of the lesion is 23.3% and 56.6% respectively with HAART and without HAART individuals.⁷

Barasch A et al⁸ reported decline in the incidence or occurrence of the oral candidiasis lesion in the HIV +subjects which is in accordance with the present study in which it was seen that the prevalence of oral candidiasis is 23.3% with HAART and is remarkably 56.6% in case of non HAART group. The prevalence of HIV associated periodontal disease in the pre- HAART era, vary widely both in developed and developing countries. Indicatively, reported rates of prevalence for linear gingival erythema range between 9% and 50%, for necrotizing ulcerative gingivitis between 11% & 25% and necrotizing ulcerative periodontitis between 1% & 18% and it is may be due to advent of the HAART therapies.⁹

The higher prevalence of mucosal hyper pigmentation in patients as HAART has been linked with increased melanin production in the epithelium associated with increased release of α -melanocyte stimulating hormone as a result of systematic ketoconazole and zidovudine therapy.²

In a study conducted by Poonam et al¹, a reduction in the prevalence of oral lesions has been reported in HIV infected patients receiving HAART and regular use of HAART had probably reduced the prevalence of oral lesions, especially oral hairy leukoplakia and pseudomembranous candidiasis. The reduction in the prevalence of oral lesion is attributed to the immune recovery on treatment with HAART.

Comprehensive guidelines for the prevention of the most prevalent and life threatening opportunistic infections in person infected with the HIV virus have recently

developed by CDC and the infectious disease society of America specific notes on guidelines for pediatric population are included in every sections, although a majority of cases firm pediatric recommendations await the result of controlled clinical trials. Routine childhood vaccines are important for pediatric patients who are infected with HIV. In general live viral vaccines and live bacterial vaccines should not be given to patients with AIDS or to patients with other clinical manifestations of HIV infections.¹⁰ Side effects or intolerance to antiretroviral therapy occur with moderate frequency. Drug related toxicity may be acute, occurring soon after a drug has been administered; subacute occurring within days of administration or late occurring after prolonged drug administration. Severity may vary from mild to severe life threatening. Identification of the responsible agent allows substitution of a similar agent to which virus is susceptible, children who initiate or change to a new HAART regimen need to be followed to assess effectiveness, adherence, tolerability, and side effects of the regimen.¹¹

CONCLUSION

The present study found that HIV infected patients receiving HAART predominantly combination of stavudine, lamivudine, nevirapine, zidovudine and efavirenz for a period of less than a year, had a significantly lower prevalence of oral lesion particularly oral candidiasis, oral hairy leukoplakia, parotid gland enlargement and cervical lymphadenopathy. There was significant increase in hyperpigmentation in HAART group than that of non HAART group which was due to possible side effects of anti-retroviral therapy. Progress in the treatment of pediatric HIV infection has been made over the past decade with significant reduction in morbidity and mortality. Understanding the principles of selecting HAART regimens and vigilance for toxicities are important for optimal management of HIV infected infants and children where access to medication is not a problem, the biggest challenge to optimizing HAART is to maintaining adherence to medications a challenge that requires ongoing assessment and interventions as the patient moves from the infancy to adolescence. More studies preferably longitudinal need to be conducted for longer periods of time in order to get better picture on the efficacy of HAART in reducing oral lesions in children in our settings.

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