Study of amplitude of accommodation in patient with Human Immunodeficiency Virus infection on Anti Retro virus Treatment

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Abstract
Introduction: Human Immunodeficiency Virus [HIV] is known to cause premature ageing leading to reduction in amplitude of accommodation. It is associated with many other ocular and systemic diseases.
Aim: The primary objective was to find out if HIV-positive patients on Anti Retroviral Treatment [ART] have significantly reduced amplitude of accommodation compared with controls. The secondary objective was to investigate accommodative impairment in relation to factors such as age, CD4 count and current antiretroviral treatments.
Method: It was a cross sectional, open and prospective single center study in a tertiary care hospital in Western Maharashtra. It involved 200 HIV-positive patients on ART aged from 35 years to 45 years with no previous history of eye problems and 200 age-matched controls.
Results: Blur reported by HIV patients using Royal Air Force [RAF] ruler for 35-39 years age group was 27.94% [19/68] while for control group it was 2.08%[2/96], [p value <0.001] Reduced amplitude of accommodation below age expected norms was also observed. For age group 40-45 years, reduction in amplitude of accommodation found for HIV patients and control was 92.42% and 95.09% respectively, [p Value <0.001] Accommodation failure was not related to CD4 count or current ART being used.
Conclusion: This study has identified accommodative failure in a significant proportion of HIV-positive patients on ART aged between 35 and 45 years. This problem may be under-recognized. The need for near correction for the pre-presbyopic age is often overlooked. Accommodation failure was not related to CD4 count or current ART being used.
Keywords: Amplitude of accommodation, RAF ruler, HIV, ART.

Introduction
It has been observed that a significant proportion of HIV-positive patients on ART complained of difficulty in accommodation at ages below that of presbyopic age (40 yrs). A literature review showed that the question of HIV associated impairment of accommodation has received little attention till date. Wu and associates¹ reported significant reduced amplitudes of accommodation in a small sample of 10 patients with AIDS compared with controls. However, till date the only published survey to provide a quantitative estimate of accommodative failure across different ages in HIV-positive patient has been by Their felder and his associates in 1994². They reported reduced amplitude of accommodation outside normal limits in two thirds of their patients.
The study by Their felder and associates was before the advent of Highly Active Antiretroviral Therapy (HAART). Since the advent of HAART, there has been a decrease in the incidence of AIDS-related opportunistic infections such as cytomegalovirus (CMV) and disseminated Mycobacterium avium complex. Study by Westcott and associates in 2001 on 43 HIV patients aged between 25-35 yrs found that age groups 25-34 yrs had reduced amplitude of accommodation when compared with age expected normal individuals. The decline in the incidence of opportunistic infections and improved survival rates are likely to make failure of accommodation an increasingly significant clinical problem. Accommodative failure is important for optometrists to recognize as the prescription of presbyopic correction makes it one of the most easily treated ocular manifestation of HIV infection.

Aim
The primary aim of this study was to investigate the extent of accommodative insufficiency in a cohort of HIV-positive patients on ART. A secondary aim was to investigate for possible associations between accommodative impairment and factors such as age, CD4 count and combination of ART being used by patients.

Method
It was a cross sectional study. It comprised of 200 HIV patients and 200 age matched controls. Subject with significant ocular, medical or therapeutic histories known to effect accommodation such as diabetes mellitus, hypertension and cataract were excluded from the study. A detailed history was taken of patients previously diagnosed as HIV positive. All subjects underwent refraction and acceptance to ensure that they had Best corrected visual acuity [BCVA] 6/6 or better in both eyes. These patients were regular users of ART. Patients were invited to take part in the study irrespective of whether they were, or were not, suffering from accommodative difficulties. The study was approved by the hospital ethics committee. All patients and controls gave informed consent prior to being included in the study. Only outpatients were included in the study. Terminally ill or bedridden patient were excluded from the study. They were subjected to orthoptic assessment and RAF ruler was used to assess the amplitude of accommodation.

Testing procedure
Pupil diameter was recorded prior to testing to ensure that there were no pupillary abnormalities evident which could affect accommodation amplitude. No pupil size differences were identified between the patient and control group. The amplitude of accommodation was assessed using a traditional push up method using a RAF ruler. The subjects were told to report when the test card (N5 print) becomes blurred and difficult to read as it was moved toward the patient. The test was repeated three times unilocularly and the average of the three test results was taken into consideration.

Results
All variables were tested for normality. To test the hypothesis that the amplitudes of accommodation were significantly different, non parametric analysis was done. Applying test of normality for data, it was found that data was not normally distributed. Therefore, Mall Whitney Test which is non-parametric test of statistical significance was used to check if there was any difference between the two groups. P value <0.001, was considered significant.

From the table 1 it is clear that the amplitude of accommodation is hampered in HIV infected patients on ART [mean 23.36cms] when compared with the control group [14.93cms]. To analyze the effect of age on accommodative amplitude, the subjects were further divided into two equal age group intervals of 35-39 years and 40-45 years. Variance analysis showed no
difference at the \( p<0.05 \) level of significance between the mean ages of the patient versus control within each age interval. None of the patients were taking any other systemic medication at the time of the study. All the patients were on combination of antiviral agents including stavudine, lamivudine and efavirenz (SLE), zidovudine ,lamivudine and efavirenz (ZLE) stavudine, lamivudine and nevirapine (SLN) zidovudine ,lamivudine and nevirapine (ZLN) 31% of patients were on SLE/ZLE combination while 69.% were on a combination of SLN/ZLN.

CD4 count was divided in two groups, less than 250 and more than 250 [table 6], 47.5% of patient had \( >250 \) CD4 cell count where as 52.5% had CD4 count \(<250 \) cells. Anti retroviral treatment being used by the patient [table 2 and CD4 count [table 3] had no correlation with decreased amplitude of accommodation.

Table 1

| Variables | Group | Range (Mini to Maxi) Cms | Mean Cms | SD | p-value |
|-----------|-------|-------------------------|---------|----|---------|
| Blurred   | On ART | 18.00 to 46.00           | 23.365  | 7.7726 | 0.001   |
|           | Control | 12.00 to 17.00           | 14.935  | 1.1651 |         |

ART Regimen Vs Amplitude of Accommodation [Table 2]

| Amplitude of Accommodation | ART Regimen | ART Regimen | Control |
|-----------------------------|-------------|-------------|---------|
|                             | SLE/ZLE     | SLN/ZLN     |         |
| 10-15                       | 10          | 24          | 142     |
| 16-21                       | 23          | 27          | 58      |
| 22-27                       | 14          | 42          | -       |
| 28-33                       | 9           | 30          | -       |
| 34-39                       | 6           | 10          | -       |
| 40-45                       | 1           | 5           | -       |
| Total                       | 62          | 138         | -       |

Patients were divided into 2 ART regimen groups [SLE/ZLE and SLN/ZLN] and compared to check for impact of ART regimen on amplitude of accommodation, by applying t-test [ \( t=1.985, \) df 10 \( p=0.075 \)] There was no significant impact of the type of ART regimen being used and amplitude of accommodation in the patients study.
Table 3

| Amplitude of Accommodation | CD4 count | Cd4 count |
|----------------------------|-----------|-----------|
| 10-15                      | < 250     | >250      |
| 16-21                      | 18        | 18        |
| 22-27                      | 23        | 24        |
| 28-33                      | 34        | 22        |
| 34-39                      | 24        | 16        |
| 40-45                      | 5         | 11        |
|                            | 1         | 4         |

Patients were divided into 2 groups [CD4 < 250 and CD4 > 250] and compared to see if CD4 count affected amplitude of accommodation, t-test [t=0.282, df 10 p=0.784] was used. It was found that there was no significant difference between the groups.

**Discussion**

This study shows that amplitude of accommodation is significantly reduced in HIV-positive patient on ART. A study by Wu P, Williams JG, Phillips BJ, Khanna A, Friedlander SM, Goldstein DA. Loss of decreased amplitude of accommodation in the patients between 35-39 yrs, making them pre-presbyopes. They needed to go for the presbyopic correction to have quality vision for near. Just like Marc C Westcott we also did not identify any particular anti-retroviral combination associated with impaired accommodation, and CD4 count as compared with controls of same age group.

**Conclusion**

This study has identified accommodative failure in a significant proportion of HIV-positive patients on ART aged between 35 and 45 years. This problem may be under-recognized. The need for near correction for the pre-presbyopic age is often overlooked. Accommodation failure was not related to CD4 count or current ART being used.

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