Published online: 2019-09-23

Original Article

Evaluation of salivary flow rate and gustatory function in HIV-positive patients with or without highly active antiretroviral therapy

Neha Verma[1], Ranjitkumar Patil[1], Vikram Khanna[1], Vandana Singh[1], Anurag Tripathi[1]

Correspondence: Dr. Vikram Khanna
Email: drvikramkhanna@gmail.com

[1]Department of Oral Medicine and Radiology, Faculty of Dental Sciences, KGMU, Lucknow, Uttar Pradesh, India

ABSTRACT

Objectives: The aim of this study is to evaluate the salivary flow rate and gustatory changes in HIV-positive patients on highly active anti-retroviral therapy (HAART) and without HAART. We also correlated CD4 count and salivary flow rate and gustatory function in both groups. **Methods:** Sample size for each group was thirty. After obtaining informed consent, we measured salivary flow rate using Schimer's method and gustatory function using four tastants (sweet, sour, bitter, and salty) of different concentrations. The readings were recorded at 0 month, 2nd, 4th, and 6th month interval. The data obtained was statistically analyzed. **Results:** The mean salivary flow rate was decreased more in Group I as compared to Group II. The mean identification score for sweet, salty, sour, and bitter was significantly higher in Group II than Group I. The mean detection threshold score for sweet, salty, sour and bitter taste was comparatively higher in Group I than Group II. The Pearson's correlation analysis showed inverse relation between age and salivary flow rate in Group II. No significant correlation was observed in CD4 count and salivary flow rate. **Conclusion:** Along with routine oral health appraisal in seropositive patients, evaluation of salivary flow rate, and taste abnormalities should also be considered an integral part of patient assessment.

Key words: Gustatory function, highly active anti-retroviral therapy, salivary flow rate, seropositive patients

INTRODUCTION

Acquired immune deficiency syndrome has caused a major damage since its discovery. Worldwide, around 2 million new HIV patients add to the current list of the infected individuals.[1] However, advances in the knowledge of the pathogenesis, patient care, pharmacology of antiretroviral therapy has led to decrease in the incidence of the HIV patients globally.[2] Highly active anti-retroviral therapy (HAART), commonly known as HAART, has played a pivotal role in increasing the life span of the infected patients.[3]

HAART dramatically suppresses viral replication and reduces the plasma HIV-1 viral load (vLoad) to undetectable levels (<50 RNA copies/mL). It also results in substantial increase in circulating $CD4^+$ T-lymphocytes. Combination therapy uses three antiretroviral agents directed against at least two distinct molecular targets.[4] Side effect of HAART includes bloating, nausea, diarrhea, fatigue, headache, nightmares, and decreased salivary flow which leads to increase in caries index.[5,6] It has also been reported that HAART therapy affects the chemosensory system in 70% of individuals and 23% of patients reported a change in the taste sensation.[7]

Access this article online

Quick Response Code:

Website: www.eurjdent.com

How to cite this article: Verma N, Patil R, Khanna V, Singh V, Tripathi A. Evaluation of salivary flow rate and gustatory function in HIV-positive patients with or without highly active antiretroviral therapy. Eur J Dent 2017;11:226-31.

DOI: 10.4103/ejd.ejd_289_16

The cause of perversion of the taste sensation is still debatable. Some researchers believe that taste alterations results due to the progression of the disease while other implies it might be the side effect of the drug therapy, i.e., HAART. Therefore, we planned this study to evaluate the salivary flow rate and gustatory changes in HIV-positive patients with HAART and without HAART. We also correlated CD4 count and salivary flow rate and gustatory function in HIV-positive patients on HAART and not on HAART.

METHODS

After obtaining clearance from the institutional ethical committee, we started the study by dividing seropositive patients into two groups. Group I includes seropositive patients on HAART therapy and Group II includes seropositive patients not on HAART therapy. Each group comprised thirty participants.

Inclusion criteria

- HIV seropositive individuals of both sexes and all age
- HIV seropositive patients on who have been advised HAART for the first time with no prior history of anti-retroviral drugs
- HIV seropositive patients not on any antiretroviral drugs (HAART).

Exclusion criteria

- HIV seropositive diseases with any known salivary gland disease and congenital salivary gland abnormality
- HIV-seropositive individuals with any other systemic disorder and on any known medication affecting salivary flow rate and gustatory function.

All the patients were appropriately coded to maintain their confidentiality. Patients case history, current HAART medications, CD4 count, the WHO clinical staging were recorded. Patients were tested in a noise free and comfortable room with no distraction. Salivary flow rate (unstimulated) was measured using Schirmer's test. Based on the length of wetting of Schirmer test strip, reading was recorded.

The gustatory function was assessed by four freshly prepared tastant solutions of sucrose (sweet), sodium chloride (salty), citric acid (sour), and quinine sulfate (bitter) in five concentration levels with 1/2 log steps. During the procedure, patients were presented with 5 ml of a taste solution in a cup and 5 ml of distilled water in other two cups, they were instructed to sip and swish the solution for 10 s. Patients were asked to identify the taste of given solution. Every correct identification was given a score of "1" was given, and incorrect identification was scored as "0." The detection threshold of taste was measured on a scale of 1–5 (lowest to highest) for all concentrations of each taste solution.

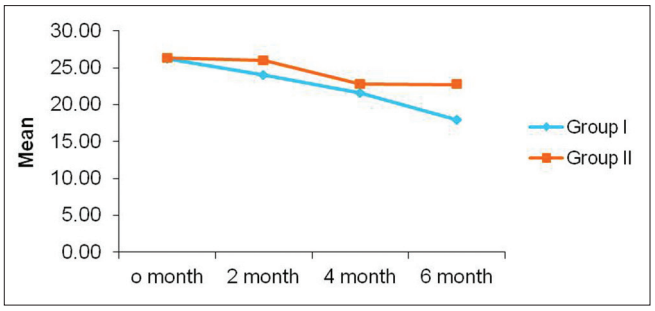

Figure 1: Mean salivary flow rate of both groups at different time intervals

Outcome measures

The outcome measures of the study were salivary flow rate and identification and detection threshold of all four taste senses (sweet, sour, salty and bitter) in both groups. The outcome measures of both the groups were assessed at the baseline visit (0 month) and consecutive visits at 2, 4, and 6 months. Co-relation of age, sex, and CD4 count with salivary flow rate and gustatory function was also evaluated.

Statistical analysis

The mean values of recorded data were analyzed with appropriate statistics. Student's *t*-test was performed to compare the variables between groups. To compare repeated measures of two groups analysis of variance was performed. The significance of mean difference within (intra) and between (inter) the groups was analyzed using Tukey's *post hoc* test. To ascertain normality and homogeneity of variance between groups Shapiro–Wilk's test and Levene's test were performed, respectively. Categorical (discrete) groups were compared using Chi-square (χ^2) test. Pearson's correlation analysis was performed to assess association between the variables.

OBSERVATIONS AND RESULT

Measure of salivary flow rate

The mean salivary flow rate was decreased in both Group I and Group II over 6 months. However, it decreased more in Group I than Group II [Figure 1].

When compared both the groups, the mean salivary flow rate showed no significant change in Group I and II at the time 0 month, 2 months, 4 months, but it was found to be significant at 6 months interval. In Group I, there was statistically significant decrease ($P < 0.001$) in the salivary flow rate at all intervals of time**.**

In Group II, there was statistically decrease in salivary flow rate at 0–4 months, 0–6 months, 2–4 months, 2–6 months. However, the decrease was not statistically significant at 0–2 months and 4–6 months ($P = 0.992$ and 1.000, respectively).

Measure of gustatory function

Sweet taste

Identification

The mean identification score for sweet taste in Group I remained constant from 0 month to 2 months and decreased, thereafter whereas, in Group II, it remained constant from 0 month to 4 months and decreased thereafter. The mean identification sweet score was significantly higher in Group II than Group I [Figure 2a].

Detection threshold

The mean detection threshold score for sweet taste in Group I and Group II remained constant from 0 month to 4 months but later on both the groups showed an increase in sweet taste threshold. The mean detection threshold score for sweet taste was comparatively higher in Group I than Group II [Figure 2b].

Salty taste

Identification

The mean identification score for salty taste in Group I and Group II remained constant from 0 to 4 months then it decreased at 6 months in Group I and increased in Group II. The mean identification score was comparatively higher in Group II than in Group I [Figure 3a].

Detection threshold

The mean detection threshold score for salty taste in Group I and Group II remained constant from 0 month to 4 months then it increased at 6 months in Group I and decreased in Group II. The mean detection threshold score was comparatively higher in Group I than in Group II [Figure 3b].

Sour taste

Identification

The mean identification score for sour taste in Group I and Group II remained constant from 0 to 2 months; thereafter, it decreased at 4 and 6 months in Group I. In Group II, it increased at 4 months and then decreased again at 6 months. The mean identification sour score was comparatively higher in Group II than Group I [Figure 4a].

Detection threshold

The mean detection threshold score for sour taste in Group I and Group II remained constant from 0 month to 2 months. It then increased at 4 and 6 months in Group I, whereas, in Group II, it decreased slightly at 4 months, but increased again at 6 months. The mean detection threshold score for sour taste was comparatively higher in Group I than Group II [Figure 4b].

Bitter taste

Identification

The mean identification score for the bitter taste in Group I and Group II remained constant from 0 to 2 months, then it was decreased at 4 and 6 months

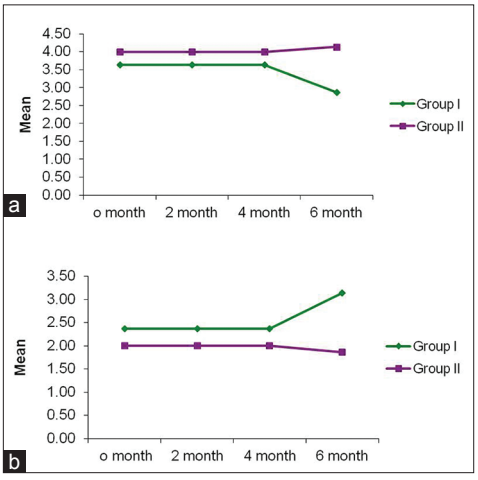

Figure 2: (a) Mean identification score for sweet taste of both groups at different time intervals. (b) Mean detection threshold score for sweet taste of both groups at different time intervals

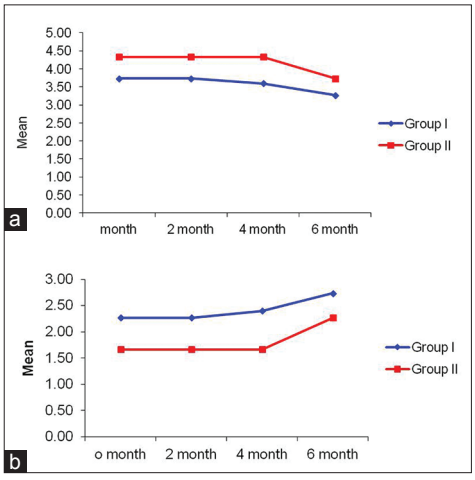

Figure 3: (a) Mean identification score for salty taste of both groups at different time intervals. (b) Mean detection threshold score for salty taste of both groups at different time intervals

in Group I. In contrast, it was constant at all-time intervals in Group II. The mean identification score for bitter taste was comparatively higher in Group II than Group I [Figure 5a].

Detection threshold

The mean detection threshold score for the bitter taste in Group II remained constant at 0,2,4 and 6 months. However for Group I, it was constant at 0 and 2 months, but it increased at 4 and 6 months, respectively. The mean detection threshold score for bitter taste was comparatively higher in Group I than Group II [Figure 5b].

Co-relation of age, sex, and CD4 count with salivary flow rate and gustatory variables

The Pearson's correlation analysis in Group I showed no significant co-relation between age, sex, and CD4 count with salivary flow rate and gustatory variables; however in Group II, a significant negative (inverse) correlation was seen between salivary flow rate and age ($r = -0.41$, $P < 0.05$) It was found that as the age increases salivary flow rate decreases or vis-a-versa. Furthermore, in Group II, the changes in sweet taste ($r = 0.58$, $P < 0.01$) showed positive co-relation with sex, whereas in salty taste ($r = -0.57$, $P < 0.01$) an inverse association was seen.

The Pearson's analysis showed a significant inverse co-relation between changes in salty taste score and salivary flow rate in Group I ($r = -0.59$, $P < 0.001$); however, it showed a positive co-relation in Group II ($r = 0.45$, $P < 0.05$). The changes in other gustatory variables showed no significant co-relation ($P > 0.05$) with CD4 count and salivary flow rate in both the groups.

DISCUSSION

Xerostomia, hyposalivation, and altered taste sensation are the common complaints of seropositive patients, and it is equally noted in adult as well as pediatric patients.[8] The change in quality and quantity of the salivary constituents will result in high caries index, deterioration of the oral health and increased chances of opportunistic infections. Although HAART is an integral part of medical management for HIV infection, owing to its various side effects, it greatly compromises the quality of life among these patients.

The ambiguity over the cause of hyposalivation or xerostomia still exists. The disease progression theory suggests that diffuse infiltration of $CD8^+$ lymphocyte in salivary glands causes suppression of salivary gland functions, whereas the other theory suggests, the adverse effect of HAART are responsible for hypofunctioning of salivary glands.[9]

Many studies have been reported to evaluate the effect of HIV infection on salivary gland and gustatory function in HIV-positive patients. In this study, HIV-positive patients on HAART and without HAART were included to assess the salivary and gustatory alterations at regular time intervals for 6 months. In this study, the salivary flow rate was reduced in HIV-positive patients on HAART as compared to those not on HAART. These findings were consistent with the studies conducted by Navazesh *et al*.[10] In contrast Johar *et al*.[11] reported increased salivary flow rate in patients on HAART, whereas Lin *et al*.[12] and Pavithra *et al*.[13] found no significant difference in patients with or without HAART.

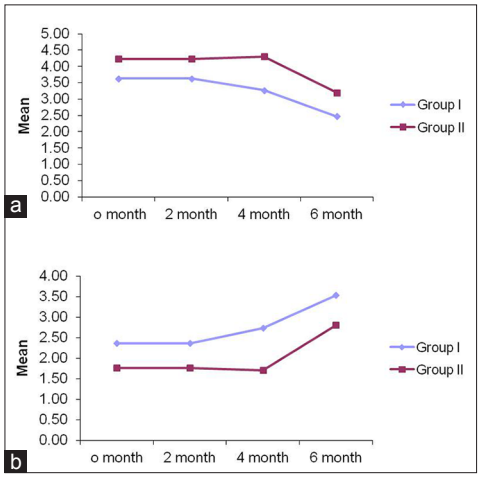

Figure 4: (a) Mean identification score of sour taste of both groups at different time intervals. (b) Mean detection threshold score for sour taste of both groups at different time intervals

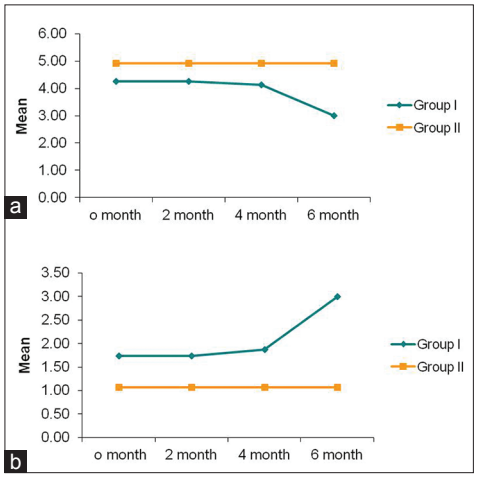

Figure 5: (a) Mean identification score for bitter taste of both groups at different time intervals. (b) Mean detection threshold score for bitter taste of both groups at different time intervals

Nittayananta *et al*. and Kumar *et al*. observed that long-term use of HAART causes a significant decrease in salivary flow rate of HIV-positive patients.[14,15] Similarly, there was a significant decrease in salivary flow rate but after long-term follow-up (4–6 months) in our study. Navazesh *et al*. suggested that individuals on long-term HAART are at a higher risk for developing salivary gland enlargement and salivary gland hypofunction altering the composition of saliva.[10] These alterations could be due to HIV infection itself, consequent immunosuppression or the effect of drugs used in HAART. These conflicting observations may be the result of the differences in HAART regimen and the method of saliva collection.

Glick *et al*. and Bretz *et al*. mentioned in their study that reduced salivary flow rate was associated with decreased CD4 count in HIV-positive individual[16,17] Kumar *et al*. also concluded that reduction in CD4 cell counts were significantly associated with reduced salivary flow rates in HIV-positive individuals who were on long-term HAART.[15] Our study found no significant co-relation between CD4 count and salivary flow rate in HIV-positive patients both with HAART and without HAART. The differences in the co-relation of CD4 count and salivary flow rate may be attributed to the variations in the upper and lower range of CD4 count of the study population. In this study, the lowest mean CD4 count was 224 cells/mm^3.

The present study showed an inverse co-relation between age and salivary flow rate in patients without HAART, whereas no co-relation was observed in patients with HAART. Here, we propose that no correlation between the patient on HAART and salivary flow rate infers to role of therapy in alteration of salivary flow and warrants further research. Sex was not found to be co-related with salivary flow rate in both the groups.

We observed significant taste alterations in HIV patients with HAART, whereas nonsignificant alterations were noted in patients without HAART, similar to the findings reported by López-Verdín *et al*.[9] Sour and bitter tastes were more affected as compared to sweet and salty tastes, which was in accordance with Raja *et al*.[7] The significant alteration in sour and bitter taste could be the result of adaptation to these tastes caused by continuous stimulation by HAART and also may have resulted in the higher detection threshold to it.

There was no significant co-relation of CD4 count and salivary flow rate and gustatory changes in our study which was in accordance with the findings of Heald *et al*.[18] López-Verdín *et al*. in their study reported that there was significant xerostomia, reduction in salivary flow rate and flavor alteration in HIV-positive patients on HAART which was consistent with our findings.[9]

The reasons for hypofunctioning of salivary gland and gustatory alterations in HIV-positive patients are being studied continuously. In the present study, significant effects of HAART were seen on salivary flow rate and gustatory functions in HIV-positive patients. No significant alterations in salivary flow rate and gustatory functions were seen in HIV-positive patients without HAART, irrespective of CD4 counts. Although previous studies reported that decrease in CD4 count, suggestive of immune suppression and HIV progression was a significant factor for the decrease in salivary and gustatory function. However, our study did not support the above theory of decrease salivary and gustatory function rather it entails the role of HAART in hypofunction and dysgeusia.

The differences in observations in the present study and other reported studies could be due to varied follow-up period and different HAART regimen. HAART could be a major etiological factor for inducing hyposalivation and taste perversion. However, further studies with larger sample size and including patients in advanced stages of HIV infection with longer follow-up period are required to discern the effects of HAART on salivary gland functions and gustatory alterations.

CONCLUSION

Reduction in salivary flow rate and alteration in gustatory function are problems of imperative concern for HIV positive patients. A significant association of these changes is seen with the use of HAART regimen. Hence, along with routine oral health appraisal in HIV-positive patients, evaluation of salivary flow rate and taste abnormalities should also become an integral part of patient assessment. Various drugs are helpful in the management of reduced salivary flow, leading to enhancement in quality of life of these patients by improving their nutritional status, immune status, and treatment compliance.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Global Statistics; 2014. Available from: http://www.unaids.org. [Last accessed on 2015 Aug 26].
2. Palmisano L, Vella S. A brief history of antiretroviral therapy of HIV infection: Success and challenges. Ann Ist Super Sanita 2011;47:44-8.
3. Broder S. The development of antiretroviral therapy and its impact on the HIV-1/AIDS pandemic. Antiviral Res 2010;85:1-18.
4. Arts EJ, Hazuda DJ. HIV-1 antiretroviral drug therapy. Cold Spring Harb Perspect Med 2012;2:a007161.
5. Ammassari A, Murri R, Pezzotti P, Trotta MP, Ravasio L, De Longis P, *et al.* Self-reported symptoms and medication side effects influence adherence to highly active antiretroviral therapy in persons with HIV infection. J Acquir Immune Defic Syndr 2001;28:445-9.
6. Diz Dios P, Scully C. Antiretroviral therapy: Effects on orofacial health and health care. Oral Dis 2014;20:136-45.
7. Raja JV, Rai P, Khan M, Banu A, Bhuthaiah S. Evaluation of gustatory function in HIV-infected subjects with and without HAART. J Oral Pathol Med 2013;42:216-21.
8. Islam NM, Bhattacharyya I, Cohen DM. Salivary gland pathology in HIV patients. Diagn Histopathol 2012;18:366-72.
9. López-Verdín S, Andrade-Villanueva J, Zamora-Perez AL, Bologna-Molina R, Cervantes-Cabrera JJ, Molina-Frechero N. Differences in salivary flow level, xerostomia, and flavor alteration in Mexican HIV patients who did or did not receive antiretroviral therapy. AIDS Res Treat 2013;2013:613278.
10. Navazesh M, Mulligan R, Komaroff E, Redford M, Greenspan D, Phelan J. The prevalence of xerostomia and salivary gland hypofunction in a cohort of HIV-positive and at-risk women. J Dent Res 2000;79:1502-7.
11. Johar N, Proctor GB, Kumar R. A comparative study of salivary compostion of HIV seropositive patients on HAART and not on HAART. J Indian Acad Oral Med Radiol 2011;23:29-32.
12. Lin AL, Johnson DA, Stephan KT, Yeh CK. Alteration in salivary function in early HIV infection. J Dent Res 2003;82:719-24.
13. Pavithra S, Ranganathan K, Rao UK, Joshua E, Rooban T, Kumarasamy N. Impact of highly active antiretroviral therapy on salivary flow in patients with human-immuno deficiency virus disease in Southern India. J Oral Maxillofac Pathol 2013;17:17-22.
14. Nittayananta W, Talungchit S, Jaruratanasirikul S, Silpapojakul K, Chayakul P, Nilmanat A, *et al.* Effects of long-term use of HAART on oral health status of HIV-infected subjects. J Oral Pathol Med 2010;39:397-406.
15. Kumar JV, Baghirath PV, Naishadham PP, Suneetha S, Suneetha L, Sreedevi P. Relationship of long-term highly active antiretroviral therapy on salivary flow rate and CD4 Count among HIV-infected patients. J Oral Maxillofac Pathol 2015;19:58-63.
16. Glick M, Muzyka BC, Lurie D, Salkin LM. Oral manifestations associated with HIV-related disease as markers for immune suppression and AIDS. Oral Surg Oral Med Oral Pathol 1994;77:344-9.
17. Bretz WA, Flaitz C, Moretti A, Corby P, Schneider LG, Nichols CM. Medication usage and dental caries outcome-related variables in HIV/AIDS patients. AIDS Patient Care STDS 2000;14:549-54.
18. Heald AE, Pieper CF, Schiffman SS. Taste and smell complaints in HIV-infected patients. AIDS 1998;12:1667-74.