Oral Cavity and Transmission of HIV: A Debatable Dilemma

Shivani Rawat, Susmita Saxena, Preeti Sharma, Gautam Adhikari

ABSTRACT

Human immunodeficiency virus (HIV) is most commonly transmitted by sexual activity. HIV is found in blood and other body fluids, including semen, vaginal fluid and saliva. Spread of the HIV from oral secretions of the millions of HIV viremic individuals, during kissing, dental treatment, biting is a very uncommon finding. The shedding of infected blood or exudates from the saliva of an infected individual usually contains only the noninfectious component of HIV and may also contain fragments or the entire noninfectious genome. The risk of HIV transmission via oral secretions is an issue of growing interest to the dental health professionals. The oral transmission of HIV remains a controversial issue and a cause of concern.

Keywords: Oral transmission, HIV, Mononuclear leukocytes.

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DISCUSSION

The oral mucosa is a stratified squamous epithelium supported by lamina propria. Unlike other mucosal sites oral cavity is rarely a site of HIV transmission. The mucosal compartmentalized mucosa-associated lymphoid tissue (MALT). Archibald et al (1992) reported only 1% incidence of infected saliva in HIV carriers, although all carriers have infectious virus in their blood. The rarity of casual oral transmission is easy to correlate with the incidence of high vaginal (27%) and high infectivity in the seminal fluid transmission.

Cohen MS et al (2000), in their study reported that HIV transmission from saliva or intimate family contact is extremely rare, and this could be attributed to low concentration of HIV-1 in saliva.

WHAT ANTI-HIV BARRIERS DOES THE ORAL CAVITY HAVE? WHAT IS THEIR ROLE?

HIV shows favorability for CD4+ receptors in the cell membrane of monocytes and lymphocytes. The most common cell type in the oral cavity is the epithelial cell; a cell type which does not express the CD4 antigen hence is not prone to infection. (Milman and Sharma, 1994). Baron S (2001) states that most of the HIV infectivity in carrier’s secretions and blood occurs as infected leukocytes rather than as cell-free HIV. Lamm (1977) also reported that human epithelial cells could be infected by HIV and transfer the infection to adjacent leukocytes, where these get neutralized by IgA. Also the transcytosis of HIV via epithelial cells can be inhibited by S-IgA, IgG or IgM. The very low presence of HIV-infected epithelial cells in the oral cavity indicates that oral mucosal cells contribute minimally to the viral load in saliva. Any free infectious HIV in mucosal secretions will have low affinity for mucosal epithelial cells of the mouth, esophagus, vagina and rectum because these cells lack the CD4 receptor for free HIV to bind.
The frequency and infectivity of saliva and the oral mucosal cells is reported to be lower than that in other secretions (Baron et al 1999). The frequency of HIV antigen detection has ranged from 0 to 35% and that of proviral DNA and viral RNA detection from 12 to 100% (Yeung et al 1993). Another study by Tamashiro and Constantine (1994) reported that the immunoglobulin content of oral fluids is similar to that of blood, but their levels are less. However, the use of an HIV IgG antibody capture assay (GAC ELISA) designed specifically for testing oral fluids, and certain routine HIV blood tests can produce encouraging results. Viral cultures from saliva have shown HIV titers in only 0 to 39% cases (Gropman et al 1984). Hence literature states that the saliva of a large proportion of HIV patients does not contain the virus.

A healthy and intact mucosa forms an excellent barrier against infection by pathogenic microorganisms including viruses. The lubricating action of the mucosal surface, low number of CD4+ cells and the diluting action of saliva dilutes the microbial load and expels microorganisms toward the gastrointestinal tract for their inactivation and destruction. A thick epithelial layer and presence of antiviral antibodies and various endogenous factors also act for the inhibitory action of oral mucosa. Saliva’s army for inhibitory HIV transmission consists of HIV-1-specific antibodies, lysozymes, peroxidases, Clq component of complement, cystatins, lactoferrin, defensins, mucins, amylase, statherins, proline-rich peptide, thrombospondin-1, histatins and secretory leukocyte protease inhibitor, ribonuclease (Table 1).

**SALIVA’S HYPOTONICITY KILLS CELLS AND THEREBY PREVENTS VIRUS MULTIPLICATION**

Baron et al (2001) reported a new potent salivary inhibitor of HIV transmission, unique hypotonicity of saliva. Saliva has the ability to rapidly disrupt (>90%) mononuclear leukocytes (Fig. 1). It is estimated that complete cell disruption and the resulting interruption of virus multiplication occurs with solutions containing the same low-salt concentration as saliva. Extreme hypotonicity, as in saliva causes cell death by osmotic swelling and bursting of cells and their plasma membrane.

Baron et al (1999) also reported salivary hypotonicity appears to destroy the cell wall of HIV-infected mononuclear

![Fig. 1: Disruption of human mononuclear leukocytes incubated at 34°C for 15 minutes with saliva compared with blood plasma](image)

<table>
<thead>
<tr>
<th>Factors</th>
<th>HIV-inhibitory mechanism</th>
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<tr>
<td>Anti-HIV antibodies</td>
<td>Neutralize and inactivate the virus IgA. Inhibits interaction between gp120 and CD4</td>
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<td>Clq component of complement</td>
<td>In presence of fibronectin, binds to the virus and produces its sedimentation</td>
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<td>Cystatins</td>
<td>Have general antimicrobial activity: Inhibit cysteine proteases</td>
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<tr>
<td>Defensins (α, β, γ, and mini-defensins)</td>
<td>Have general antimicrobial activity: Block penetration by the virus</td>
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<td>Lactoferrin</td>
<td>Binds to iron to inhibit bacterial proliferation and viral replication</td>
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<td>Lactoperoxidase</td>
<td>Inactivates virus by production of thiocyanate</td>
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<td>Lysozyme</td>
<td>Interrupts HIV replication by destroying viral membranes</td>
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<td>Ribonuclease</td>
<td>Blocks the reproduction of the virus by destroying its genetic material (metabolize select RNA)</td>
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<td>Mucins</td>
<td>Sequester and aggregate viral particles</td>
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<td>Secretory leukocyte protease inhibitor (SLPI)</td>
<td>Interact with a cellular surface molecule to limit viral entry into target cells</td>
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<td>Thrombospondin 1 (TSP-1)</td>
<td>Produces aggregation of the virus; during penetration by the virus, blocks its interactions with lymphocytes</td>
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<tr>
<td>Proline-rich proteins (PRPs)</td>
<td>Bind to gp120 of the virus, preventing its penetration of lymphocytes</td>
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<tr>
<td>Salivary agglutinins (SAG)</td>
<td>Bind to gp120 from virions, agglutinate HIV and dissociate viral envelope proteins</td>
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leukocytes, preventing them from binding to mucosal epithelial cells and producing infective HIV. Complete inhibition of virus yield occurred with mixtures of solutions containing 100 and 75% saliva, implying the killing of infected cells by saliva. While diminished inhibition of virus yield was reported with mixtures containing 75 to 25% saliva, implying partial killing of cells by saliva.

Hence, the demonstrated killing of HIV-infected leukocytes by the hypotonicity of saliva would prevent all routes of transmission, namely attachment to epithelial cells, penetration of the epithelium by infected mononuclear leukocytes and virus production. The effect of hypotonicity on any shed infectious cell-free HIV by hypotonic solutions like water and perhaps saliva may occur over hours, compared to immediate lysis of infected cells.

**CONCLUSION**

Taken together the present findings indicate that the rarity of transmission of HIV from the oral cavity may be not only due to the reported nonspecific salivary inhibitors but also largely due to hypotonic saliva-induced disruption of infected cells. Hypotonic disruption may be a major mechanism by which saliva kills infected mononuclear leukocytes and prevents their attachment to mucosal epithelial cells and production of infectious HIV, thereby preventing transmission. The conclusion is based on the limited inhibition of HIV by the reported salivary inhibitors (2 to 5-fold) compared with the 10,000-fold or higher inhibition by salivary lysis of infected leukocytes. Indeed, transmission of HIV through oral cavity is a rarity.

**REFERENCES**


**ORAL TRANSMISSION OF HIV: A Debatable Dilemma**

For health care workers, oral transmission of HIV is of prime concern and may be increased under special conditions, such as:

- Acute HIV infection where cell-free HIV is high.
- Advanced acquired immunodeficiency syndrome where cell-associated HIV is high.
- Oral sex, where the seminal fluid protects the infected cells against saliva.
- Saline irrigation of the mouth that may overcome the hypotinicity of saliva and create aerosols.
- Cofactors, such as oral ulcers, gingival bleeding (gingivitis or periodontitis) or the presence of other infections in the oral cavity.

**HIV INHIBITORY ACTIVITY OF OTHER BODY FLUIDS**

Fultz (1986) published the first study to report that the whole saliva of chimpanzees and humans protect cells susceptible to HIV infection *in vitro*. The other body fluids with an anti-HIV activity are shown in Table 2.

**SPECIAL CONDITIONS IN WHICH ORAL TRANSMISSION MAY OCCUR**

The inhibition is offset by isotonic secretions such as breast milk and semen. Orally deposited seminal fluid, milk or colostrum reverses the ability of saliva to inactivate virus-infected leukocytes by the reconstitution of salts and solutes in hypotonic saliva. The hypotonic disruption is a major mechanism by which saliva inactivates transmitting leukocytes and prevents their attachment to mucosal epithelial cells. This accounts for the paradox of successful oral transmission by the seminal fluid and milk. Hypotonic lysis of shed-infected leukocytes can be overcome by unusually large volumes of isotonic fluids in the mouth thus leading to oral transmission of HIV. Such rare conditions could be:

- Isotonic blood in the mouth- as may be in the case of oral transmission by the bite of patient who was experiencing heavy bleeding in the mouth (Lancet 1987).

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