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Review Article

IS HIV CURABLE? A PERIODONTIST FORESIGHT – A REVIEW

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A B S T R A C T

Human immunodeficiency virus (HIV) is a retrovirus in the Lentivirus group that targets CD41 T cells. HIV infection leads to lots of opportunistic infection which manifest both orally and generally .The treatment of HIV infected patients involves Antiretroviral therapy along with antibiotics for opportunistic infections. This review paper explains about the mechanism of action of ozone against bacteria and virus activity and the effectiveness of subgingival ozone therapy as an adjunct for the treatment of HIV infected patients.

INTRODUCTION

Human immunodeficiency virus (HIV) is a retrovirus in the Lentivirus group that targets CD41 T cells.

Acquired immunodeficiency syndrome (AIDS) is the end stage of the natural history of the infection and was first described in 1981. The primary receptor in humans for HIV is believed to be the characteristic 55 KD protein on the surface of CD4+ lymphocytes (T-helper cells). It is the depletion of these cells that is responsible for many of the pathological and clinical manifestations of HIV infection.A reduction in the cell-mediated immune response leads to development of various fungal, viral, and occasionally bacterial infections, as well as development of specific malignancies that can dramatically affect the health of the individual.

Oral and perioral lesions are common in patients infected with human immunodeficiency virus (HIV), are often the presenting feature, and may predict deterioration in general health and a poor prognosis.[1,2,3]

Before the advent of antiretroviral therapies, atypical lesions involving the periodontal tissues were observed, including Linear gingival erythema and a range of necrotizing periodontal diseases either restricted to the gingiva (eg, necrotizing ulcerative gingivitis), or extending further into the periodontium to involve the soft tissue attachment and alveolar bone.In this antiretroviral therapies era, studies have reported reductions in oral candidiasis and hairy leukoplakia,[1,2,3] and a decrease in the prevalence of periodontal diseases in adults with HIV.

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This paper is to review the hypothesis of using ozone therapy as an adjunt for treatment of HIV infection.

Etiology of Hiv Associated Periodontal Disease

The nature of subgingival microbial changes was observed in the affected individuals. [4,5,6,7]

As reviewed by Murray,[8] data from a considerable number of studies have determined that the subgingival bacteria detected in HIV-associated periodontal lesions are, in general, similar to what are detected in periodontal lesions seen in individuals who are not infected with HIV.

Lucht *et al*.[9]examined 10 healthy controls and 20 patients infected with HIV. In this small sample, severity of periodontal disease was related to a decrease in the number of CD4+ cells, but not the presence of recognized periodontal pathogens.

Moore *et al*.[10]studied the anaerobic microflora from subgingival sites from HIV positive patients with gingivitis or adult periodontitis and determined that essentially the same microflora were seen in HIV positive as in HIV negative individuals. They did observe that Mycoplasma salivarius was elevated when HIV infection was present. Furthermore, 13% of subjects harbored subgingival yeast, but these organisms only comprised 0.05% to 0.002% of the cultivable flora.

Zambon *et al*. [11] examined the subgingival microflora from 50 AIDS patients. Patients with variable types of periodontal disease were studied (LGE, NUG, NUP, gingivitis, and adult Periodontitis). Using culture and immunofluorescence, the microflora present were similar to what have been observed in non-HIV patients with periodontal disease.

Indirect immunofluorescence and selective culturing have been used to evaluate the subgingival microbiota associated with different forms of periodontal disease seen in association with HIV infection[12]. The presence of putative pathogens was similar for HIV periodontitis (NUP) and adult periodontitis. The microflora from the HIV-gingivitis lesions were similar to that in the HlV-periodontitis lesions, but different from conventional gingivitis. These findings led to the conclusion that HIV gingivitis may preceed HIV periodontitis.

In a subsequent report, Murray[13] and coworkers used DNA probes to evaluate the occurrence of periodontal pathogens in HIV-associated periodontal lesions.
The DNA probe-detected profile of periodontal pathogens for HIV periodontitis (NUP) was similar to that seen for adult periodontitis.

Rams *et al*. and Zambon *et al*.[11] detected unusual subgingival pathogens, including Enterobacter cloacae, Pneumoniae, and Clostridium species. This association of unusual pathogens and HIV periodontitis has also been observed in a number of case reports.

Host Response in hiv Infection

The host response in immunocompetent individuals with periodontal disease involves a complex series of events, with contributions from the acute inflammatory, humoral,immune, and cellular immune responses.

Ryder *et al*[15],. examined peripheral blood PMN activity in HIV individuals with HIV associated periodontitis and intraoral candidiasis.As compared to controls, PMN from HIV patients demonstrated an increase in the percentage of cells that phagocytized microspheres, and an increase in both the oxidative burst and actin polymerization. The enhanced response may have been the result of the absence of an intact cellular immune response.[16]

PMN function in HIV infection has been studied, and alterations in the activity of these cells that characterize the acute inflammatory response have been observed. PMN chemotaxis has been reported to be reduced in patients with AIDS-related complex (ARC), but this was not observed in patients with AIDS.

In contrast, other studies have reported HIV patients with adult periodontitis and controls. They determined that PMN-derived matrix metalloproteinases in GCF and saliva from H1V patients were present in the activated form, and proposed that these activated enzymes may contribute to periodontal destruction in HIV patients.

Besides a reduced number of T-helper cells and altered PMN function, another modification of the host response associated with HIV infection that may have an impact on periodontal disease is an elevated IgG antibody titer in serum.[19] This appears to be a compensatory mechanism that represents an attempt by the humoral immune arm to respond to challenges in the absence of an adequate cellular immune response.[18,19]

Steidley *et al*.[20] observed a complete absence of T cells in the gingival tissue from HIV individuals. In contrast, Odden *et al*.[21] detected T cells in gingival biopsies from HIV positive and HIV negative individuals. As expected, the CD4+/CD8+ ratio in tissue was decreased in the HIV positive patients, but this ratio tended to be higher than what was observed in the peripheral blood of these patients.

Elbim *et al*.[17] demonstrated increased expression of the adhesion molecule CD lib/CD 18, increased action polymerization, and increased production of H2O2 by PMN from patients with HIV infection.

Ozone and its Mechanism of Action

The pharmacological effects of ozone underlies in its chemical and biochemical properties. The pharmacological properties of ozone are depending on ozone being a triatomic oxygen molecule, reacting with organic compounds containing double bonds and adding the three oxygen atoms to the unsaturated bond with the formation of ozonides.

This reaction is of great importance, since ozone causes the split of the double bonds with a reaction called ozonolysis. In an aqueous medium (i.e., blood), the ozonides are immediately transformed into stable hydroperoxides having the ability to release oxygen when the pH increases, as it occurs in protonic environments. Such a physical-chemical characteristic is typical of degenerative processes and/or ischemic conditions. The lipoperoxides derived from the breaking of a chain of ozonides lose the hydrophobicity characteristic of lipids and become soluble in water since they are short-chain lipid compounds. It is generally understood that the toxic effects of ozone are mediated through free radical reactions, although ozone is not a radical species [22].

Two different mechanisms may be advocated to explain the ozone-derived radical formation: a direct mechanism involving the oxidation of biomolecules to give classical radical species (hydroxyl radical) and a mechanism involving the radical-dependent production of cytotoxic, nonradical species (aldehydes) [22].

Antimicrobial effect: Ozone works destructively against bacteria, fungi, and viruses. The antimicrobial effect of ozone is a result of its action on cells by damaging its cytoplasmic membrane due to ozonolysis of dual bonds and also ozone-induced modification of intracellular contents (oxidation of proteins loss of organelle function) because of secondary oxidants effects. This action is non-specific and selective to microbial cells; it does not damage human body cells because of their major antioxidative ability.

In viral infections the ozone action lies in the intolerance of infected cells to peroxides and change of activity of reverse transcriptase, which takes part in synthesis of viral proteins. Being a very strong oxidant it joins with biomolecules containing cysterine, methionine, histidine (all being part of bacterial cell membranes). The main targets of their attack are the thiol groups of the amino acid cysteine. As a result of the reaction of ozone with unsaturated fatty acids of a lipid sheath of a virus the lipid sheath of a virus melts[23].

Immunostimulating Effect: Ozone influences cellular system. It stimulates proliferation of immunocompetent cells and synthesis of Immunoglobulins. It also activates function of macrophages and increases sensitivity of micro-organisms to phagocytosis. As a response to this activation through ozone, the body's immune cells produce special messengers called cytokines. These molecules in turn activate other immune cells, setting off a cascade of positive change throughout the immune system, which is stimulated to resist diseases. This

means that the application of medical ozone is extremely useful for immune activation in patients with immune deficit. Ozone causes the synthesis of biologically active substances such as Interleukins, Leukotrienes and Prostaglandins which is beneficial in reducing inflammation and wound healing. Ozone in high concentration causes immunodepressive effect whereas in its low concentration immunostimulating effect.[23]

Newer Method of Ozone Administration (Local Intrapocket Delivery of Antibacterial Drugs)

For an antimicrobial agent to be successful, the pathogen must be known and it should be susceptible to the drug and not readily develop resistance for an adequate period of time. The periodontal pocket provides a natural reservoir bathed by gingival crevicular fluid which is easily accessible for the insertion of a delivery device. The GCF provides a leaching medium for the release of a drug from the solid dosage form and for its distribution throughout the pocket. Moreover, the periodontal diseases are localized to the immediate environment of the pocket, enabling the periodontal pocket a natural site for treatment with local sustained-release delivery systems.The sustained-release dosage forms maximize the therapeutic effect of antimicrobials by maintaining a constant plasma drug concentration over a prolonged period of time in a controlled manner. So it is hypothized that ozone (formulated as ozone oil) can be delivered inside the periodontal pocket where it exhibits its action [24].

Potential Advantage of local Antimicrobial drug Delivery into Periodontal Pocket

1. It can improve patient acceptance and compliance.
2. This route is more possible for direct access to target diseases/various periodontal diseases.
3. This may reduce oral health care treatment cost.
4. It offers avoidance of GI tract with problems of oral drug administration.
5. It can serve as a reliable route for drug administration in very ill patient who are not able to swallow.
6. It can provide rapid absorption due to rich blood supply in comparison with transdermal.
7. It bypasses the first pass metabolism by the liver.
8. It can offer increase therapeutic efficacy of the drug.
9. It offers close proximity to blood flow.
10. This route is safe and convenient route.
11. It can produce longer duration of action.
12. It offers noninvasive, painless, and simple application.[24].

CONCLUSION

Dentistry is changing as we are now using modern science to practice dentistry. In comparison with classical medicine modalities for HIV positive patients such as antibiotics and disinfectants, ozone therapy is quite inexpensive, predictable and conservative. The ozone therapy has been more beneficial than present conventional therapeutic modalities. This state of the art technology allows us to take a minimally invasive and conservative approach .Treating patients with ozone therapy reduces the treatment time with a great deal of difference and it eliminates the bacterial count more precisely.[22] The treatment is completely painless and increases the patients acceptability and compliance with minimal adverse effects. Although more clinical research has to be done to standardize indications and treatment procedures of ozone therapy, still many different approaches are so promising, or already established, that hopefully the use of ozone therapy becomes a standard treatment as an adjuvant for HIV positive patients.

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