

## Management of Periodontal Disease with Doxycycline: An Update

Srithi Srinath

Saveetha Dental College, Chennai- 77, Tamil Nadu, India

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### ABSTRACT

To manage periodontal disease with the use of doxycycline drug. An update to the present findings of doxycycline in managing periodontal disease. Periodontal disease is one of the most common microbial infections in adults. It is an inflammatory disease of bacterial origin that affects the tooth-supporting tissues. There are two major types of periodontal disease: gingivitis and periodontitis. Periodontitis is characterized by general inflammation of the periodontal tissues. Antibiotics given orally and at standard doses have some limited applications for periodontal disease. They are typically given for an acute infection. Specific antibiotics used in periodontal disease include: Tetracycline antibiotics includes tetracycline hydrochloride, doxycycline, and minocycline are the primary drugs used. They not only have anti-bacterial actions but also reduce inflammation. Short-term use of standard-dose doxycycline is used for treating acute periodontal infections and for eliminating inflammation. Metronidazole in combination with tetracycline or amoxicillin may be used for severe and chronic periodontal disease. Atridox is a doxycycline gel that conforms to the gum surface and then solidifies. PerioChip is a chip that is placed into the gum pocket after scaling. Periodontal disease when left untreated may cause cardiac diseases in systemic disorders. Hence this review helps in proper management of periodontal health.

**Keywords:** doxycycline, periodontal disease, antibiotics, periostat, atridox

### INTRODUCTION

Periodontal disease is a most common dental disease. Gingival inflammation due accumulation of plaque and calculus causes gingivitis. Sometimes gingivitis can progress to periodontitis. Periodontitis is more severe form of periodontal disease. This can cause progressive loss of alveolar bone, increased loss of attachment to tooth and increase in pocket depth. There no known cure for periodontitis. Periodontal disease, on other hand can be treated and prevented<sup>1</sup>. The risk factors of periodontitis are smoking which causes loss of attachment<sup>2</sup>, obesity<sup>3</sup>, specific microorganism<sup>4</sup>, genetic factors<sup>5</sup> and aging<sup>7</sup>. The one of greatest challenges are in elimination of bacteria from oral cavity which is cause of formation of biofilm causing periodontal disease. Eliminating bacteria from oral cavity is not possible. Moreover the bacteria causing periodontal disease is opportunistic bacteria<sup>1</sup>. Some specific microorganism that cause periodontitis are usually present in the mouth. They are Porphyromonas gingivalis, Tannerella forsythia and Actinobacillus actinomycetemcomitans, prevotella intermedia, P gingivalis, and Fusobacterium nucleatum<sup>8</sup>. Perioceutics is pharmacologic agents specifically developed to better manage periodontitis, is emerging to aid in the management of susceptible patients who develop periodontal disease. Mechanical therapy like brushing, flossing & tooth scaling<sup>9,10</sup>. Antiseptics can be used topically or subgingivally. Some of the antiseptics used to treat periodontitis and gingivitis are listerine is available over-the-counter<sup>11,12</sup>, Triclosan<sup>13</sup> and Periochip. Periochip (Dexcel Pharmaceuticals, Israel) is an orange-

brown, biodegradable, rectangular chip rounded at one end that has an active ingredient of chlorhexidine gluconate (2.5 mg) that is released into the pocket over a period of 7 to 10 days<sup>14</sup>. Antibiotics like Atridox, which is second FDA-approved locally delivered tetracycline<sup>15</sup>. Doxycycline is an antibiotic used for treatment of periodontal disease, especially in case of aggressive periodontal disease<sup>16</sup>. Aggregatibacter actinomycetemcomitans (formerly known as Actinobacillus actinomycetemcomitans) is often the causative pathogen that invades the epithelium and connective tissue, eluding mechanical debride. Doxycycline and minocycline are semisynthetic analogs of tetracycline HCl<sup>17</sup>. Doxycycline is one of the most commonly used group of tetracycline drugs and inexpensive of the broad-spectrum antibiotic drugs currently in use<sup>18,19</sup>. Doxycycline inhibits protein synthesis. It is given orally or paraeneterally and is absorbed by gastrointestinal tract and excreted by kidneys<sup>20,21</sup>. Doxycycline is well tolerated<sup>20</sup>.

### DOXYCYCLINE

Doxycycline is one the most commonly used broad spectrum antibiotics and belongs to the tetracycline class of antibiotics<sup>22</sup>.

#### *Mechanism of action*

Doxycycline is a bacteriostatic drug<sup>20,22,23</sup>. They inhibit protein synthesis by binding to 30S subunit of ribosome of the susceptible organism reversibly. Thereby preventing the binding of aminoacyl transfer RNA<sup>22, 23</sup>.

#### *Pharmacokinetics*

Doxycycline is a well absorbed orally or parenterally for treatment<sup>20,22-24</sup>. It is well distributed throughout the body and is highly protein bound. It is concentrated in the bile. It is excreted in kidney and has a half life of 18-22 hours<sup>22-26</sup>.

#### *Anti inflammatory property*

At subantimicrobial doses, doxycycline reduces inflammation via anticollagenolytic, antimatrix-degrading metalloproteinase, and cytokine down regulating properties<sup>27</sup>. Doxycycline inhibits the nitric oxide synthesis. This activity is another possible pathway by which tetracyclines may function as anti-inflammatory compounds<sup>28</sup>. This suggests that the direct inhibition of nitrate release is the main mechanism of the anti-inflammatory activity of doxycycline in septic shock<sup>29</sup>.

*Available dosage forms:* Gel, capsule

#### *Doxycycline gel*

Doxycycline hyclate (Atridox) is a locally delivered tetracycline. It is mainly involved in preventing some of the specific microorganism like *Aggregatibacter actinomycetemcomitans* (formerly known as *Actinobacillus actinomycetemcomitans*)<sup>16</sup>. Atridox allows controlled release of drug for 7 days with 10% formulation of doxycycline in a bioabsorbable, "flowable" poly-DL-lactide and N-methyl-2-pyrrolidone mixture delivery system. This is provided with two pre filled syringes to be mixed at chair-side and applied subgingivally to the base of the pocket through cannula. The flowable polymer gel of Atridox fills and conforms to pocket morphology, then solidifies to a waxlike substance after contact with GCF (Gingival Cervicular Fluid). Significant reductions (60%) in anaerobic pathogens are sustained for up to 6 months after placement of Atridox<sup>31</sup>. In patients with chronic adult periodontitis, the application of this doxycycline gel at baseline and 4 months resulted in reductions in probing depths (1.3 mm) and gains in clinical attachment (0.8 mm) equivalent to SRP (scaling and root planing) alone at 9 months after baseline<sup>32</sup>. An important findings from these studies was that for the Atridox treatment group, smoking status did not seem to affect the outcome of clinical parameters such as probing depth reductions and clinical attachment level gains, whereas smokers and even former smokers did not respond as well to mechanical therapy alone<sup>33</sup>. A recent study supports these findings, indicating that locally applied Atridox improves the healing following nonsurgical therapy in smokers<sup>34</sup>. The side effect profile was equivalent to placebo. It is likely that this agent will be used not as a mono therapy for the management of periodontal disease but as an adjunct to mechanical therapy. Removal of the plaque and calculus deposits by SRP has proved to be effective. Disruption of the biofilm improves on the efficacy of antimicrobial agents<sup>35</sup>.

#### *Subantimicrobial Dose Doxycycline*

Although the pathogenesis of periodontitis is initiated by periodontopathic bacteria within the gingival sulcus and also caused by the response of the host to the presence of the bacteria, manifesting in the release of cytokines and matrix metalloproteinases. It is understood that it is the host tissues (the patient's own tissues) that degrade

connective tissue, resulting in attachment loss, bone destruction and progression of periodontitis<sup>37-39</sup>. By modifying the host response, clinical outcomes may be enhanced. This may promote therapeutic benefit resulting in a reduction of gingival inflammation, bleeding probing depths and a gain in clinical attachment levels. Periostat, a low dose 20mg. Doxycycline formulation taken twice daily, therefore, is an important new therapy to combat against Refractory Periodontitis when used as an adjunct to scaling and root planing. This low dose doxycycline, part of the tetracycline family does not create bacterial resistance<sup>40</sup>. On a clinical basis, when a patient presents for periodontal evaluation after the completion of initial periodontal therapy, including scaling and root planing, and there continues to be persistence in gingival bleeding and/or gingival inflammation, the introduction of a six to nine month therapeutic regimen of Periostat to suppress enzymatic activity is indicated. This treatment approach has been shown to have a particular benefit in smokers, where signs of gingival bleeding are often masked by the smoking<sup>41</sup>.

#### *Adverse effects*

Doxycycline is well tolerated. It causes nausea, diarrhoea, rash, photoonycholysis and photosensitivity in both children and adult<sup>22-24,43</sup>. It also causes phlebitis and pain during parenteral admixtures at the site of infusion. It is responsible for growth retardation and enamel hypoplasia<sup>22-24,44</sup>. It is contraindicated from second half of the pregnancy to seven years in children because they have harmful effects of the bone and tooth development<sup>20</sup>.

## **CONCLUSION**

Periodontal disease is common disease that has to be treated in required time. Otherwise it will cause systemic effects as in cardiovascular system. Doxycycline is more effective in treating periodontal diseases through various dosage forms.

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