Comparative Evaluation Of The Efficacy Of Neem And Tetracycline When Incorporated In A Local Drug Delivery System When Used As An Adjunct To Scaling And Root Planing: A Clinico-Microbiological Study

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Abstract

Background: Antimicrobial agent has been effectively used systemically and locally in management of periodontal disease. Local drug has an advantage of higher antimicrobial concentration in subgingival site. Presently large number of herbal product researches in oral use in various from. The study researches neem extract when incorporated in LLD system used as adjunct to scaling and root planing.

Methods: The study included a total of 15 patients having chronic periodontitis (7 males and 8 females) with an average age of 25-55 yrs. The subjects were assessed clinically for Plaque index, Gingival index, probing pocket depth and microbiologically for the subgingival bacteria counts of Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum, Aggregatibacter actinomycetemcomitans. All clinical parameters were assessed at baseline (0 days), 1 month and 3 months. Full mouth scaling and root planing was performed. 3 groups were made Group A- scaling and root planing, Group B- scaling and root planing along with placement of tetracycline fibers, Group C- scaling and root planing along with placement of neem fibers. The 3 selected non adjacent sites were randomly assigned to one of the groups. The test sites in group B & C received intra pocket placement of tetracycline & neem fiber respectively.

Result: Results showed an reduction in the PPD, gingival index and plaque index as well as the counts of the bacteria in all three groups. Higher reduction was observed in both test groups as compared to control.

Conclusion: Herbal extracts such as Neem extracts exhibited good antibacterial property, and was found to be marginally better though not statistically significant than commercially available tetracycline fibres.

Keywords: Local drug delivery system, tetracycline fiber, neem fiber, Scaling root planing

I. Introduction

Periodontal diseases is caused due to host- microbial interaction with large number of anerobic periodontal pathogens contributing in tissue destruction. Pathogenic bacteria are known to liberate their toxins evoking an inflammatory response of the host causing initiation and progression of periodontal disease. The tooth surface and the sub gingival area gets colonized by these microbes and forms the biofilm which consist of communities of microorganisms embedded in a glycocalyx. This extracellular matrix plays a very important role in maintaining the integrity of the biofilm as well as preventing desiccation and attack by harmful agents. The bacteria in the biofilm helps in production of enzymes such as ß-lactamase which acts against antibiotics or catalases or superoxide dismutases against oxidizing ions, thereby making these agents ineffective.

Therefore, the best way to manage these biofilms is to mechanically disrupt them. This is the principal which is the basis of our prevention and therapeutic strategies to manage periodontal disease. It has certain limitations: It may not be effective to eliminate the putative pathogens from the subgingival areas as they may colonize in sites like root concavities or furcations. For the management of periodontitis antimicrobial agents may be used as an adjunct to scaling and root planing.

Various investigators have advocated the use of antimicrobials, in both ways, systemically as well as topically for the management of periodontitis¹. Systemic antimicrobial are known to have numerous side effect & harmful drug interaction. On the other hand a local route of drug delivery can attain 100-fold higher concentrations of an antimicrobial agent in subgingival sites when compared with a systemic therapy.

Local antibiotic placement also reduces the risk of developing drug-resistant microbial populations at non oral body sites². Various devices using active agents like tetracycline and its derivatives, metronidazole and chlorhexidine have been used for this purpose. Among these Tetracycline have been the most widely studied agents. They are broad spectrum antibiotics that effect anaerobic and facultative organisms.
Presently a large number of herbal products are researched for oral use in form of mouth rinses, gels etc. herbal extract & have an advantage of cost effective, minimal side effect & good patient compliance.

Neem leaves are used in the treatment of gingivitis and periodontitis is also efficacious in the treatment of oral infections and plaque growth inhibition in treating periodontal disorders. Neem also has broad range antibacterial activity. It removes toxins from the body, purifies the blood and neutralizes damaging free radicals. So, locally it may also have an effect in enhancing healing. Neem extract contains: Azadiractin—the active principal, Glycosides—antimicrobial, Sterols Luminols—anti—inflammatory and Flavenoids.

The present study is an attempt to determine the efficacy of Azadirachta indica (neem) extract fiber (25 mg/g) & tetracycline fiber as a local drug delivery system along with scaling and root planing in the management of moderate to severe chronic periodontitis.

II. Material And Methods

Tetracycline fiber (Periodontal Plus AB) consists of 25 mg of pure fibrillar collagen containing approximately 2 mg of evenly impregnated tetracycline HCL. Preparation of neem fiber: Leaves of Azadirachta indica (neem) were identified from agriculture area of Jaipur city. They were further authenticated by a botanist. Leaves where thoroughly washed with sterile distilled water and shaded dried for 1 month. 25 gm of shaded dried powdered leaf form was macerated. The maceration process was done to obtain an extract by the process of solvent extraction. The liquid extract was finally subjected to rotatory evaporator. After complete solvent evaporation the solvent extract was preserved in vacuum at 40°C in an air tight bottle.

The study was conducted on patient visiting the outpatient department of Periodontology and Implantology, Jaipur dental college, Jaipur. Inclusion and exclusion criteria: Patient should have atleast 3 non adjacent sites with periodontal pocket ranging 4 to 7 mm. Patient in good systemic health. Patient requiring premedication or on medication such as antibiotic, anticoagulant, steroid or on hormonal therapy were excluded. Pregnant women and lactating mother were excluded. Subject with history of allergy to tetracycline were excluded. Subject who were unable to comply with follow up visit were excluded.

A written inform consent was taken. Total of 15 patient of both sexes in age group of 25-55 years where included in the study.

Baseline reading for Plaque index (Turesky- Gilmore- Glickman modification of the Quigley and Hein plaque index 1970), gingival index (Loe and Silness, 1963) and probing pocket depth by using UNC-15 were recorded & microbiological sample were collected using a area specific gracey curette and immediately transferred into vial containing thioglycollate transport media. Full mouth scaling and root planing was performed and 3 groups were made Group A- scaling and root planing, Group B- scaling and root planing along with placement of tetracycline fibers, Group C- scaling and root planing along with placement of neem fibers. The 3 selected site were randomly assigned to one of the groups. The test sites in group B & C received intra pocket placement of tetracycline & neem fiber respectively. The clinical and microbiological parameters were further recorded at 1 month & 3 months intervals.

III. Results

Mean ± Sd of Plaque Index at various interval of various group subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Interval</th>
<th>Basal</th>
<th>At 1 month</th>
<th>At 3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRP</td>
<td>1.79 ± 0.53</td>
<td>0.73 ± 0.21</td>
<td>0.79 ± 0.22</td>
<td></td>
</tr>
<tr>
<td>Tetracycline</td>
<td>1.70 ± 0.49</td>
<td>0.53 ± 0.19</td>
<td>0.58 ± 0.20</td>
<td></td>
</tr>
<tr>
<td>Neem</td>
<td>1.62 ± 0.51</td>
<td>0.49 ± 0.22</td>
<td>0.51 ± 0.18</td>
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</tbody>
</table>

Mean ± Sd of Gingival Index at various interval of various group subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Interval</th>
<th>Basal</th>
<th>At 1 month</th>
<th>At 3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRP</td>
<td>1.71 ± 0.58</td>
<td>0.71 ± 0.17</td>
<td>0.80 ± 0.22</td>
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<tr>
<td>Tetracycline</td>
<td>1.58 ± 0.59</td>
<td>0.53 ± 0.21</td>
<td>0.57 ± 0.15</td>
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<tr>
<td>Neem</td>
<td>1.57 ± 0.53</td>
<td>0.47 ± 0.14</td>
<td>0.49 ± 0.19</td>
<td></td>
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</tbody>
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Mean ± Sd of Probing pocket depth at various intervals of various group subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Interval</th>
<th>Basal</th>
<th>At 1 month</th>
<th>At 3 month</th>
</tr>
</thead>
<tbody>
<tr>
<td>SRP</td>
<td>5.78 ± 0.67</td>
<td>5.01 ± 0.46</td>
<td>4.95 ± 0.54</td>
<td></td>
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<tr>
<td>Tetracycline</td>
<td>5.80 ± 0.65</td>
<td>4.45 ± 0.41</td>
<td>3.45 ± 0.39</td>
<td></td>
</tr>
<tr>
<td>Neem</td>
<td>5.81 ± 0.70</td>
<td>4.34 ± 0.37</td>
<td>3.19 ± 0.30</td>
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</table>
The increase in clinical parameter could be attributed to the microbial colonization which occur 3-4 weeks after SRP, which in turn may results in increased values for the clinical parameter assessed.

In group B (test group- tetracycline): PI, GI and PPD decreased at 1 month as compared to baseline which was found to be statistically highly significant. This goes in accordance with 

Hung HC 2002 study in which SRP reduced PPD by more than 1 mm for sites with medium initial PPD & by about 2 mm for sites with deep initial PPD.8

The findings in the present study showed that the PI, GI and PPD increased at 3 months interval as compared to 1 month interval. This increase in clinical parameter could be attributed to the microbial recolonization which occurs at 3-4 weeks after SRP, which in turn may results in increased values for the clinical parameter assessed.

In group B (test group- tetracycline): PI, GI and PPD decreased at 1 month as compared to baseline which was found to be statistically highly significant. This goes in accordance with study done by M Panwar 2009 9 who found similar clinical result with tetracycline along with SRP, the result in reduction in clinical parameter may be attributed to the bacteriostatic effect of tetracycline against gram negative species. Tetracycline have an added anti-collagenase action and also known to inhibit bone resorption and promote attachment of fibroblast to root surface. The results are in agreement Heijji et al 1991 10 who found greater PPD reduction in SRP & tetracycline as compare to SRP alone. The result goes in concurrence with M Radvar 1996 11 study in which significant reduction in MGI scores were seen in group in which SRP with tetracycline fiber placement was done.

The result obtain from the study are not in accordance with study done by Thomas et al 199812 who did not found any significance in clinical parameter such as PPD & clinical attachment gain when tetracycline fiber was used with SRP versus SRP alone.

In 3 month interval the PI, GI has slightly increased as compare to 1 month interval which was found to be statistically not significant. This increase in PI and GI in clinical parameter may be attributed to the bacteriostatic effect of tetracycline against gram negative species. Tetracycline have an added anti-collagenase action and also known to inhibit bone resorption and promote attachment of fibroblast to root surface. The results are in agreement Heijji et al 1991 10 who found greater PPD reduction in SRP & tetracycline as compare to SRP alone. The result goes in concurrence with M Radvar 1996 11 study in which significant reduction in MGI scores were seen in group in which SRP with tetracycline fiber placement was done.

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Microbial count for specific bacteria like Pg, Pi, Fn and A.a was assessed at BL 1 month and 3 month. Sampling was done using area specific gracey curette. Curette is a common method used for collecting subgingival bacterial sample as has been demonstrated in study by Sangeeta singh 2009[4].

At 1 month as compared to BL the bacterial count in all 3 group was reduced which was found to be statistically highly significant. The result are going in hand with study done by Haffajee et al 1997 which showed reduction in bacterial count post SRP.

At 3 month bacterial count increased on comparison to 1 month count in all 3 groups. The bacterial counts for all the microorganisms assessed in control group were considerably higher as compared to test group.

Inter comparison of microbiological result between control & two test group Pg, Pi, Fn, A.a in both test group showed reduction as compare to control. Mombbelli et al 1997[6] reported that tetracycline fiber were able to suppress but not eliminate p.g, as tetracycline bind to the bacterial 30s ribosomal sub unit & inhibit protein synthesis in the bacterial cell.

The present study is the 1st of its kind in vivo study in which anti-bacterial effect of neem has been studied on periodontal pathogens such as A.a, P.g, P.i, F.n. Neem extract has an effect on bacterial property such as bacterial adhesion thereby preventing colonization & bacterial aggregation. Neem has gallotannins which reduce bacterial binding to the tooth surface. Neem effectively inhibit glucosyltransferase activity which in turn reduces bacterial adhesion. Kakiuchi et al 1986[3] reported that galloyl radical of the tannis was important for inhibition of glucan activity &there by having an effective anti-plaque activity.

The reduction in Pg, Pi, A.a was marginally higher in the neem group but was not statistically significant. Reduction was higher in the test groups as compared to the control group.

Conclusion: Local drug delivery of tetracycline and neem enhanced the periodontal status clinically and reduced pathogenic bacteria counts. Herbal extracts such as Neem extracts exhibited good antibacterial property, and was found to be marginally better though not statistically significant than commercially available tetracycline fibers. Further investigation using larger sample size, long term studies using different vehicles and concentration can be conducted to affirm the observations of our study.

References
[13]. Patel VK, Venkatakrishna BH. A study to determine the most effective method for reducing plaque formation and the levels of bacteria on the tooth surface. Ind J Clinical Pharmacol Ther Toxicol 2005; 16 (6): 76-81.