Therapeutic Efficacy Of Clindamycin Gel As An Adjunct To Scaling And Root Planing Therapy In Chronic Periodontal Disease

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Summary – Clindamycin, a lincosamide antibiotic, has been under-recognized as an antimicrobial agent for use in dentistry. The aim of the present work was to evaluate clinical efficacy of 2% clindamycin gel in addition to the basic mechanical periodontal therapy. At baseline, scaling and root planing (SrP) was performed at all 50 subjects (control group and test group). Clindamycin gel was applied after SrP only in the test group. Clinical measurements including periodontal pocket depth (PPD), clinical attachment level (CAL), bleeding on probing (BOP) and plaque index (PI) were done at baseline, and at 3 and 6 months after treatment. Compared to baseline, the PPD and CAL values significantly decreased in the test group (p<0.05) and were statistically lower (p<0.05) compared to control group. PPD reduction of 2.42 mm was obtained in the test group and could be generally considered as clinically significant. A PPD reduction greater than 2 mm indicated that clindamycin gel could be used efficiently as an adjunct to SrP. Also, between-group difference in BOP and PI scores was statistically significant 6 months after treatment. In conclusion, the application of clindamycin gel in combination with SrP enhanced the efficacy of non-surgical periodontal therapy in reducing pocket depth and improving attachment levels in chronic periodontitis subjects and had additional benefits over mechanical therapy alone.

Key words: Periodontal diseases – therapy; Anti-infective agents, local; Clindamycin

Introduction

Chronic adult periodontitis is an inflammatory disease that results in destruction of the soft tissue and supporting bone structure of the periodontium¹. Certain gram-negative bacteria have been implicated in the pathogenesis of this disease, including Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Prevotella intermedia and Tannerella forsythia.

In healthy adults, the resident oral microflora remains relatively stable owing to a dynamic balance achieved by inter-bacterial and host-bacterial interactions. However, variations in the microflora can be attributed to the direct effect in periodontitis².

The treatment of chronic periodontitis is focused on arresting destruction of the periodontal support of the teeth by eliminating pathogenic bacteria present in the inflamed pocket. It is performed by mechanical scaling and root planing (SRP) and the efficacy of this procedure is well documented³. However, variations in the depth of periodontal pockets often result in variable effectiveness of SRP. Also, in many cases, mechanical therapy alone cannot completely eliminate periodontal pathogens present in periodontal pockets, as they are inaccessible to the instruments. Complementing mechanical therapy with adjunctive antibacterial agents, usually in the form of irrigants,
systemic or local antibiotics may enhance treatment effects and overcome the limited efficacy of conventional treatment.

Systemic antibiotics enter periodontal tissues and periodontal pocket via serum and are effective in certain forms of periodontal disease such as aggressive periodontitis. The main disadvantage of systemic therapy is that only a small proportion of the total drug dose reaches the subgingival microflora and periodontal pocket. Also, the use of systemic antibiotics can result in bacterial resistance and very often causes undesirable side effects such as nausea, diarrhea, fever, abdominal pain and pseudomembranous colitis that may be induced by long term usage. In addition, local drug application is a relatively simple procedure to perform and, moreover, patient acceptance is better as compared with invasive procedures such as surgical treatment.

Recently, a new approach using local systems containing antibiotic or antiseptic drugs has been introduced. The local tissue concentration of a drug can be enhanced by incorporating the active agent into controlled release delivery systems to be placed directly in the periodontal pocket. Controlled release devices that contain tetracycline hydrochloride, doxycycline, minocycline, metronidazole or ofloxacin for direct pocket placement are commercially available in various countries as an useful adjunct to SRP in reduction of probing depth.

Clindamycin, a lincosamide antibiotic that has been in use worldwide for more than 30 years, has been consistently effective in the treatment of infections involving a wide spectrum of facultative and strictly anaerobic bacteria. The clinical value of clindamycin in a number of medical studies is well known, but it has been under-recognized as an antimicrobial agent for use in dentistry. It has been shown to be active against a range of gram-negative species, including Porphyromonas species, Prevotella species, Bacteroides fragilis group, Veillonella species and Fusobacterium species. In addition to its antimicrobial properties, clindamycin has anti-inflammatory activities. Its effectiveness for the treatment of periodontal disease has been investigated in a limited number of studies.

The aim of this study was to evaluate and analyze clinical results and efficacy of a six-month treatment of periodontal disease using 2% clindamycin gel as an adjunctive therapy to SRP.

Materials and Methods

Fifty patients, 27 male and 23 female, mean age 47.6 years, took part in this study. The population group was recruited at Dental Clinic in Niš among patients with periodontitis and in good general health, who required periodontal treatment. Patients completed a health history questionnaire to ensure that they were medically qualified for participation in the study. A consent form was signed by each patient after thorough explanation of the nature of this study. The study was approved by the Ethics Committee of the Medical Faculty, University of Niš.

Patients were included in the study if they had at least one pocket, from 5 up to 7 mm in depth. Oral hygiene recommendations were reinforced at the first visit and each subsequent appointment. Radiographic bone loss was recorded dichotomously (presence or absence) in each quadrant to confirm the diagnosis. Patients with any antimicrobial therapy, nonsteroidal anti-inflammatory drugs, corticosteroid therapy, or patients with any periodontal therapy in the preceding 6 months, having known or suspected allergy to lincosamide antibiotics, smokers (current or past), or subjects using tobacco in any other form, alcoholics, and pregnant or lactating females were excluded from the study.

At baseline, all patients received SRP, but in all instances the subgingival instrumentation was carried out after recording baseline measurements. Clinical measurements were carried out at the deepest periodontal pocket from each chosen tooth at baseline, and at 3 and 6 months after therapy. Clinical response was assessed by measuring probing depth (PPD, to the nearest millimeter from the free gingival margin to the base of the pocket), clinical attachment level (CAL, it was recorded to the nearest millimeters from the cemento-enamel junction), gingival bleeding on probing (BOP), and plaque index (PI) based on a modified score of 0 to 3. BOP was evaluated using a scoring scheme, where 0 = no bleeding within 10 seconds after probing; 1 = bleeding within 10 seconds after probing; and 2 = bleeding on probing. Plaque scores were recorded as follows: 0 = no plaque present; 1 = plaque covering not more than 1/3 of the tooth; 2 = plaque covering more than 1/3, but not more than 2/3 of exposed tooth surface; and 3 = plaque covering more than 2/3 of exposed tooth surface.
For further investigations, all patients were divided into two groups. Only SRP was done in 25 patients (control group), and the other 25 patients received SRP plus clindamycin gel (test group). Clindamycin gel was supplied in a disposable applicator containing 10 mg clindamycin (as hydrochloride) in 500 mg of gel. The gel was applied directly into each periodontal pocket of 5 to 7 mm or more with an endodontic syringe with a needle that had a special tip that was inserted to the bottom of the pocket. A sufficient amount of gel was used to fill each pocket up to the gingival margin. Final follow up visits were 3 and 6 months later.

Statistical analysis was performed by descriptive and analytical statistics methodology using standard data processing programs MS Excel and SPSS program package version 15.0. The Student’s paired t-test was used to compare data on PPD and CAL from baseline to those at 3 and 6 months for each treatment group and between treatment groups. The level of significance was set at p<0.05. Testing of score values for BOP and PI was done by variant analysis with subsequent post-hoc test for homogeneous data or by Pearson $\chi^2$-test and Mann-Whitney U test for non-homogeneous data. The level of significance was set at p<0.05.

### Results and Discussion

Periodontal disease essentially comprises of a group of oral infections with dental plaque as the primary etiological factor, which results in inflammatory lesions of the supporting tissues. Removal of the cause of infection and its effects is the primary aim of both non-surgical and surgical treatment regimens. The major non-surgical therapeutic approach involves mechanical SRP. The infective nature of the disease has led to the widespread use of antimicrobials, especially systemic or local antibiotics, as an adjunct to SRP\textsuperscript{11}.

Clindamycin has not been extensively used in periodontal therapeutics, especially applied locally as gel. This clinical trial was performed to examine clinical efficacy of subgingivally administered 2% clindamycin gel in combination with SRP non-surgical treatment of periodontal pockets affected by chronic periodontitis. During the treatment, subgingival administration of 2% clindamycin gel produced no systemic adverse effects and was generally well tolerated. Also, none of the patients had discoloration of teeth or other systemic adverse reactions, especially pseudomembranous colitis.

Table 1 and Table 2 summarize the results of clinical measurements. At baseline, the mean values of clinical measurements revealed no significant between-group differences. Three months after the treatment, a statistically significant between-group difference was found for PPD (p<0.05), but not for CAL, BOP and PI. At 6 months after initial treatment, statistically significant differences between control group (SRP) and test group (SRP + clindamycin gel) were recorded for all examined clinical parameters.

### Table 1. Comparison of periodontal pocket depth and clinical attachment level mean values in test and control group patients at different examination intervals

<table>
<thead>
<tr>
<th>Examination interval</th>
<th>PPD (mean ± SD [mm])</th>
<th>CAL (mean ± SD [mm])</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test n=25</td>
<td>Control n=25</td>
</tr>
<tr>
<td>Baseline</td>
<td>6.04±0.68</td>
<td>5.92±0.67</td>
</tr>
<tr>
<td>At 3 months</td>
<td>4.76±0.65</td>
<td>5.45±0.57</td>
</tr>
<tr>
<td>At 6 months</td>
<td>3.62±0.31</td>
<td>5.56±0.65</td>
</tr>
<tr>
<td>Total difference from baseline</td>
<td>2.42±0.44</td>
<td>0.36±0.29</td>
</tr>
<tr>
<td>p-value\textsuperscript{b}</td>
<td>*p&lt;0.001</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

PPD = periodontal pocket depth; CAL = clinical attachment level; SD = standard deviation; n = number of patients; p-value between treatment groups; *p-value between paired means; \textsuperscript{a}statistical significance p<0.05
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The adjunctive use of locally delivered antibiotics can provide additional benefits compared to the conventional SRP therapy. In general, the clinical findings in our study with clindamycin gel are consistent with those reported on the use of other locally delivered antibiotics\textsuperscript{12-15}.

Clindamycin works primarily by binding to the 50s ribosomal subunit of bacteria. This agent disrupts protein synthesis by interfering with the transpeptidation reaction, which thereby inhibits early chain elongation. In addition to the direct antibacterial effect on ribosomal units, clindamycin has a number of unique pharmacological features that enhance its clinical efficacy and reaches high concentrations in saliva, gingival cervical fluid and bone. The ability of clindamycin to reach high intracellular concentrations and extended activity inside the bacterium yields a post-antibiotic effect by which the antimicrobial remains active although serum concentration levels are subinhibitory\textsuperscript{10}. Local clindamycin therapy has been investigated for the treatment of periodontal disease in a limited number of studies\textsuperscript{16,17}. In 1993, Sauvêtre \textit{et al.} described the effect of 1% clindamycin gel on the microbial flora of periodontal pockets deeper than 5 mm, but clinical data were not presented\textsuperscript{17}.

This is the first paper describing the effectiveness and clinical results of local clindamycin therapy as an adjunct to SRP in the treatment of chronic adult periodontitis. The reduction of all clinical parameters observed in this study with clindamycin gel therapy was generally maintained in most patients throughout the observation period. However, in the control group, the noticeable changes in CAL were observed at 3 months after therapy and remained relatively invariant for up to 6 months after therapy. In the test group, reduction of PPD and CAL had statistically significant values at 3 and 6 months after treatment compared to baseline (Table 1). A 2-mm reduction in probing depth is considered as clinically relevant\textsuperscript{3,11}. In our work, PPD reduction of 2.42 mm was obtained in the test group and could be generally considered as clinically significant. A PPD reduction greater than 2 mm indicated that clindamycin gel could be used efficiently as an adjunct to SRP. Also, plaque scores were reduced and it was expected owing to the repeated instructions on oral hygiene. Bleeding scores were reduced owing to SRP, improvement of plaque scores and use of clindamycin gel.

Our findings related to clinical improvements after clindamycin gel administration are very similar to other studies indicating significant improvement of clinical measurements in patients that received SRP and topical doxycycline, tetracycline, azithromycin, minocycline or metronidazole therapy\textsuperscript{12-15,18-20}.

As stated, the results of the present study showed that clindamycin gel was a good adjunct to SRP therapy at the examined depth of periodontal pocket. Also, we confirmed that mechanical treatment combined

\textbf{Table 2. Comparison of score values for bleeding on probing and plaque index of test and control group patients at different examination intervals}

<table>
<thead>
<tr>
<th>Examination interval</th>
<th>BOP Score</th>
<th>Test n=25</th>
<th>Control n=25</th>
<th>( p )-value</th>
<th>PI Score</th>
<th>Test n=25</th>
<th>Control n=25</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>\p=0.573</td>
<td>1</td>
<td>6</td>
<td>8</td>
<td>\p=0.872</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>13</td>
<td>15</td>
<td>\p=0.596</td>
<td>2</td>
<td>10</td>
<td>9</td>
<td>\p=0.664</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>11</td>
<td>8</td>
<td></td>
<td>3</td>
<td>9</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>At 3 months</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>\p=0.488</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>\p=0.671</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>18</td>
<td>17</td>
<td>\p=0.522</td>
<td>1</td>
<td>12</td>
<td>6</td>
<td>\p=0.234</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3</td>
<td>7</td>
<td></td>
<td>2</td>
<td>11</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>At 6 months</td>
<td>0</td>
<td>9</td>
<td>3</td>
<td>\p&lt;0.05</td>
<td>0</td>
<td>7</td>
<td>4</td>
<td>\p&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>15</td>
<td>16</td>
<td>\p&lt;0.05</td>
<td>1</td>
<td>15</td>
<td>12</td>
<td>\p=0.062</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1</td>
<td>6</td>
<td></td>
<td>2</td>
<td>3</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

BOP = bleeding on probing; PI = plaque index; \( n \) = number of patients; *Pearson \( \chi^2 \)-test; **Mann-Whitney test; statistical significance for both tests \( p<0.05 \)
with clindamycin gel application was more effective and clinical improvements were predominant.

Conclusion

Within the limits of this study, we found significant reduction of all clinical parameters in the test group compared to the control group. Hence, it can be concluded that the utilization of clindamycin gel in combination with SRP enhances the efficacy of non-surgical periodontal therapy in reducing pocket depth and improving attachment levels in chronic periodontitis subjects, so this antimicrobial therapy is very useful as an adjunct treatment. Although plaque control and SRP remain important and essential in periodontal therapy, topical application of clindamycin along with SRP had additional benefits over mechanical therapy alone.

References

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Sažetak

TERAPIJSKA UČINKOVITOST KLINDAMICIN GELA KAO DODATAK BAZIČNOJ TERAPIJI KRONIČNE PARODONTOPATIJE

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Klindamicin, linkozamidni antibiotik, je u širokoj upotrebi u stomatologiji. Cilj ovoga rada je bio procijeniti kliničku učinkovitost 2% klindamicin gela kao dodatne terapije bazičnoj terapiji kronične parodontopatije. Bazična terapija provedena je u svih 50 pacijenata (kontrolna skupina i ispitna skupina). Klindamicin gel je primijenjen nakon bazične terapije parodontopatije samo u ispitnoj skupini. Praćeni su sljedeći klinički parametri: dubina parodontalnog džepa (DPDZ), razina pripojnog epitela (NPE), indeks krvarenja (IKr), plak indeks (PI). Mjerenje indeksa provedeno je prilikom prve terapije te tri i šest mjeseci nakon tretmana. DPDZ i NPE vrijednosti su bile značajno smanjene u ispitnoj skupini (p<0,05) i bile su statističke niže u odnosu na kontrolnu skupinu (p<0,05). Smanjenje dubine parodontalnog džepa za 2,42 mm zabilježeno je u ispitnoj skupini i može se smatrati klinički značajnim. Ovo smanjenje pokazuje da klindamicin gel ima terapijski učinak kao dodatak bazičnoj terapiji u liječenju kronične parodontopatije. Također je evidentirana statistička razlika između skupina u IKr i PI šest mjeseci nakon terapije. Zaključuje se da primjena klindamicin gela u kombinaciji s bazičnom terapijom parodontopatije povećava učinkovitost nekirurške terapije.

Ključne riječi: Periodontalne bolesti – terapija; Antiinfektivna sredstva, lokalna; Klindamicin