

# Custom Tray Application of Peroxide Gel as an Adjunct to Scaling and Root Planing in the Treatment of Periodontitis: Results of a Randomized Controlled Trial after Six Months

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## Abstract

- **Objective:** Scaling and root planing (SRP) is the primary non-surgical treatment for periodontitis, but its effectiveness is limited. Consequently, various adjunctive therapies have been investigated to improve clinical outcome. This study evaluated the clinical effects of one SRP procedure alone or combined with local administration of hydrogen peroxide gel using customized trays for the treatment of subjects with chronic periodontitis over a period of six months.
- **Methods:** An examiner-blind clinical trial was conducted among 30 subjects with moderate to advanced periodontitis who were randomized to SRP alone or SRP combined with prescription custom-tray application (Perio Tray<sup>®</sup>) of 1.7% hydrogen peroxide gel (Perio Gel<sup>®</sup>) for a period of three months, then extended to six months. Following impressions for the test group, all subjects brushed twice daily with a regular dentifrice and toothbrush for a four-week acclimation phase to standardize oral conditions (while trays were fabricated) prior to initiating the treatment phase. SRP was performed three weeks after baseline, and clinical assessments, *i.e.*, pocket probing depth (PPD) and bleeding index (BI), were conducted at baseline and after two, five, 13, and 26 weeks of peroxide gel applications. Clinical variables were compared by ANCOVA and paired t-tests after each treatment interval.
- **Results:** A total of 13 test and 15 control subjects completed the original three-month trial, of whom 10 test and 13 control subjects finished the three-month extension. After two weeks of peroxide gel use prior to SRP, mean PPD for the test group significantly decreased from baseline by 0.21 mm and mean BI significantly dropped by 0.14; clinical parameters for the control group were unchanged. Two weeks following SRP, mean PPD significantly decreased from baseline by 0.65 mm for the test group and 0.17 mm for the control; mean BI significantly dropped by 0.17 for the test group and 0.05 for the control. Ten weeks following SRP, mean PPD decreases were 0.77 mm for the test group and 0.13 mm for the control, and mean BI reductions were 0.14 for the test group and 0.00 for the control. For subjects who completed the three-month extension (*i.e.*, 23 weeks post-SRP), mean PPD decreases were 0.72 mm for the test group and 0.13 mm for the control, and mean BI reductions were 0.05 for the test group and 0.01 for the control. Analysis of deeper pockets (*i.e.*, > 5 mm at baseline) showed the same relationship for PPD, but with larger differences between groups. For example, after two weeks of peroxide gel use prior to SRP, mean PPD decreased by 0.48 mm for the test group compared to 0.04 mm for the control. Two weeks after SRP, mean PPD decreased from baseline by 1.40 mm for the test group and 0.60 mm for the control, and 10 weeks after SRP by 1.57 mm for the test group and 0.58 mm for the control. After the extension (*i.e.*, 23 weeks post-SRP), mean PPD changed from baseline by 1.50 mm for the test group and 0.55 mm for the control. With the exception of BI at 23 weeks post-SRP, all reductions cited above for the test group were statistically significantly different from the control group for both PPD and BI for all comparisons.
- **Conclusion:** When compared with SRP alone, clinical improvements in PPD (*e.g.*, ~1.0 mm for pockets > 5 mm at baseline) were maintained for up to six months after SRP with adjunctive use of 1.7% hydrogen peroxide gel, locally administered using prescription customized trays in the treatment of subjects with moderate to advanced periodontitis.

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## Introduction

Currently, the primary non-surgical treatment for chronic periodontitis consists of supra- and subgingival plaque (biofilm) removal and mechanical debridement to reduce the periodontal bacterial load.<sup>1,2</sup> This localized, professionally administered therapy, commonly referred to as scaling and root planing (SRP), usually results in clinical improvement and can temporarily decrease the progression of the disease.<sup>3,4</sup> Nevertheless, SRP alone has significant limitations since it is mechanically impossible to eliminate subgingival

bacteria from areas inaccessible to periodontal instruments,<sup>5</sup> as well as reservoirs in dentin tubules and epithelial cells.<sup>6</sup> Consequently, viable bacteria that remain after SRP regenerate, and bacteria constantly introduced into the mouth result in new biofilm formation.<sup>7-10</sup> As a result, it is necessary to repeat SRP at least every three months for periodontal maintenance.

For these reasons, numerous adjunctive treatments have been investigated and currently many sustained or controlled-release local

delivery agents (LDAs) that provide antimicrobial or chemotherapeutic activity as adjuncts to SRP are widely used, including various systemic and topical antibiotic therapies recommended by the American Academy of Periodontology for deeper pockets ( $\geq 5$  mm) of chronic periodontitis patients.<sup>11</sup> Nevertheless, despite the use of these adjunctive treatments, clinical and immunological manifestations of disease often persist and sometimes progress.<sup>12</sup> In addition, for both patients and clinical practitioners several problems and limitations are associated with the use of these therapies, including home care restrictions for brushing/flossing around treated sites, unsuitability for shallow pockets ( $< 5$  mm), biofilm resistance to antibiotics, drug allergies/sensitivities, potential overgrowth of resistant and/or commensal microorganisms, and concerns about judicious drug use in general.

Thus, there is still a need to find other approaches, preferably localized treatments which will safely and effectively reduce inflammation and disease progression in patients with chronic periodontitis. Topical peroxide application can circumvent many of these limitations and has been shown to reduce plaque and gingival inflammation.<sup>13-15</sup> Aqueous hydrogen peroxide at low concentrations, which has long been used as an oral debriding agent and wound cleanser,<sup>16</sup> also has an extensive history of topical application in

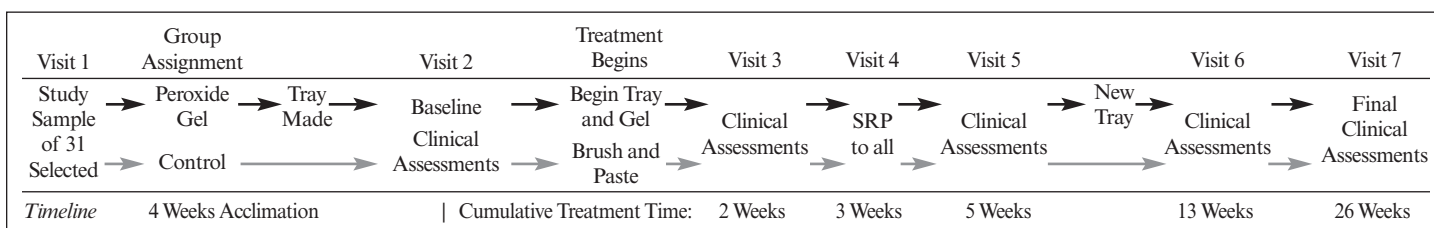
with SRP alone. In order to determine if these clinical improvements might be maintained in subjects for six months without additional SRP therapy, the trial was extended for another three months.

## Materials and Methods

### Experimental Design

The experimental design was a randomized, controlled, examiner-blind, parallel group study to evaluate the effects of subgingival placement of hydrogen peroxide gel with a custom-fabricated prescription tray as an adjunct to mechanical debridement (SRP) to treat existing periodontitis. This report presents the addition of six-month data to an already published three-month study.<sup>26</sup> The detailed experimental procedures were described in this previous publication; therefore, they are somewhat abbreviated here.

The overall study was divided into three phases: 1) a pre-SRP phase consisting of a four-week acclimation period and a three-week treatment period prior to SRP; 2) a 10-week post-SRP treatment phase with clinical assessments after two and 10 weeks; and 3) a 13-week treatment phase extension with clinical assessments at completion. A flow chart of the experimental study design and subject participation is provided in Figure 1.



**Figure 1.** Flow diagram showing recruitment and different phases of study design. All subjects were given brush and paste to use starting at Visit 1.

mouthrinses, dentifrices, and antiseptic gels, and a long-term safety record.<sup>17,18</sup> Additionally, tray delivery of peroxide gel appears to be effective for supragingival and subgingival biofilm management.<sup>19,22</sup>

Still, the challenge for peroxide use in treating periodontitis has been to identify a method for its delivery deep into periodontal pockets for sufficient time to have significant therapeutic effect.<sup>17</sup> Use of a prescription custom-fabricated dental tray (Perio Tray<sup>®</sup>, Perio Protect LLC, St. Louis, MO, USA) overcomes gingival crevicular fluid flow to deliver peroxide directly into the sulcus.<sup>23</sup> When 1.7% hydrogen peroxide gel was introduced via a prescription tray into periodontal pockets as an adjunctive chemical therapy before and after SRP, case studies indicated evidence of subgingival biofilm debridement and reductions in bleeding on probing and pocket probing depths.<sup>20,24,25</sup> An advantage of the prescription tray delivery approach is that patients can use it daily at home between office visits to deliver peroxide (and other medications) into periodontal pockets of all depths, allowing for adjunctive care at the earliest stages of disease.

In a previous report, prescription tray local delivery of a 1.7% hydrogen peroxide gel was evaluated as adjunctive therapy to SRP in chronic periodontitis patients over three months.<sup>26</sup> The clinical results of this randomized, controlled trial in subjects with moderate to advanced periodontitis demonstrated that this adjunctive treatment provided statistically significant improvements in gingival bleeding and pocket depths at sites throughout the mouth, in both shallow ( $\leq 5$  mm) and deep ( $> 5$  mm) pockets, when compared

### Subject Population

A study population of 31 qualifying adults was selected by screening exams from volunteers who were identified as suitable subjects with chronic periodontitis, based on the classification system of the American Academy of Periodontology.<sup>27</sup> Periodontitis was classified as mild (pocket depth  $\leq 4$  mm), moderate (pocket depth 5–7 mm), or severe (pocket depth  $> 7$  mm).

All eligible subjects were fully informed of the purpose and timeline of the study, as well as potential risks and benefits of participation, and signed a Research Study Information and Consent Form. Prior to initiation of clinical procedures, the protocol and all study documents were approved by an independent institutional review board (IRB). With IRB approval, a Consent Form Addendum was administered to those subjects who were willing to continue in a three-month extension.

### Inclusion and Exclusion Criteria

Inclusion criteria were adults (30–70 years of age) in good general health, with 12 or more natural teeth, moderate to severe generalized periodontitis (one site with pocket depth  $> 5$  mm in at least two quadrants), no mechanical debridement for greater than six months prior to the study, and willingness to comply with instructions and procedures for the duration of the study. Exclusion criteria included professional periodontal therapy before study enrollment, extensive calculus deposits, significant oral soft tissue pathology or tooth mobility, orthodontic bands, fixed appliances or partial dentures, need for

prophylactic antibiotics prior to dental treatment, therapy with systemic antibiotic medications within the previous month, systemic condition or disease (e.g., diabetes, immunological disorders), drug allergies or adverse effects following use of oral hygiene products, genetic predisposition to periodontitis, and pregnant or lactating females.

### **Clinical Assessments**

The following clinical assessments were performed throughout the study by the same examiners who were blinded to the treatment.

- Oral soft tissue health (OST) was determined by means of a comprehensive visual inspection of the oral cavity.
- Pocket probing depth (PPD) was measured using a manual calibrated periodontal probe (WHO Periodontal Probe) as the distance in millimeters from the gingival margin to the attached periodontal tissue.
- Bleeding index (BI) was determined by stroking with a probe along the inner wall of the gingival crevice.<sup>28</sup>

Clinical measurements were taken at six sites (mesio-buccal, buccal, disto-buccal, mesio-lingual, lingual, disto-lingual) of each tooth, except third molars (168 possible sites).

### **Study Schedule**

At Visit 1, a screening exam was performed to identify adults with chronic generalized periodontitis, and subjects were randomly assigned to one of two treatment arms. Subjects assigned to the peroxide/tray group had a dental impression taken which was sent to a laboratory for preparation of custom-fabricated trays. Following enrollment, all subjects received a regular toothbrush and dentifrice, replenished as needed, to use for the study duration. They began an acclimation phase by brushing twice each day to standardize home oral care and oral conditions for both groups.

Approximately four weeks later at baseline (Visit 2), assessments for OST, BI, and PPD were performed. Subjects assigned to the test group received their trays which they began using with peroxide gel at home for 15 minutes four times per day. After two weeks (during which subjects in the test group performed the peroxide/tray treatments), clinical assessments were performed for OST, BI, and PPD (Visit 3). A week later (Week 3, Visit 4) all subjects received full-mouth SRP. At the SRP visit, subjects in the test group were instructed to reduce tray/peroxide gel usage to two times per day for 15 minutes for the remainder of the trial.

Following SRP, subjects began a 10-week treatment period during which they continued their home treatment regimens. After two weeks (Week 5, Visit 5) OST, BI, and PPD were performed for all subjects, and impressions for new trays were taken for subjects in the test group. The same clinical assessments were performed 10 weeks (Week 13, Visit 6) and 23 weeks after SRP (Week 26, Visit 7). A study schedule summary follows:

- Visit 1 Screening
- Visit 2, Baseline: Assess OST, BI, PPD; tray and peroxide use begins for test group
- Visit 3, Week 2: Assess OST, BI, PPD
- Visit 4, Week 3: Full-mouth debridement and scaling for all subjects
- Visit 5, Week 5: Assess OST, BI, PPD
- Visit 6, Week 13: Assess OST, BI, PPD

- Visit 7, Week 26: Assess OST, BI, PPD

### **Randomization and Allocation to Treatment**

Subjects were sequentially assigned consecutive identification numbers during enrollment (Visit 1). Allocation to treatment was accomplished by an investigator, who was not directly involved with examination or treatment procedures, by stratifying subjects according to pocket depth and number of pockets with a depth  $\geq 6$  mm. Within each stratum, subjects were randomly assigned according to tobacco use and gender to a treatment group, resulting in distribution into two groups with similar periodontal conditions and demographic factors. The treatment identification code was kept concealed from all individuals directly involved in the assessments until all examinations were concluded.

### **Treatment Procedures**

Both groups of subjects brushed twice daily (morning and evening) with a marketed dentifrice (Crest® Cavity Protection Toothpaste, Procter & Gamble Co., Cincinnati, OH, USA) and an adult, flat-trim bristle profile toothbrush (American Dental Association, Chicago, IL, USA).

All subjects received full-mouth scaling and root planing (SRP) using ultrasonic and hand instruments by two licensed dental hygienists, who had extensive experience with periodontal pocket debridement and were under no time restriction. A licensed dentist, who was experienced with periodontal debridement, administered local anesthetic only if needed. Subjects were randomly assigned in equal numbers for each treatment group to each hygienist who was unaware of group assignment.

For subjects assigned to the test group, impressions of maxillary and mandibular arches were taken with irreversible hydrocolloid material, and yellow stone models were poured and sent with a prescription of the patient's presenting conditions at screening to an FDA-registered dental laboratory for fabrication of custom, ethylene-vinyl copolymer trays (Perio Trays). Thickness of the prescription tray seal and length and thickness of extensions were determined by precise measurements on the models provided in conjunction with the subject's periodontal probing depth measurements.

First use of trays and 1.7% hydrogen peroxide gel was supervised by an instructor and, if needed, adjustments were made to trays so they would seat completely and comfortably in the subject's mouth while maintaining an adequate seal. Each subject applied a thin ribbon of gel throughout tooth indentations to provide a dosage of  $\sim 0.75$  gram in each tray.

Treatment frequency varied depending on the stage of the study as follows:

- Baseline Exam (Visit 2) to SRP (Week 3, Visit 4): 4 treatments per day, 15 minutes each
- SRP (Week 3, Visit 4) to Final Exam (Week 26, Visit 7): two treatments per day, 15 minutes each

Thus, for the three-week period following the baseline, subjects used  $\sim 6.0$  grams of gel per day, and for the 23-week period following SRP, subjects used  $\sim 3.0$  grams of gel per day.

Subjects documented tooth brushing and peroxide/tray applications on a diary for the entire treatment phase. Subject compliance was estimated throughout the treatment phase by reviewing diaries and by weighing toothpaste and peroxide gel tubes.

### Data Analysis

Analyses were performed on data from all subjects who were administered a full-mouth scaling and debridement (SRP) during the treatment phase of the study. Subject-wise mean scores for PPD and BI were calculated based on all measured sites, or on subsets of all measured sites as indicated.

Efficacy data analysis consisted of between-treatment and within-treatment (longitudinal) comparisons of PPD and BI at all examination time points using parametric procedures. Between-treatment comparisons employed analysis of variance (ANOVA) for baseline data and analysis of covariance (ANCOVA) for follow-up data. In addition, within-treatment comparisons of baseline versus follow-up mean scores were performed using paired t-tests. All comparisons were performed using two-sided hypothesis tests, and employed a 0.05 level of significance.

## Results

### Demographics and Subject Retention

Initially, 63 adult volunteers were assessed for eligibility and 28 were excluded because they failed inclusion/exclusion criteria, had scheduling problems, or other reasons for not participating. At screening (Visit 1), 35 subjects were examined, and four were disqualified for failing the pocket inclusion criterion; 31 subjects were enrolled. Prior to SRP, one subject in the test group stopped product use and another relocated; in the control group, one subject was disqualified for antibiotic use. Thus, 28 subjects completed all clinical assessments through Visit 6; 17 females/11 males, 20 non-smokers/eight smokers, with a mean age of 54.8 years (range 33–69 years). Of these, 23 subjects elected to continue participation for the 13-week extension, and all completed the final clinical assessments at Visit 7; 14 females/9 males, 18 non-smokers/5 smokers, with a mean age of 52.9 years (range 33–68 years).

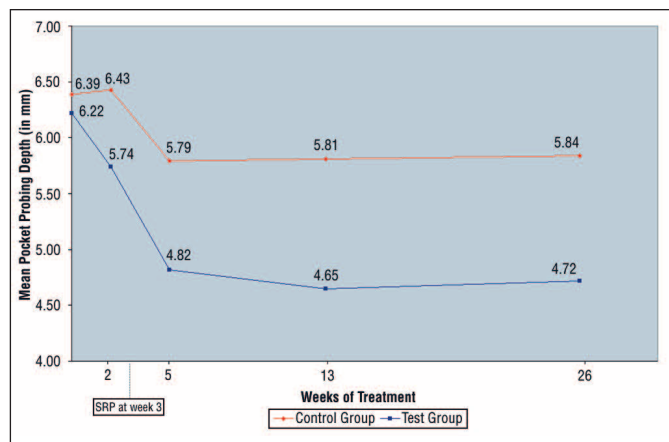
### Compliance and Adverse Effects

For subjects in the test group, the tray/peroxide treatment generally was well received. Diary entries and amounts used (based on tube weights) for both dentifrice and peroxide gel indicated that subjects satisfactorily followed treatment instructions.

Three subjects in the test group reported sensitivity that they associated with peroxide/tray use. One subject had mild intermittent sensitivity to cold that was localized to one tooth with recession, and also experienced occasional discomfort when positioning trays due to a TMJ problem. Two subjects initially reported mild, generalized, intermittent sensitivity immediately after treatment, but it resolved with subsequent use. The only other treatment condition associated with peroxide/tray use reported by subjects was an improvement (*i.e.*, whitening) in the color of their teeth.

### Pocket Probing Depth Clinical Findings

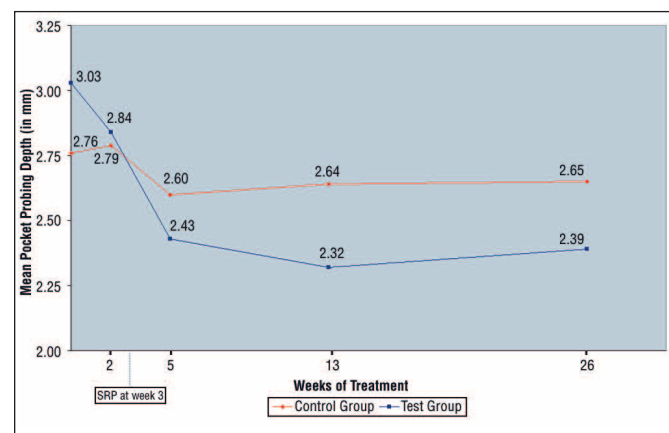
Figure 2 provides whole mouth PPD data for all examined sites at baseline with deep pockets (*i.e.*, > 5 mm) of both treatment groups after two weeks of test product use prior to SRP, and after five, 13, and 26 weeks (*i.e.*, two, 10, and 23 weeks post-SRP). No statistically significant difference was found between



**Figure 2.** Pocket probing depth measurements (in mm) - subjectwise analysis of whole-mouth data for deep pockets (*i.e.*, PPD sites > 5 mm) at baseline. Between-group comparison for change from baseline at 26 weeks:  $p = 0.0002$ .

the test and control groups at baseline (Visit 2). However, following two weeks of tray/peroxide treatment prior to SRP, the test group exhibited a significant decrease ( $p < 0.0001$ ) in PPD from baseline that also was significantly different ( $p < 0.0001$ ) from the control group, which did not change from baseline. Two weeks after SRP (five weeks from baseline), both groups showed decreases in pocket depth. However, the same relationship between treatment modalities occurred in which the test group had statistically lower PPD values ( $p < 0.0001$ ) than the control group. This same pattern continued 10 weeks after SRP (13 weeks from baseline) and again 23 weeks after SRP (26 weeks from baseline). A highly significant PPD reduction ( $p = 0.0001$ ) from baseline of 1.50 mm was observed for the test group compared to 0.55 mm for the control group at the final exam after 26 weeks of treatment (Visit 7). For all comparisons, the reductions for the test group (tray/peroxide + SRP) were statistically greater ( $p < 0.004$ ) than the control (SRP only), reflecting an average improvement in deep pocket depth over SRP of approximately 1 mm that persisted for six months.

Figure 3 provides the same whole mouth PPD comparisons for all examined sites at baseline with shallow pockets (*i.e.*,  $\leq 5$  mm). These data also produced highly significant PPD reductions ( $p = 0.0001$ ) of more than 0.6 mm from baseline compared to



**Figure 3.** Pocket probing depth measurements (in mm) - subjectwise analysis of whole-mouth data for shallow pockets (*i.e.*, PPD sites  $\leq 5$  mm) at baseline. Between-group comparison for change from baseline at 26 weeks:  $p < 0.0001$ .

just 0.1 mm for the control group at the final exam after 26 weeks of treatment (Visit 7). The reductions from baseline for the test group (tray/peroxide + SRP) were statistically greater ( $p < 0.0001$ ) than the control (SRP only) for all comparisons. The differences in PPD data between groups were highly significant for all post-SRP comparisons, indicating on average that shallow pocket depths improved by ~0.25 mm two weeks after SRP and then improved further to ~0.5 mm after three months, where they remained until completion of the study extension after six months.

Figure 4 is a 5 mm pocket threshold evaluation for both groups, indicating the percentage of deep pockets (*i.e.*, >5 mm) at baseline that changed to shallow pockets (*i.e.*, ≤ 5 mm) after two, five, 13, and 26 weeks (*i.e.*, one week before SRP and two, 10, and 23 weeks after SRP). After two weeks of tray use (*i.e.*, one week before SRP), the test group had 28% of sites with pockets that changed from greater than 5 mm to less than or equal to 5 mm, whereas the control group had only 2% of sites that changed. After five weeks of tray use (*i.e.*, two weeks after SRP), the test group had 57% of sites that converted versus approximately 30% for the control group, and after 13 weeks of tray use (*i.e.*, 10 weeks after SRP), the test group increased to 76% of sites while the control group remained at 30%. After 26 weeks of tray use (*i.e.*, 23 weeks after SRP), the number of conversion sites for test and control groups were similar to those observed after 13 weeks with 72% and 28%, respectively.

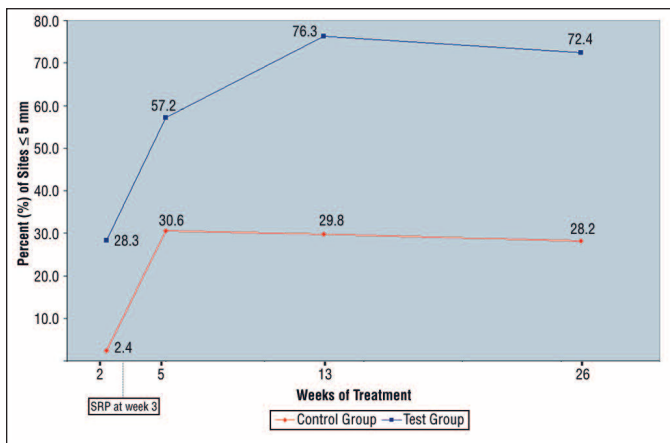


Figure 4. Pocket probing depth threshold evaluation measuring changes from baseline in percentage of PPD sites > 5 mm at baseline and ≤ 5 mm at subsequent time periods.

Figure 5 provides a more detailed presentation of the changes in PPD over the course of the trial, showing the distribution of PPD scores as percentages for sites with deep pockets (*i.e.*, > 5 mm) at baseline. Both groups began with similar deep pocket distributions of approximately 70% 6 mm sites and 30% ≥ 7 mm sites. After 2 weeks of tray use in the test group prior to SRP, there was a decrease in the percentage of 6 mm and ≥ 7 mm sites and an increase in 5 mm sites, whereas the control group remained unchanged. Two weeks following SRP (*i.e.*, at the 5-week visit), the test group had a pronounced decrease in deep pocket sites (*i.e.*, 6 mm and ≥ 7 mm) and a similar increase in the number of 4 mm and 5 mm sites. The control group had a slight decrease in ≥ 7 mm sites and a larger decrease in 6 mm sites with an increase primarily in 5 mm sites. Ten weeks after SRP (*i.e.*, at the 13-week visit), the test group had a further decrease in the percentage of

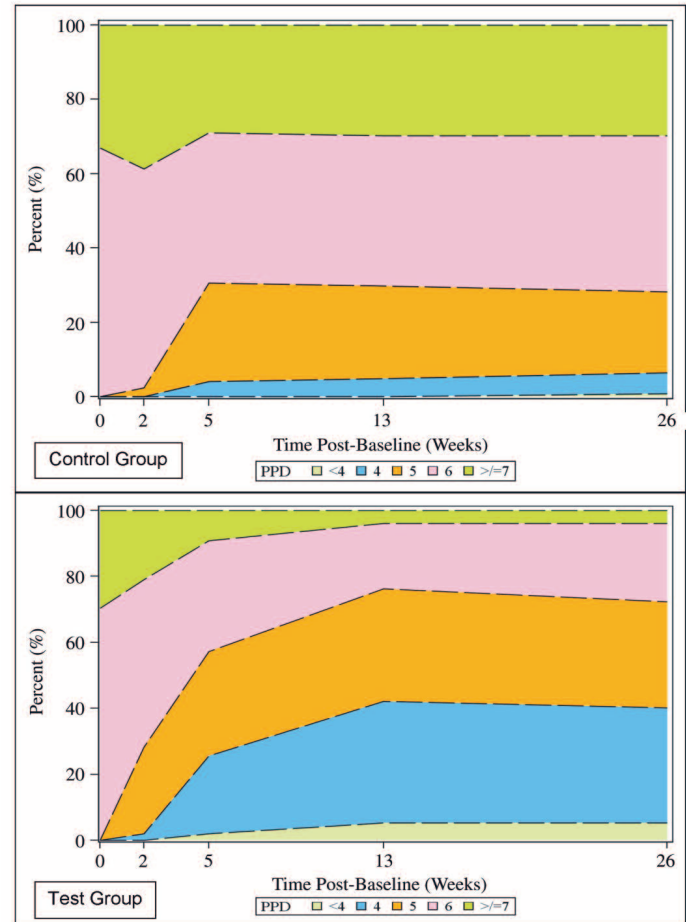
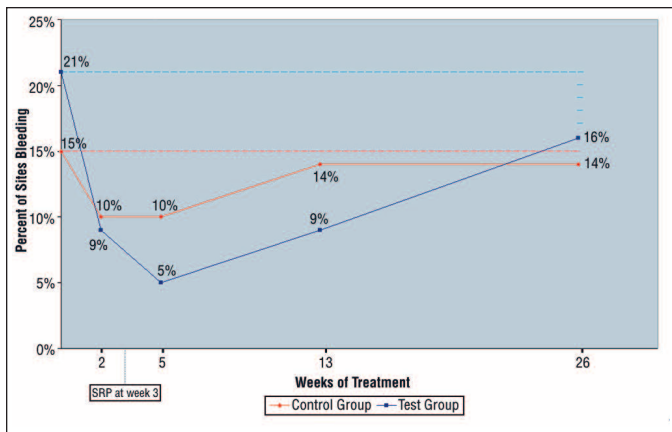


Figure 5. Percentage distribution of pocket probing depth scores on sites with baseline PPD > 5 for subjects completing the 26-week visit.

deep pockets and a continued increase in shallow pockets, particularly 4 mm and 5 mm sites, but some < 4 mm sites as well. Similar percentages, reflecting shifts from deep to shallow pockets, continued 23 weeks after SRP (*i.e.*, at the 26-week visit). In contrast, the control group had no further changes in the distributions between deep and shallow pockets 10 and 23 weeks after SRP.

### Bleeding Index Clinical Findings

Figure 6 presents whole mouth BI data for both groups two weeks after baseline (one week prior to SRP) and five, 13, and 26 weeks after baseline (*i.e.*, two, 10, and 23 weeks post-SRP). For the test group, the data produced significant BI reductions ( $p < 0.02$ ) from baseline for visits after two, five, and 13 weeks, and a reduction that approached significance ( $p = 0.07$ ) after 26 weeks compared to the control group, which produced a significant reduction only at five weeks after baseline (*i.e.*, two weeks post-SRP). A statistically significant difference was not observed between the test and control groups at baseline (Visit 2), but after two weeks of tray/peroxide treatment prior to SRP, the test group exhibited a reduction in bleeding that was statistically different ( $p < 0.014$ ) from the control group. In addition, reductions for the test group (tray/peroxide + SRP) were statistically greater ( $p < 0.002$ ) than the control (SRP only) for comparisons at subsequent exams (five and 13 weeks), except at 26 weeks ( $p > 0.050$ ).



**Figure 6.** Percentage of bleeding sites - subjectwise analysis of whole-mouth data for all pockets. Between-group comparison for change from baseline at 26 weeks:  $p = 0.0002$ .

## Discussion

This randomized, examiner-blind, parallel-design clinical trial compared the effectiveness of daily treatment with 1.7% hydrogen peroxide gel using prescription custom-fabricated dental trays as an adjunct to one scaling and root planing (SRP) procedure over a period of six months. The results demonstrated that the peroxide gel-prescription tray treatment regimen in combination with SRP was statistically significantly more effective than traditional SRP therapy alone in reducing pocket depths and bleeding both two weeks and 10 weeks after SRP, and pocket depths 23 weeks after SRP. Moreover, although all the data are not provided herein as was done previously for data up to three months,<sup>26</sup> the effectiveness of the peroxide gel-prescription tray system after six months was manifested at all sites throughout the mouth, and encompassed both initially deep ( $> 5$  mm) and shallow ( $\leq 5$  mm) periodontal pockets.

This clinical trial also demonstrated that the use of the peroxide gel-prescription tray regimen for two weeks prior to SRP significantly decreased pocket depths and bleeding without mechanical intervention. This finding supports case studies<sup>20,24,25,29</sup> prior to this study that emphasized minimally invasive dentistry without full-mouth debridement or SRP, and it advocates that the use of the peroxide gel-prescription tray regimen may reduce the scope and frequency of more invasive procedures, *e.g.*, full-mouth SRP, which increase risk, especially to medically compromised patients, of introducing pathogenic bacteria into the bloodstream.<sup>30,31</sup> Based on the results of this six-month study, prescription tray delivery of hydrogen peroxide is an adjunctive debridement therapy that was effective before and after full-mouth mechanical procedures in reducing PPD and BI, and in maintaining PPD improvements of  $\sim 1$  mm over SRP alone for up to six months. General consensus in the periodontal literature is that a difference of 1 mm between treatments for pocket depth at initially deep sites is clinically relevant.<sup>32,33</sup> These reductions compare favorably with those reported for other well-known adjunctive LDA treatments, *e.g.*, Atridox®, Arestin®, and Periochip®.

Comparisons of reductions in bleeding scores to those obtained in other studies are limited by the fact that a standard method for assessing bleeding is not universally used. Nevertheless, gingival

bleeding scores were reduced significantly by adjunctive use of the peroxide gel-prescription tray regimen relative to SRP alone during the first three months of this trial. However, after six months' use the difference between groups had diminished, and it was no longer statistically significant. The reason for the lessening of the BI reduction at six months is uncertain, but there are several possible explanations: 1) Only ten subjects in the test group completed the six-month assessments, thus limiting the trial's ability to differentiate bleeding effects; 2) The peroxide gel-prescription tray system is adjunctive, and SRP was completed only once; 3) To maintain their improvements, certain subjects (*e.g.*, due to rapid calculus formation) are unable to extend maintenance visits to six months, and needed additional SRP therapy; and 4) Biofilms in deeper pockets recolonized, due either to inherent limitations of SRP or from infected epithelial cells, and seeded into nearby tissues. Thus, patients with extensive disease that is less responsive to therapy may benefit by additional SRP or by surgical intervention while using the adjunctive treatment regimen. Other instances in which adjunctive therapy may be less effective for controlling bleeding include sites where subgingival calculus remains or reforms, presence of endoperiodontal lesions or granulomatous tissue, cracked teeth, and occlusion trauma.

In this study, the control group 23 weeks after SRP had a mean PPD reduction from baseline of 0.55 mm for initial pocket depths  $> 5$  mm. This change falls within the range of improvements for SRP six months post-treatment in other recently reported studies.<sup>34,37</sup> Although reductions produced by SRP are dependent on initial PPD values and other study variables, subgingival debridement combined with oral hygiene instruction is generally an effective treatment modality. When an effective modality is used as a gold standard of comparison, it may be difficult to show any adjunctive effect in addition to the original treatment, as has been the case with other interventions.<sup>34,35</sup> Therefore, it is noteworthy that highly significant clinical reductions were observed in subjects treated with 1.7% hydrogen peroxide gel in prescription custom-fabricated dental trays as an adjunct to SRP, and that the PPD improvements were maintained for six months.

The improvements in the percentage of sites exhibiting PPD greater than 5 mm at baseline and less than or equal to 5 mm at subsequent visits for both groups follows a parallel trajectory between two and five weeks, the visit just before and after SRP, indicating a similar effect of SRP on all subjects. However, a noteworthy difference is that the test group, which used the trays and peroxide gel from baseline, had a considerable improvement before SRP was performed three weeks after baseline, and this improvement (over and above that from SRP) continued after SRP, whereas the control group improvement due to SRP alone was maintained for the duration of the trial. Since surgery is generally considered necessary for sites with persistent PPD greater than 5 mm, these data suggest that surgical intervention may be needed less frequently for patients who daily administer 1.7% hydrogen peroxide gel in prescription trays as an adjunct to SRP.

Prescription-tray delivery of 1.7% hydrogen peroxide gel overcomes most of the limitations and problems associated with

the use of LDAs, such as home care restrictions around LDA sites, microbial overgrowth, bacterial resistance to antibiotics, patient drug allergies and sensitivities, and retention problems, and offers some potential advantages to patients: 1) can be used at home between office visits; 2) is non-invasive; 3) puts no restrictions on brushing or flossing around treatment sites; 4) is beneficial as full-arch treatment for numerous deep and/or bleeding pockets; 5) is possible for earlier adjunctive intervention than with other time-released LDAs; 6) can place medication into periodontal pockets of all depths, theoretically allowing for adjunctive care at the earliest stages of disease; and 7) delivers low-concentration hydrogen peroxide gel, which is a safe, well-known, oral debriding agent and wound cleanser.<sup>23</sup> In addition, while the prescription tray delivery approach requires daily use to be effective, subjects in this trial generally were receptive to administering treatments using properly fitted trays, especially after observing rapid improvements in their oral condition.

### Conclusions

When compared with SRP alone, the adjunctive use over six months of 1.7% hydrogen peroxide gel, locally administered using prescription customized trays for the treatment of subjects with moderate to advanced periodontitis, demonstrated clinical improvements in pocket depths and bleeding. Application of the peroxide/tray system for two weeks prior to SRP decreased gingival bleeding and pocket depth from baseline and when compared to the SRP control. Use of the prescription tray delivery of peroxide as adjunctive debridement care, compared with SRP alone, exhibited activity at all sites examined throughout the mouth, and was effective in reducing disease severity in both shallow ( $\leq 5$  mm) and deep ( $> 5$  mm) pockets, decreasing PPD in the latter by 1.50 mm versus 0.55 mm for SRP after 23 weeks.

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