Effects of hyperbaric oxygen therapy on the treatment of severe cases of periodontitis

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ABSTRACT

Objectives: To evaluate the effect of hyperbaric oxygen therapy (HBO₂) as an adjunct to scaling and root planing (SRP) in the treatment of severe cases of chronic periodontitis.

Materials and Methods: In 20 patients diagnosed with severe generalized chronic periodontitis (pockets > 7 mm) with bleeding on probing, SRP was rendered in all pockets. Additionally, five consecutive hyperbaric sessions were administered in 10 patients after random allocation (SRP + HBO₂). Clinical parameters were assessed at baseline up to six months: plaque index, bleeding on probing, probing depth, clinical attachment level and benzoyl-DL-arginine-naphthylamide (BANA) test.

Results: SRP + HBO₂ resulted in greater probing reduction and attachment gain than SRP alone three months after treatment (p < 0.001). The BANA test was negative after one week only for sites in the SRP + HBO₂ group (p < 0.05). However, SRP + HBO₂ failed to show a significant difference from SRP group after 3 months, where all BANA sites became negative (p > 0.05).

Conclusion: Our data suggest that hyperbaric oxygen therapy had a short-term beneficial effect on pocket reduction and bacterial elimination, and may be considered a potential adjunct therapeutic option to improve the clinical outcomes of scaling in severe cases of chronic periodontitis.

INTRODUCTION

Hyperbaric oxygen therapy (HBO₂) has been recommended when host compromising factors and/or comorbidities such as diabetes, collagen vascular disease, radiation exposure, trauma and vasculitis are present and might not result in good outcomes with the standard of practice treatments – or when the disease recurs in this group of patients (1). Fourteen conditions are approved for treatment with HBO₂ therapy: air or gas embolism, carbon monoxide poisoning and smoke inhalation, carbon monoxide poisoning complicated by cyanide poisoning, clostridial myonecrosis (gas gangrene), crush injury, compartment syndrome, decompression sickness (the “bends”), enhancement of healing in select problem wounds, exceptional blood loss (anemia), necrotizing soft tissue infections, osteomyelitis (refractory), radiation tissue damage (osteoradionecrosis), skin grafts and flaps (compromised) and other acute traumatic ischaeas (1).

The beneficial effects of hyperbaric oxygen therapy (HBO₂) as an adjunct in the management of periodontitis have been reported (2,3,4,5,6,7). The biological plausibility is based on the fact that oxygen tension is lower in deeper periodontal pockets (8), and this might favor a faster colonization of residual pockets by periodontopathogens (9,10,11). Hyperbaric therapy refers to placing the patient in a chamber to breathe oxygen produced at greater than one atmosphere. When oxygen is breathed at a pressure of 2 ATA (atmospheres absolute), it causes vasoconstriction by decreasing the blood flow rate by up to 20%. The normal tissue PO₂ is 30 to 40 mmHg, but in ischemia caused by infection, trauma or edema, oxygen levels fall much lower. Below 30 mmHg, fibroblast and
leukocyte functions are severely compromised. Hypoxia (15mmHg) stimulates angiogenesis and capillary budding (if the periphery of the hypoxic area has adequate perfusion/oxygenation). Hyperbaric oxygen increases collagen formation for capillary growth and arcing by providing the required matrix to support this process (12). HBO2 also promotes fibroblast replication, collagen formation and increased bactericidal function of leukocytes to take place while the patient is in the hyperbaric chamber (13). Surprisingly, compensation occurs by increasing the tissue oxygen tension (pO2), which may reach 250 to 300mmHg when hyperbaric oxygen is applied (12). In periodontal tissues, HBO2 has demonstrated beneficial effects on periodontal healing by raising the oxygen tension in the pocket (4,5,6,7).

In order to overcome possible failures in the periodontal treatment (14), and considering the antimicrobial and healing aspects of HBO2, the objective of the present study was to evaluate the immediate clinical effects of HBO associated with SRP in the treatment of cases of severe generalized chronic periodontitis.

MATERIALS AND METHODS
Experimental design
This was a parallel-group, randomized, single-blind preliminary clinical trial on treatment of severe generalized chronic periodontitis with hyperbaric oxygen therapy (HBO2). Following the CONSORT flowchart of the study (Figure 1, Page 109), the patients were randomly divided into two groups: SRP+HBO2—onestage scaling/root planing, followed by five consecutive hyperbaric sessions; and the SRP group—one stage scaling/root planing.

The following parameters were measured: plaque index (PI), bleeding on probing (BoP), probing depth (PD), and clinical attachment level (CAL). Clinical outcomes were evaluated at one week, one month and three months. Randomization was achieved by the use of sequentially numbered, identical containers containing SRP+HBO2 or SRP. The protocol for five consecutive HBO2 sessions was determined by the authors in this pilot study, as it was not found in the literature and established protocol for the use of HBO2 in periodontitis cases.

Study population
This preliminary (pilot) study was designed with 20 subjects (12 men, 8 women, mean age 37.3 years) selected from a pool of 360 patients referred to the Periodontal Clinic of the School of Dentistry at Bahian Science Foundation (FBDC, Bahia, Brazil). The patients had an initial diagnosis of severe generalized chronic periodontitis. Diagnosis was determined according to the American Academy of Periodontology-AAP (20) guidelines: presence of more than 30% of periodontal sites with pockets with more than 5mm of probing depth and more than 4mm of clinical attachment loss, bleeding on probing and calculus (20).

Exclusion criteria
Patients were excluded according to the following criteria: smoking, pregnancy or lactation, antibiotics or periodontal treatment within the last six months, a diagnosis of aggressive periodontitis, trauma from occlusion or endodontic lesions. According to an accurate clinical examination performed by a hyperbaric medical doctor (MD), the HBO2 contraindications (12) served as exclusion criteria. The only absolute contraindication to hyperbaric oxygen therapy was from patients with untreated pneumothorax; relative contraindications were included: upper respiratory infections, high fevers, emphysema with CO2 retention, history of thoracic surgery, malignant disease and middle ear barotrauma; and patients taking or have recently taken the following drugs: doxorubicin (Adriamycin®), disulfiram (Antabuse®), Cis-platinum and mafenide acetate (Sulfamylon®).

Ethics
The experiments of this research were undertaken with the understanding and written consent of each subject and in full accordance with ethical principles (World Medical Association Declaration of Helsinki, version VI, 2002). Subjects were also informed about the study outline and signed informed consent form in accordance with the Brazilian Council of Health Guidelines. The Brazilian Research Ethics Committee approved the protocol.
Baseline examination (Day 0) was carried out, including assessments of PI and BOP (14), and PD and CAL (16). At each recall visit, supportive periodontal therapy was provided, including monitoring and oral hygiene instruction. Re-evaluations were carried out on days 7, 15, 30, 60 and 90 after treatment. One calibrated examiner, who was unaware of the treatments, performed all examinations. Calibration included duplicate full-mouth assessment of 10 patients with disease severity similar to those included in the trial (kappa=0.9).

Hyperbaric oxygen sessions
The patients from SRP+HBO₂ group attended two HBO₂ sessions for five consecutive days, as determined by the authors, just after the SRP session. The patients used a multiplace HBO₂ chamber located at the Sagrada Familia Hospital (Salvador, BA, Brazil) under the supervision of a hyperbaric medicine specialist. For each session, patients were exposed to a pressure of 2.4 ATA, breathing pure oxygen for 72 minutes, with an air break of 15 minutes in the middle of the session. According to Hasson & Nahlieli (17), HBO₂ is absolutely contraindicated for individuals
with optical neuritis, viral infections and malignant tumors. There are no definitive studies on the application of HBO₂ for subjects with respiratory infections and pregnant women. The indication to patients with psychological disturbances is restricted because of the difficult management, and individuals submitted to otological or thoracic surgeries.

**BANA test**

The benzoyl-DL-arginine-naphthylamide (BANA) test was used in accordance with Loesche, et al. (18) to verify the presence of periodontopathogens by the trypsin activity in subgingival plaque at baseline, on Day 7 and after three months of treatments. In each patient, the deepest sites were selected for sample collection. Subgingival plaque samples were collected with site-individual sterile curettes (Hufriedy, USA) to avoid the possibility of cross-contamination from the same patient.

**Statistical analysis**

After checking for normality of data, the periodontal clinical parameters and BANA test were compared between groups by means of the Wilcoxon Rank Sum test for each experimental period. The intragroup analysis of all parameters was performed by means of the Friedman test ($\alpha = 5\%$).

**RESULTS**

**Patient selection**

Among 360 patients screened, only 20 patients fulfilled the exclusion criteria and presented a diagnosis of severe generalized chronic periodontitis according to the classification of AAP (20). Ten of 20 patients were randomized to the SRP+HBO₂ group, while an equal number was randomized to the SRP group-only management. All 20 patients initially selected and randomized have completed the trial (*Figure 1*). Plaque index (PI) and bleeding on probing (BoP) plaque and gingivitis presented high scores at baseline for all groups. After three months, there was a reduction in PI and BoP for all groups ($p<0.05$). However, no statistical differences were detected between groups after three months’ follow-up. Table 1 (*above*) summarizes these data.

**TABLE 1**

<table>
<thead>
<tr>
<th>PI – PLAQUE INDEX</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SRP+HBO₂ (n=10)</td>
<td>before</td>
<td>68.3%</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>32.2%</td>
</tr>
<tr>
<td>SRP (n=10)</td>
<td>before</td>
<td>79.4%</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>45.2%</td>
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<table>
<thead>
<tr>
<th>BoP – BLEEDING ON PROBING</th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SRP+HBO₂ (n=10)</td>
<td>before</td>
<td>63.62%</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>18.67%</td>
</tr>
<tr>
<td>SRP (n=10)</td>
<td>before</td>
<td>78.28%</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>28.34%</td>
</tr>
</tbody>
</table>

Table 1. Plaque index (PI) and bleeding on probing (BoP) at baseline (before) and at three months (after) treatments.

**Probing depth (PD) and clinical attachment level (CAL)**

Intragroup analysis showed a significant improvement in all parameters for both groups after the three-month period ($p<0.05$). However, an intergroup analysis showed that SRP+HBO₂ treatment presented the highest reduction in PD and gain in CAL after three months, compared with the SRP alone ($p<0.001$). No differences in gingival recession were observed. Data are presented in Tables 2 and 3 (*facing page*).

**BANA test**

The intragroup analysis showed all baseline BANA-positive pocket sites became negative at re-evaluation after three months ($p<0.05$) for both groups. Intergroup analysis showed that only the sites from SRP+HBO₂ group were BANA-negative at Day 7 ($p<0.05$); however, the BANA test did not present any difference between groups after three months (*Table 4*, facing page).
**DISCUSSION**

The present preliminary study was designed to investigate the short-term effect of hyperbaric oxygen therapy (HBO\textsubscript{2}) as adjunctive to scaling and root planing in patients suffering from extremely severe generalized chronic periodontitis. HBO\textsubscript{2} improved clinical parameters as to probing depth and attachment level, indicating that it could have beneficial effects on the initial periodontal treatment outcome. Furthermore, after seven days the HBO\textsubscript{2} treatment killed periopathogens that present trypsin-like activity (BANA test), while SPR sites became negative to BANA only after three months, indicating a possible short-term elimination and inhibition of recolonization by periodontopathogens (Porphyromonas gingivalis, Prevotella intermedia, Aggregatibacter actinomycetemcomitans).

Microorganisms can secrete different enzymes that can destroy collagen and growth factors. When the oxygen concentration in gingival tissue is low, the amount of bacteria in the periodontal pockets increases. HBO\textsubscript{2} seems to effectively decrease the amount of bacteria and simultaneously inhibit collagenase secretion. A study by Rabkin & Hunt (21) showed that oxygen at 2.0 ATA could inhibit the growth of certain pathogens related to periodontitis.

HBO\textsubscript{2} has shown bactericidal/bacteriostatic effects on actinomyces, bacteroides, and streptococcus (23). A study of Signoretto et al (7) showed a two-month lasting effect of HBO\textsubscript{2}/SRP therapy on reducing up to 99.9% the gram-negative anaerobe loads of the subgingival microflora, therefore decreasing the initial recolonization of the periodontal pockets. The results of Signoretto showed that the amount of anaerobic microorganisms decreased in all groups, but this occurred faster in the HBO\textsubscript{2} group, as demonstrated by the present study. A series of papers published by Chen (5,6,19,24,25, 26) indicated that the beneficial effects of HBO\textsubscript{2} on periodontal treatment outcome could last for

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**TABLE 2**  
<table>
<thead>
<tr>
<th></th>
<th>SRP (n=10)</th>
<th>SRP+HBO\textsubscript{2} (n=10)</th>
<th>p=Wilcoxon test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>6.57±2.4</td>
<td>7.40±3.3</td>
<td>0.921</td>
</tr>
<tr>
<td>Day 7</td>
<td>5.57±1.5</td>
<td>4.23±1.3</td>
<td>0.004</td>
</tr>
<tr>
<td>Day 15</td>
<td>5.37±1.4</td>
<td>3.80±1.2</td>
<td>0.006</td>
</tr>
<tr>
<td>Day 30</td>
<td>5.50±1.4</td>
<td>3.60±1.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Day 60</td>
<td>5.50±1.2</td>
<td>3.90±1.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Day 90 (3 mo)</td>
<td>5.47±1.1</td>
<td>3.70±1.3</td>
<td>0.000</td>
</tr>
</tbody>
</table>

p=Friedman test: 0.007 0.000

Table 2. Probing depth (PD) means values in millimeters at Days 0, 7, 15, 30, 60 and 90 (p-value for intra-group and intergroup analysis).

**TABLE 3**  
<table>
<thead>
<tr>
<th></th>
<th>SRP (n=10)</th>
<th>SRP+HBO\textsubscript{2} (n=10)</th>
<th>p=Wilcoxon test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>6.80±2.2</td>
<td>7.47±3.3</td>
<td>0.775</td>
</tr>
<tr>
<td>Day 7</td>
<td>5.80±1.4</td>
<td>4.30±1.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Day 15</td>
<td>5.60±1.4</td>
<td>3.87±1.3</td>
<td>0.005</td>
</tr>
<tr>
<td>Day 30</td>
<td>5.73±1.3</td>
<td>3.67±1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Day 60</td>
<td>5.73±1.3</td>
<td>3.97±1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Day 90 (3 mo)</td>
<td>5.70±1.5</td>
<td>3.77±1.4</td>
<td>0.000</td>
</tr>
</tbody>
</table>

p=Friedman test: 0.007 0.000

Table 3. Clinical attachment level (CAL) means values in millimeters at days 0, 7, 15, 30, 60 and 90 (p-value for intra-group and intergroup analysis).

**TABLE 4**  
<table>
<thead>
<tr>
<th></th>
<th>SRP (n=10)</th>
<th>SRP+HBO\textsubscript{2} (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Day 7</td>
<td>83%</td>
<td>0%</td>
</tr>
<tr>
<td>Day 90 (3 mo)</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 4. BANA test (median of BANA positive sites) at baseline, Day 7 and after three months.
longer than one year. They concluded that the effect of hyperbaric oxygen on periodontitis appears to involve the inhibition of growth and reproduction of subgingival plaque at the base of pockets, inhibiting initial bacterial recolonization (4,19,24,25,26).

Probing depth and clinical attachment were affected by the adjunctive HBO in the present study, probably due to the enhanced connective tissue proliferation and greater fibroblast collagen production in periodontal tissues (4). However, healing might initially enhance an immunologic or antimicrobial effect promoted by the oxygen therapy, followed by a greater fibroblastic activity (27,28,29,30), greater angiogenesis (2,3,31,32,33) and revascularization of compromised tissue (12,17,24,25,26,34,35).

In the United States, CMS (Center for Medicare /Medicaid Services) recognizes hyperbaric oxygen therapy as a reimbursable treatment for the 13 UHMS-approved conditions. An HBO2 session can cost anywhere from $100 to $200 in private clinics to more than $1,000 in hospitals. U.S. physicians may prescribe HBO2 for “off-label” conditions such as Lyme disease, stroke and even migraines. Such patients are typically treated in non-hospital affiliated HBO2 facilities or under research protocols at hospital affiliate HBO2 units. In the United Kingdom, the National Health Service finances most HBO2 chamber operations. The authors agree that HBO2 therapy could be considered a real option in dentistry, as the present study has demonstrated some evidence of clinical applicability and viability of this treatment modality in the dental practice.

Despite the fact that this study was a preliminary evaluation of HBO2 effects on periodontitis in a limited number of assigned patients, the contra-indications and the periodontal diagnosis of severe generalized periodontal cases were also considered as limitations in the present study. Nevertheless, the authors agreed that adjunctive HBO2 is still a potential option for treatment in selected cases in the practice, especially for patients with diabetes and advanced periodontitis. Meanwhile, the molecular mechanisms of HBO2 therapy in periodontal disease outcomes need further investigation. Indeed, longitudinal studies are necessary to investigate the long-term beneficial effects of hyperbaric oxygen therapy on severe cases of periodontitis.

CONCLUSIONS

Within the limitations of this preliminary study, the present study seeks to provide additional evidence regarding the benefits of HBO2 as an adjunct in the treatment of periodontitis, especially in the severe generalized cases.

REFERENCES
