Adjunctive Hyperbaric Oxygen Therapy promotes successful healing in patients with refractory Crohn’s disease

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ABSTRACT

PURPOSE: To investigate the adjunctive effect of Hyperbaric Oxygen Therapy in a group of patients with refractory Crohn’s disease.

METHODS: A total of 29 subjects with refractory Crohn’s disease were submitted to daily sessions of Hyperbaric Oxygen Therapy, in a 2800 Sechrist Monoplace Hyperbaric Chamber (Sechrist, USA) pressurized to 2.4 ATA. Each session lasted 2 hours. The endpoint was closure of entero-cutaneous fistulas and complete healing of Pyoderma Gangrenosum and perineal Crohn’s disease.

RESULTS: A total of 829 HBOT sessions were performed and no complications were noted. Overall success rate was 76% (22 cases). Pyoderma Gangrenosum and entero-cutaneous fistulas had the highest successful healing rates (100% and 91%, respectively). Perineal Crohn’s disease healing rate was 65%.

CONCLUSION: Adjunctive Hyperbaric Oxygen Therapy promoted satisfactory healing in a group of patients with refractory Crohn’s disease.

Key words: Hyperbaric Oxygenation. Crohn Disease. Cutaneous Fistula. Pyoderma Gangrenosum.
Introduction

Crohn’s disease (CD) is a chronic inflammatory condition resulting from aberrant immune system activation. The disease primarily affects the gastrointestinal system but other organs may be involved.

Clinical manifestations are heterogeneous and may vary from mild cases (abdominal pain, changes in bowel habit and weight loss) to serious complications such as acute abdomen, perineal sepsis, fistulizing disease and colorectal cancer. The course of the disease is usually relapsing but some individuals may experience continuous inflammation.

Since CD cannot be cured, most treatment options aim the induction and maintenance of remission by controlling inflammation. Surgery is usually recommended for non-responsive or complicated cases.

Some studies have shown benefits of hyperbaric oxygen therapy (HBOT) especially in the treatment of complex perineal wounds, pyoderma gangrenosum (PG) and fistulizing disease. HBOT is a treatment modality that consists in 100% oxygen breathing in pressurized chambers. The improvement with HBOT is attributed to local events (such as neovascularization and reduced hypoxia, stem cell mobilization/differentiation and extracellular matrix formation) and systemic effects (decrease in proinflammatory cytokines and biomarkers of oxidative stress).

The purpose of this study was to evaluate the adjunctive effect of HBOT in a group of patients with pharmaco-refractory perineal Crohn’s disease (PCD), enterocutaneous fistulas (ECF) and PG.

Methods

Patients

A prospective institutional review board–approved study was conducted at Clinics Hospital-University of São Paulo (Ribeirão Preto, SP, Brazil). A total of 29 patients with pharmaco-refractory CD associated with ECF, PCD or PG were selected to HBOT, from 2008 to 2015. An informed written consent was provided in all cases. Hyperbaric sessions were performed at Hyperbaric Medicine Center-São Paulo Hospital (Ribeirão Preto, SP, Brazil) that keeps a prospective, database of all sessions.

Hyperbaric oxygen therapy

Daily HBOT sessions were performed in a 2800 Sechrist Monoplace Hyperbaric Chamber (Sechrist, USA) pressurized to 2.4 ATA and lasted 2 hours, each. The number of sessions was not constant and varied according to the clinical outcome of patients in order to obtain the best results. Basic care of chronic cutaneous lesions was maintained throughout the entire treatment and included cleaning and dressings, antibiotics and surgical debridement when needed. The result of HBOT was classified as satisfactory or unsatisfactory, when improvement could not be noted.

Results

The most common indication for HBOT was PCD (n=15 / 51.7%) followed by ECF (n=8 / 27.5%) and PG (n=3 / 10.3%). An association between ECF and PCD was noted in 1 (3.5%) case. Concomitant ECF and PG were found in 1 (3.5%) patient. One patient (3.5%) exhibited all three complications. Table 1 summarizes some of the patients and treatment characteristics.

The median number of sessions was 20 (range, 10-86). A total of 829 HBOT sessions were performed and no complications were noted. Overall success rate was 76% (22 cases). Figure 1 illustrates some cases before and after HBOT. PG and ECF had the highest successful healing rates (100% and 91%, respectively). PCD completely healed in 65% of the cases. The remaining patients had an unsatisfactory response and needed major surgery surgeries (intestinal diversion with proctectomy or abdominal-perineal amputation of the rectum).
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ECF: enterocutaneous fistula, PCD: perineal Crohn's disease, PG: pyoderma gangrenosum
The complete pathogenesis of CD is unclear. Animal models of colitis have shown that intestinal hypoxia may be observed as inflammation aggravates. This hypoxic microenvironment, in thus, is a potent stimulus to further inflammation and apoptosis via increases in hypoxia-inducible transcription factor (HIF) levels. This state of perpetual inflammation can be halted by increases in tissue oxygenation. Measurements of oxygen tension on perineal wounds may exhibit increases up to 35 times after HBOT. Perianal disease can be found in up to 35-45% of CD patients. Anorectal abscesses, fissures and fistulas are the most common findings. Appropriate treatment involves the use of symptomatic medication, local care (cleansing and sitz baths), antibiotic therapy and immunomodulators in some cases. Surgery is usually recommended for resistant or complex perineal wounds. Care should be taken to avoid extensive damage since poor healing may be found, specially if severe proctitis is present.

Reported response rate for perineal disease treated in regimens of hyperoxygenation range from 75-100%. In the present study, complete healing of PCD was obtained in the majority of patients. Although minor surgical procedures were necessary to remove devitalized tissues and control infection, no intestinal diversion or proctectomy was necessary in the group that responded to HBOT.

The effects of HBOT in complex wounds include: decreased inflammation and tissue edema, mobilization of stem cells, neovascularization, fibroblasts growth and extracellular matrix formation. Those changes in wound microenvironment are powerful stimuli towards healing and could explain some of the results found in CD patients with complex wounds. The same rationale could be used to explain the pain relief, systemic corticosteroids reduction and accelerated healing in PG patients.

The use of HBOT in enterocutaneous fistulas may be appropriate if output volume is low. Complicated Fistulas with higher debit, chronic course, labiate, with satellite collection and distal obstruction may have an initial conservative approach; yet, surgery is usually the definite treatment. In the present study, treatment of ECF with HBOT was considerate excellent; however, patients were evaluated immediately after the HBOT sessions and there is no long-term follow-up. Healing failure was found in only one patient with a chronic fistula of high output volume. This successful healing rate may be explained by the systemic antinflammatory properties of HBOT.

The results of this research are encouraging since patients who were refractory to maximum medical treatment obtained high healing rates; however, the small number of patients, the short-term follow-up and the lack of a control group limit our conclusions. Part of the good results could be explained by the close monitoring of patients that included daily clinical evaluations, intensive wound care and optimization of medical therapy. A prospective controlled study could solve this problem; yet, it would be ethically questionable to create a control group and deny a possibility of treatment in patients with an aggressive condition and limited therapeutic options. This pattern of limitation is shared by most studies that deal with HBOT in severe/refractory CD. The authors believe that a randomized controlled trial with HBOT in CD patients in earlier stages of disease is necessary and will contribute to reduce biases.
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Conclusion

A high healing rate was observed in a group of patients with complicated and refractory CD after HBOT. No complications were found during the procedure. The results suggest that HBOT may have an adjunctive role in CD complications. Further investigation is necessary to strengthen our findings.

References


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