Hyperbaric Oxygen for Perianal Crohn’s Disease

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Perianal involvement in Crohn's disease is common (<= 50%), distressing, and frequently refractory to treatment. Clinical features include painful induration and stenosis, discharging fistulas, and fissures. The pathogenesis of these lesions is unclear, but local ischemia and secondary anaerobic infection may play a role. Following three sporadic reports of successful treatment with hyperbaric oxygen (HBO), we undertook a trial of this method in 10 patients with refractory perianal disease. These patients' perianal Crohn's disease had not responded to treatment that included local medications, salicylates, corticosteroids, metronidazole, or 6-mercap-topurine were treated. Treatment was administered in a hyperbaric chamber at a pressure of 2.5 atm absolute. Each session lasted 90 min, and each course consisted of 20 daily sessions. Complete healing occurred in 5 patients after one to two courses. In an additional 2, after three courses, 1 patient improved but did not heal, and 2 did not improve. No adverse effects were noted by any of the 10 patients. Follow-up of 18 months did not reveal any recurrence. These preliminary results confirm that HBO therapy is a safe and efficient therapeutic option for perianal Crohn's disease.

Key Words: Crohn's disease-Perianal involvement-Hyperbaric oxygen therapy.

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Crohn's disease involves the perianal region in <= 50% of patients (1) and causes painful induration, abscesses, fistulas with discharge, and fissures, which are extremely distressing to the patient and refractory to treatment (2,3). The reason for these lesions is poorly understood (4,5). Their indolent nature is compatible with ischemia and secondary bacterial invasion as possible pathogenetic factors. Wakefield et al. (5) conducted morphological studies that demonstrated occlusive fibrinoid lesions of the arteries supplying areas of the intestine affected by Crohn's disease. Hypoxia can compromise wound healing (6), whereas improved tissue oxygenation can restore a favorable cellular milieu in which the wound healing process and host antibacterial mechanisms, particularly against anaerobes, are enhanced (6,7).

Following sporadic case reports of the successful integration of hyperbaric oxygen (HBO) treatment in patients with fistulas due to Crohn's disease (8-10), we undertook a trial of this therapy in 10 consecutive patients, some of whom had not responded to prolonged conventional therapy with salicylates, corticosteroids, metronidazole, and 6-mercaptopurine. Our results are reported here.

METHODS

Ten patients with Crohn's disease involving the perianal region were treated with HBO. Perianal disease was selected as the only obvious parameter to follow objectively. In most of the patients, activity of the disease, as demonstrated by the Harvey Bradshaw activity index (11), was relatively low grade except for the perianal disease (Table 1).

Inclusion Criteria

The treatment was offered to all patients with perianal Crohn's disease who were willing to undergo the 90-mm daily sessions in the hyperbaric chamber. Each had a complete physical examination and routine blood tests, as well as chest x-ray and ear, nose, and throat (ENT) examination before therapy. The nature and severity of the perianal disease were documented before and after each course of therapy.

HBO was administered in a multiplace hyperbaric chamber constructed by Drager, Germany. A course of 20 daily treatments (6 times weekly) was given (100% oxygen for 90 mm at a pressure of 2.5 atm absolute). The patients were reexamined at the end of the treatment period. A further treatment of 20 sessions was administered if complete resolution had not occurred. The patients were reexamined, and a decision was made regarding a third course.

TABLE 1. Patients with Crohn's disease treated with hyperbaric oxygen

No	Age, Sex	Crohn's index before/after therapy	Duration of disease(duration of perianal disease)	G.I. involvement	Perianal involvement	Concomitant medication	20 treatment assessment	40 treatment assessment	60 treatment assessment
1	58, F	154/148	3 yr (2 yr)	Colon	Fistual on buttock, Perianal infiltration	Sulfasalazine	Complete healing		
2	30, M	83/92	4 yr (6 mo)	Terminal ileum Rectum	Perianal infiltration	Mesalazine	Complete healing		
3	36, F	268/245	14 yr (8 yr)	Colon	2 perianal fistulas to skin, 1 to vagina Severe anal narrowing and infiltration (digital examination impossible)	Sulfasalazine	Closure of 2 fistulas Improved anal diameter	Improved inflammation, less narrowing, resolution of abdominal pain and bloating	Further improvement Resolution of stenosis
4	51, F	154/138	24 yr (6 mo)	Colon	Perianal fistula and infiltration	Mesalazine	Closure of fistula infiltration remains	Complete healing	
5	34, F	150/150	14 yr (4 mo)	Colon	Perianal fistula and infiltration	Sulfasalazine	Closure of fistula infiltration remains	Complete healing	
6	30, M	308/312	13 yr (12 yr)	Diffuse small and large bowel	Severe disease with a fistula and 8 cm circular infiltration	Mesalazine	Improved fistula Infiltration reduced	3 cm infiltration, new fistula	
7	59, M	92/90	40 yr (10 yr)	Diffuse small and large bowel	Perianal fistula	Prednisone Sulfasalazine Imodium	Complete healing		
8	64, M	62/66	11 yr (1 yr)	Large bowel	2 fistulas and infiltration	Sulfasalazine	Closure of fistulas	less infiltration	Complete healing
9	40, M	374/360	12 yr (8 yr)	Small bowel	20 cm infiltration, 6 fistulas, 1 fistula to groin	Mesalazine	Closure of 3 fistulas and 1 to groin	No further improvement	No further improvement
10	34, M	34/34	18 mo (same)	No intestinal involvement	8 fistulas, severe infiltration	None	Closure of 4 fistulas	Improved inflammation	Healing

*Cases 4 and 10 are discussed in greater detail under "Representative Cases" subsection of "Results." See ref. 11.

Cost

The estimated cost of treatment is $100 per hour. This was covered in full by the patients' medical insurance.

RESULTS

The results are summarized in Table 1. Improvement occurred in 8 of 10 patients. In 3 patients, complete healing of perianal lesions occurred after a single course; in 2, after two courses. In 3 patients, three courses were required. Two patients did not improve. None of the patients reported side effects.

REPRESENTATIVE CASES

Case 4

A 51-year-old woman developed perianal disease after a 24-year history of Crohn's colitis with an active fistula and circumferential perianal infiltration. She had been treated with Mesalazine only.
The fistula closed after 20 treatments, but there was residual scarring and inflammation. She was given a further 20 treatment sessions, with complete resolution of the perianal disease that has been maintained for 18 months of follow up on maintenance mesalazine only.

Case 10

A 34-year-old man developed severe perianal disease without any bowel involvement. Examination revealed severe inflammatory induration and 8 fistulas. Treatment for 1 year with salicylates, steroids, and metronidazole was ineffective. After one course of HBO treatment, 4 fistulas closed, and after two additional courses his disease healed.

DISCUSSION

HBO, the inhalation of 100% oxygen at a pressure >1 atm (12), is now an established mode of therapy for a variety of medical conditions (12-14). These conditions include chronic wounds in diabetes and the complications of trauma and radionecrosis (15), including radiation damage to the gastrointestinal tract (16). The therapeutic effect of HBO is due to the physiological effect of hyperoxia. Although the inhalation of high concentrations of oxygen has a limited impact on total hemoglobin oxygen content, it produces an increase in the amount of dissolved oxygen in the plasma that is directly proportional to the rise in the ambient pressure. When 100% oxygen is breathed at an absolute pressure of 3 atm, the plasma oxygen content increases from 0.32 to 6.8 vol% (17). This considerable increase in the amount of oxygen that can be delivered and made available to the tissues under conditions of high pressure is probably of great importance in cases where improved tissue oxygenation is required. Hypoxia can appear in normally perfused tissue that is the site of an inflammatory reaction. HBO at an absolute pressure of 2 atm has been shown to improve tissue oxygenation in this situation (18).

The perianal lesion of Crohn's disease is in many ways a "chronic non healing wound" because of its indolent nature, its refractoriness to treatment, and the possible role of local ischemia in its pathogenesis (2,3,5). The chronic non healing wound is an established indication for HBO therapy (12-14). The best results have been reported for diabetic wounds, in which microangiopathy, ischemia, and hypoxia are important pathophysiological factors. When a high partial pressure of oxygen is breathed, there is correction of the surrounding hypoxia at sites supported by diseased vessels. The intermittent correction of wound hypoxia by HBO therapy elevates oxygen tensions in ischemic or infected wound tissue (19). Enhanced tissue oxygenation has a vasoconstrictive effect believed to reduce tissue edema (20) and restore fibroblast proliferation, collagen synthesis (21), and capillary angiogenesis (22). Thus, oxygen may be the wound's most essential nutrient (14).

Because of its location, the perianal lesion may be prone to bacterial contamination. Oxygen also has an antimicrobial effect, particularly on anaerobes (7). It plays a crucial role in the cellular response to infection. Neutrophils require molecular oxygen as a substrate for microbial killing by phagocytes, a process that depends on the formation of free radicals. The oxidative burst observed in neutrophils after the phagocytosis of bacteria involves a 10- to 15-fold increase in oxygen consumption (23,24). This oxidative antimicrobial system virtually ceases to function under conditions of hypoxia. A tissue $P0_2$ >= 30 mm Hg is considered necessary for normal oxidative function (25). Partial pressure of oxygen in diseased or injured tissue is often < 30 mm Hg (19). Improved oxygenation leads to restoration of white blood cell function and renewal of adequate antimicrobial action.

HBO is administered in a hyperbaric chamber in which 100% oxygen is breathed at pressures greater than atmospheric. The multiplace chamber used in this study is compressed with air, and oxygen is delivered to patients at the ambient pressure via a mask. In such a chamber, <= 20 patients may be treated simultaneously and are always accompanied by a trained attendant during treatment. Instrumentation and all the requirements for critical care support are on hand inside the chamber.

Our present series confirms the encouraging results reported in previous isolated case reports. In all our patients with mild or moderate disease and in some with severe disease, healing was complete after a single course of hyperbaric treatment and has been maintained for <= 18 months following treatment. In some of the severe cases, there was also remarkable improvement although several courses were required. Because systemic activity of Crohn's disease was relatively low grade in all patients reported here, possible effects of HBO on other manifestations of Crohn's disease could not be estimated from this study (see activity indexes, Table 1).

HBO is a safe form of therapy (26-28). No side effects were noted in this group of patients. Therefore, it should be considered in patients suffering from perianal Crohn's disease who have failed to respond to conventional therapy. Definitive proof of the efficacy of this mode of therapy requires a well controlled double blind study that we think is well worth doing.

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