

# Hyperbaric Oxygen as Successful Monotherapy for a Severe Ulcerative Colitis Flare

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## Lay Summary

This report presents a case of severe ulcerative colitis treated with hyperbaric oxygen as successful monotherapy.

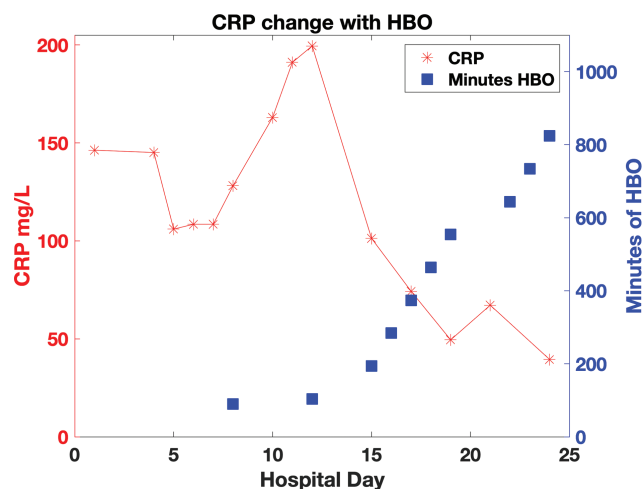
**Key Words:** inflammatory bowel disease, ulcerative colitis, hyperbaric oxygen therapy, IBD flare, pyoderma gangrenosum.

## CASE REPORT

Hyperbaric oxygen (HBO<sub>2</sub>) has promise as an ulcerative colitis (UC) adjunctive treatment but, to our knowledge, has not been used as a single-agent treatment for an ulcerative colitis flare.<sup>1</sup> We report on a 33-year-old man with severe UC who received HBO<sub>2</sub> alone for a flare. He was admitted with fever, abdominal cramping, 8 bloody bowel movements a day, skin pustules, and a C-reactive protein (CRP) of 146.3 mg/L. Prior UC treatments included adalimumab and infliximab, which both resulted in antibody-mediated hypersensitivity reactions. He developed pyoderma gangrenosum while on vedolizumab, so this medication was stopped. Tofacitinib was considered but was thought to be too risky because of its association with herpes infections and because he was healing from a shingles episode. Because the skin pustules might be persistent shingles, he did not receive intravenous steroids to avoid progression to disseminated herpes. He did not want a colectomy. With limited treatment choices that did not suppress his immune system further, other options were needed.

He began HBO<sub>2</sub> on hospital day 8 and was discharged on hospital day 24. He received 10 treatments at 2.4 ATA with a marked reduction in both CRP and stool frequency (Figure 1). He continued to a total of 30 HBO<sub>2</sub> treatments at 2.4 ATA for 90 minutes over a month and a half while insurance approval for ustekinumab was pursued. Forty-three days after admission, however, his CRP began to rise again coincident with his *Clostridioides difficile* screen turning positive. However, his pyoderma gangrenosum had resolved. He was started on ustekinumab for maintenance therapy 57 days after admission and did well.

Hypoxia and hypoxia signaling pathways play a role in the pathogenesis of inflammatory bowel disease, causing inflammation and disrupting the microbiome.<sup>2</sup> HBO<sub>2</sub> delivers 100% oxygen at pressures greater than atmospheric, reducing hypoxia in the bowel and altering hypoxia-inducible factor 1 and heme oxygenase pathways.<sup>3,4</sup> The hypoxia-inducible factor 1 and heme oxygenase pathways may play protective



**Figure 1.** The patient's C-reactive protein (CRP) declined markedly with hyperbaric oxygen (HBO) therapy. The left y-axis shows the CRP level and the right y-axis shows the cumulative number of minutes of HBO given. A single treatment usually provides 90 minutes of HBO, although initially the patient could not always tolerate the full 90 minutes in the chamber.

roles in IBD, enhancing both epithelial and immune function.<sup>5</sup> Furthermore, HBO<sub>2</sub> reduces inflammatory cytokines, including interleukin-1, interleukin-6, and tumor necrosis factor  $\alpha$ , and may also affect the gut microbiome.<sup>4,6,7</sup>

HBO<sub>2</sub> is a novel UC treatment and has been given adjunctively with other therapies for flares.<sup>1</sup> In this case, HBO<sub>2</sub> was used as single-agent therapy, which supports using HBO<sub>2</sub> for treating these flares. For severe disease or for patients unable to tolerate steroids and other immunomodulatory medications, HBO<sub>2</sub> is safe and may improve outcomes.

## Conflicts of Interest

None declared.

## References

- 1 Dulai PS, Buckey JC Jr, Raffals LE, et al. Hyperbaric oxygen therapy is well tolerated and effective for ulcerative colitis patients hospitalized for moderate-severe flares: a phase 2A pilot multicenter, randomized, double-blind, sham-controlled trial. *Am J Gastroenterol*. 2018;113(10):1516-1523.
- 2 Cummins EP, Crean D. Hypoxia and inflammatory bowel disease. *Microbes Infect*. 2017;19(3):210-221.
- 3 Parra RS, Lopes AH, Carreira EU, et al. Hyperbaric oxygen therapy ameliorates TNBS-induced acute distal colitis in rats. *Med Gas Res*. 2015;5:6.
- 4 Gonzalez CG, Mills RH, Kordahi MC, et al. The host-microbiome response to hyperbaric oxygen therapy in ulcerative colitis patients. *Cell Mol Gastroenterol Hepatol*. 2022;14(1):35-53.
- 5 Glover LE, Colgan SP. Hypoxia and metabolic factors that influence inflammatory bowel disease pathogenesis. *Gastroenterology* 2011;140(6):1748-1755.
- 6 Weisz G, Lavy A, Adir Y, et al. Modification of in vivo and in vitro TNF-alpha, IL-1, and IL-6 secretion by circulating monocytes during hyperbaric oxygen treatment in patients with perianal Crohn's disease. *J Clin Immunol*. 1997;17(2):154-159.
- 7 Colgan SP, Curtis VF, Campbell EL. The inflammatory tissue microenvironment in IBD. *Inflamm Bowel Dis*. 2013;19(10):2238-2244.