Contents lists available at Wolters Kluwer - Medknow

Medical Gas Research

journal homepage: www.medgasres.com

Oxygen therapy in ischemic colitis

Jamil Nasrallah, Ali Dheyaa Marsool, Alaa Mohammed Oudah, Abdulrahman Abbas Al-Husseini, Jobran Toami, Hiba Hamdar*

Ischemic colitis (IC) is a condition induced by ischemia that occurs as a result of reduced blood supply to a colon segment, leading to tissue damage and inflammation.[1, 2] It is most commonly arisen with abdominal cramping and urgency and, at times, with rectal bleeding, which leads to severe discomfort for the patient Although treatments to improve blood flow and alleviate symptoms exist, there is a pressing need to explore novel therapies to enhance patient outcomes and prevent complications.[1] Targeted oxygen therapy is an emerging area of research. Given that IC results from inadequate blood flow, which leads to insufficient oxygenation, evidence suggests that controlled oxygen delivery could nourish vulnerable tissues and promote faster recovery.[2] As oxygen therapy has shown promise in treating wounds and other hypoxic conditions, its application to the colon appears both plausible and promising. Utilizing this established medical treatment has the potential to improve quality of life and offer new promise for IC patients. Targeted oxygen therapy may be a novel approach to facilitate tissue repair and prevent severe complications, as oxygen shortage is central to IC pathophysiology. This perspective discusses the pathophysiological rationale for oxygen therapy for IC, summarizes current clinical evidence, and addresses practical considerations for its use in clinical practice.

Pathophysiology of IC: IC occurs when blood flow to the colon is compromised, resulting in insufficient oxygen delivery and cellular damage. This is most common in "watershed" zones, where arterial supplies converge and blood flow is naturally more tenuous.[3] When the colon's tissues lose their oxygen supply, an inflammatory cascade occurs.

Inflammation and increased permeability of the gut lining result from the release of mediators by abused cells that draw immune cells into the tissue area. Hypoxia in colonic mucosa causes cellular dysfunction, mitochondrial dysfunction, and generation of reactive oxygen species, which, in turn, aggravate local tissue damage.[3, 4] The inflammatory mediators tumor necrosis factor-α and interleukin-6 contribute to intestinal permeability and epithelial destruction.[4] The tissue may become necrotic in extreme situations, increasing the risk of a major infection and a perforation.[2, 3] A common stage of this pathophysiological mechanism is the mismatch between the oxygen demand and the colon's limited blood supply. This vicious loop causes inflammation, tissue damage, and more irreversible damage if treatment is not received.[1-3]

Rationale for oxygen therapy in IC: ***Physiological basis of oxygen therapy:*** Reduced blood flow to the colonic mucosa causes IC, which in turn causes inflammation, damage to the epithelial barrier, and hypoxia of the colon tissue.[5] Oxygen imbalance, oxidative damage, and tissue destruction result from the gastrointestinal system's need for an optimum oxygen supply. An inflammatory reaction will be triggered if there is ischemia, which will further harm the tissues and veins and complicate matters. Hyperbaric oxygen therapy (HBOT) presents vast promise because patients breathe 100% oxygen under high pressure, thus greatly enhancing the diffusion of oxygen to the oxygen-starved tissues and accelerating healing.[5] Moreover, oxygen therapy inhibits fluid leakage into the interstitial space and prevents the extravasation of inflammatory mediators through stabilization of endothelial cells and reduction of vascular permeability. Oxygen therapy may lessen the ischemia-reperfusion damage cycle and aid in the restoration of intestinal barrier integrity by enhancing microcirculatory activity.[6]

Experimental and clinical evidence supporting HBOT in ischemic conditions: Research has shown that HBOT is effective in treating ischemic disorders such as intestinal ischemia, myocardial infarction, and stroke. It has been demonstrated that intestinal tissues are protected against oxidative mitochondrial damage by hyperoxygenation.[7] HBOT strengthened intestinal barriers, decreased inflammation, and aided in vascular repair in animal models of ischemia-reperfusion injury.[7] HBOT's function in inflammatory bowel disorders, which histologically resemble IC, is further supported by clinical data.

A systematic review of HBOT in Crohn's disease and ulcerative colitis reported significant improvements in clinical symptoms and inflammatory markers, supporting its potential for IC management.[8] Additionally, studies on perianal fistulizing Crohn's disease indicate that HBOT enhances wound healing by addressing local hypoxia and promoting tissue regeneration through angiogenesis.[9] These findings, rooted in the vascular and inflammatory etiology of IC, suggest that HBOT could be a valuable treatment component. A meta-analysis of HBOT in Crohn's disease and ulcerative colitis demonstrated reduced inflammatory markers and disease severity, indicating potential benefits for IC.[10]

Alternative oxygen delivery methods: Although HBOT shows promise, it is resource-intensive and not widely accessible. Normobaric oxygen therapy, which delivers oxygen at atmospheric pressure, has been explored as an alternative.[6] However, studies suggest that normobaric oxygen therapy is less effective than HBOT for mild to severe hypoxia in colonic ischemia due to its limited oxygen transport capacity.[6] Future research should compare these modalities to determine optimal patient selection and treatment protocols. Emerging approaches, such as transcutaneous oxygen therapy and perfluorocarbon-based oxygen carriers, also warrant investigation for delivering oxygen to ischemic regions.[4, 11]

Potential mechanisms of benefit: HBOT exerts powerful anti-inflammatory effects due to increased expression of antiinflammatory mediators and decreased expression of pro-inflammatory cytokines.[10] The treatment has been indicated for suppression of tumor necrosis factor-alpha and interleukin-6, key players in the inflammatory response of IC. Antioxidant enzymes that counteract oxygen free radicals and prevent additional tissue damage are also more active when oxygen levels are higher.[10] **Figure 1** summarizes the therapeutic benefits of HBOT in IC. The ischemia state is shown to have hypoxia, inflammation, and malfunction of the epithelial barrier, whereas HBOT encourages oxygenation, angiogenesis, and epithelial repair. Restoring vascularization is another crucial function of HBOT. Sufficiently high vascular endothelial growth factor levels in an HBOT regimen almost certainly lead to angiogenesis, including improved microcirculatory perfusion. These factors collectively contribute to tissue regeneration in IC. Enhanced oxygenation supports new blood vessel formation, reduces vascular permeability, and accelerates colonic mucosal repair.[8]

HBOT also supports the intestinal epithelial barrier by promoting mucin production, particularly mucin 2, which strengthens the barrier layer. Additionally, HBOT enhances tight junction protein expression, reducing intestinal permeability and preventing bacterial translocation in ischemic conditions.[9]

MEDICAL GAS RESEARCH
www.medgasres.com

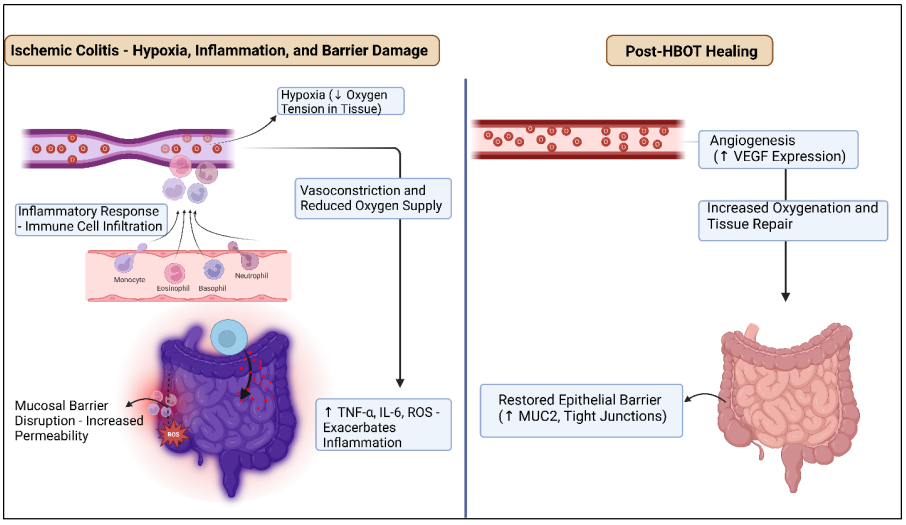

Figure 1 | **Pathophysiology of ischemic colitis (left panel) and therapeutic effects of HBOT (right panel).** The ischemic state is characterized by hypoxia, inflammation, and barrier disruption, while HBOT enhances oxygenation, promotes angiogenesis (↑VEGF), and restores epithelial integrity (↑MUC2, tight junctions). Created with BioRender.com. HBOT: Hyperbaric oxygen therapy; IL: interleukin; MUC2: mucin 2; ROS: reactive oxygen species; TNF: tumor necrosis factor; VEGF: vascular endothelial growth factor.

Challenges and limitations: No high-quality data, such as meta-analyses or randomized controlled trials, currently support oxygen or HBOT for IC. Current guidelines recommend antibiotics and supportive care, with no evidence for alternative pharmacological treatments.[11] HBOT's limited availability, requirement for specialized facilities, and need for multiple sessions over days make it impractical for critically ill patients. Patients with unstable IC at risk of perforation often require immediate surgery, rendering oxygen therapy ineffective in such cases. Moreover, many IC patients are elderly with pulmonary or cardiac comorbidities, making prolonged hyperbaric sessions challenging. Accessibility and cost further limit its feasibility.[11] Although oxygen therapy is a supportive strategy rather than a cure-all, it may be useful in certain moderate situations. In patients with full-thickness necrosis or peritonitis, it cannot take the place of surgery, and it is still challenging to identify those who might benefit. As a result, its clinical use is restricted.

Priorities and future directions: Despite the potential of oxygen therapy in IC, several questions remain. A key issue is whether normobaric or hyperbaric oxygen delivery is more effective. Normobaric oxygen is administered at atmospheric pressure, while hyperbaric oxygen is delivered at higher pressures.[6] Future studies should determine the optimal oxygen dose, treatment duration, and the relative benefits and risks of each approach.

Further research is needed to elucidate biological roles of oxygen in inflammation and tissue repair. Though oxygen is required for tissue repair and inflammation, the pathways are unknown. Understanding the pathways better will lead to the possible development of new drugs or combination therapy. Patient-specific protocols of oxygen treatment based on patient parameters such as illness severity, age, and comorbidities can make treatment better. According to a 2014 study by Dulai et al.[12] on inflammatory bowel disease hyperbaric oxygen treatment, patient individualization of HBOT regimens, i.e., variation in session frequency and pressure of oxygen, can maximize therapy benefits and reduce side effects. This approach could enhance patient selection for IC, addressing present challenges in identifying potential individuals. Practical limitations, such as the scarcity of hyperbaric chambers and high costs, also need addressing.[11] Developing accessible and cost-effective delivery methods or integrating oxygen therapy into standard care could enhance its clinical utility.

Conclusion: Although oxygen therapy may have significant potential for IC treatment, further investigations are required before wide clinical application. Studies should focus on overcoming current limitations and optimizing treatment protocols. If future research confirms its efficacy and establishes precise guidelines, oxygen therapy could accelerate recovery in IC, leading to improved patient outcomes.

Jamil Nasrallah, Ali Dheyaa Marsool, Alaa Mohammed Oudah, Abdulrahman Abbas Al-Husseini, Jobran Toami, Hiba Hamdar*

Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon (Nasrallah J, Toami J)

University of Baghdad/Al-Kindy College of Medicine, Baghdad, Iraq (Marsool AD, Oudah AM, Al-Husseini AA)

Plovdiv Medical University, Plovdiv, Bulgaria (Hamdar H)

Medical Learning Skills Academy, Beirut, Lebanon (Hamdar H)

***Correspondence to:** Hiba Hamdar, MD, hamdarhiba95@gmail.com.
https://orcid.org/0000-0002-4488-7323 (Hiba Hamdar)

Date of submission: March 29, 2025
Date of decision: June 10, 2025
Date of acceptance: June 27, 2025
Date of web publication: August 18, 2025

https://doi.org/10.4103/mgr.MEDGASRES-D-25-00093
How to cite this article: *Nasrallah J, Marsool AD, Oudah AM, Al-Husseini AA, Toami J, Hamdar H. Oxygen therapy in ischemic colitis. Med Gas Res. 2026;16(2):178-179.*

References

1. Sun MY, Maykel JA. Ischemic colitis. *Clin Colon Rectal Surg*. 2007;20:5-12.
2. Ahmed M. Ischemic bowel disease in 2021. *World J Gastroenterol*. 2021;27:4746-4762.
3. Washington C, Carmichael JC. Management of ischemic colitis. *Clin Colon Rectal Surg*. 2012;25:228-235.
4. Nathan C. Immunology: oxygen and the inflammatory cell. *Nature*. 2003;422:675-676.
5. Dulai PS. The potential role of hyperbaric oxygen therapy in patients with inflammatory bowel disease. *Gastroenterol Hepatol*. 2024;20:753-755.
6. Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. *Plast Reconstr Surg*. 2011;127 Suppl 1:131S-141S.
7. Xiao YD, Liu YQ, Li JL, et al. Hyperbaric oxygen preconditioning inhibits skin flap apoptosis in a rat ischemia-reperfusion model. *J Surg Res*. 2015;199:732-739.
8. Lansdorp CA, Gecse KB, Buskens CJ, et al. Hyperbaric oxygen therapy for the treatment of perianal fistulas in 20 patients with Crohn's disease. *Aliment Pharmacol Ther*. 2021;53:587-597.
9. van der Post S, Jabbar KS, Birchenough G, et al. Structural weakening of the colonic mucus barrier is an early event in ulcerative colitis pathogenesis. *Gut*. 2019;68:2142-2151.
10. Rossignol DA. Hyperbaric oxygen treatment for inflammatory bowel disease: a systematic review and analysis. *Med Gas Res*. 2012;2:6.
11. Hung A, Calderbank T, Samaan MA, Plumb AA, Webster G. Ischaemic colitis: practical challenges and evidence-based recommendations for management. *Frontline Gastroenterol*. 2021;12:44-52.
12. Dulai PS, Gleeson MW, Taylor D, Holubar SD, Buckey JC, Siegel CA. Systematic review: the safety and efficacy of hyperbaric oxygen therapy for inflammatory bowel disease. *Aliment Pharmacol Ther*. 2014;39:1266-1275.