A Monograph for Health Care Providers

Radiation Induced Hemorrhagic Cystitis

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Radiation induced hemorrhagic cystitis (HC) can occur as early as 3 months after radiation or may not become evident for many years. Significant Grade 3-4 HC occurs in 3 – 8% of post pelvic radiation patients despite advances in administration technique and delivery. Historically, severe hemorrhagic cystitis was associated with a 44% mortality rate despite aggressive urinary diversion and cystectomy. Radiation causes chronic fibrosis, endarteritis and progressive tissue hypoxia of the bladder submucosa and muscular tissue with eventual scarring, mucosal sloughing and symptomatic hemorrhagic cystitis. Radiated tissue is rendered hypoxic, hypocellular, and hypovascular to the point that the tissue is no longer able to heal spontaneously resulting in recurrent symptomatic hematuria.

Traditional treatment methods include bladder irrigation, cauterization, oral or IV agents, intravesical chemical instillation, iliac artery embolization, urinary diversion, and cystectomy.

Hyperbaric oxygen therapy (HBOT) improves oxygenation and induces angiogenesis within radiation damaged tissues among other beneficial effects. Several studies have shown a 76 – 100% response rate with patients demonstrating complete or partial symptomatic improvement, even in those patients refractory to multiple prior medical, cystoscopic, or intravesical therapies.

Medicare and most private insurers cover this effective treatment.

What is Hyperbaric Oxygen?

Hyperbaric oxygen (HBO) is a daily treatment, in which a patient breathes 100% oxygen at pressure greater than normal atmospheric pressure in a hyperbaric chamber.

HBO therapy systemically delivers 100% oxygen at 2-3 times greater than atmospheric pressure. This elevated pressure within the hyperbaric chamber results in a 10-15 fold increase in plasma oxygen concentration, which translates to arterial oxygen values of between 1,500 and 2,000 mmHg. The steep oxygen gradient provided by HBO produces a four-fold increase in the diffusing distance of oxygen from functioning capillaries.

On average most treatment regimens for radiation cystitis will be 90 - 120 minutes long with the number of treatment being highly individualized.

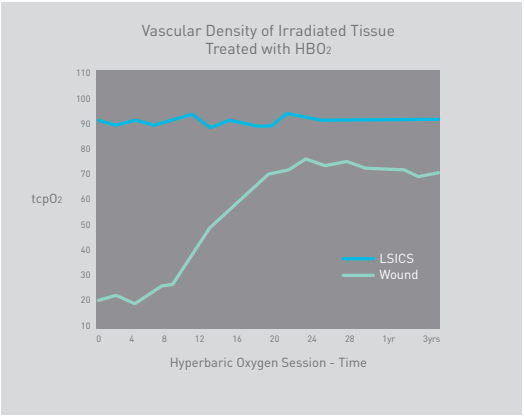
Hyperbaric oxygen has been proven to have no enhancing effects on cancer or metastatic growth.

What are the Beneficial Mechanisms Associated with HBO as related to Radiation Cystitis?

Several beneficial mechanisms of action are associated with intermittent exposures to hyperbaric oxygen (daily treatments). HBO is the only intervention that has been demonstrated to increase the number of blood vessels in irradiated tissue.

Delayed radiation injuries are typically seen after a latent period of three months to several years. Although the etiology of radiation injuries may vary somewhat among different organ systems, the hallmark of delayed radiation injury remains the same, endarteritis with tissue hypoxia and secondary fibrosis.

Solid evidence demonstrates that hyperbaric oxygen can produce neovascularization in irradiated (ischemic) tissue while reducing fibrosis. The following is a brief description of this process.



Tissue oxygen levels increase in irradiated tissue with hyperbaric oxygen therapy, returning to 80% of normal at about 20 twenty treatments. These oxygen levels are sustained following cessation of treatment.[7]

In normal wound healing, both hypoxia and normal amounts of oxygen are necessary for the different phases of healing. Hypoxia stimulates macrophages to release angiogenesis factors and mitogens which in turn stimulate fibroblast replication. For fibroblasts to synthesize collagen, normal levels of oxygen are required.

Intermittent hyperbaric oxygenation allows for periods of hypoxia between daily treatments. During these hypoxic periods, angiogenesis factor is released which causes capillary budding. New capillaries, however, cannot advance unless they are surrounded by a collagen matrix. Hyperbaric oxygen raises the oxygen tension in tissue sufficient for collagen formation to take place at greater distances from damaged/functioning capillaries.

A minimum of 20 mmHg partial pressure of oxygen is required for fibroblast proliferation and collagen production to start (irradiated tissue is often far below this level). In normal tissue at atmospheric pressure this tension of oxygen exists up to 30 microns away from the capillary wall. Under hyperbaric conditions this tension can be maintained up to 280 microns away.

This rich collagen matrix allows capillary buds to invade rapidly and form a new advancing vascular system that returns perfusion to within normal limits, thus allowing the tissue to heal.

Reference

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