HBOT: The Antidote to Soft Tissue Radionecrosis

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Objectives

- Understand pathophysiology of Soft Tissue Radionecrosis.
- Learn the role of Hyperbaric Oxygen Therapy in the treatment and management of Soft Tissue Radionecrosis.
- Help identify patients that could benefit from HBOT for treatment of Soft Tissue Radionecrosis.

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Pre-test Questions

1. Which of the following is not an effect of tissue exposed to radiation?

   A. Impaired revascularization

   B. Incapacitation to produce normal cells and collagen

   C. Hypoxic and fibrotic tissue

   D. All are effects of radiation

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Pre-Test Questions

2. True or False: Hyperbaric Oxygen therapy can serve as monotherapy in the treatment of Soft Tissue Radionecrosis.

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Pre-Test Questions

3. Which is a Contraindication to HBOT?

   A. Claustrophobia

   B. COPD

   C. Cisplastin

   D. URI

   E. All the above are contraindications

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Epidemiology

- 1.2 Million cases of invasive cancer diagnosed yearly
  - 50% of these will receive radiation
    - 3-5% will develop delayed effects of radiation
      - 18,000-30,000 patient per year

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Normal Pathophysiology

In normal wound healing, blood vessels adjacent to wound become temporarily dilated and hypertrophied in an effort to deliver higher levels of fibronectin into their vascular wall. By day 5 post-injury, these “mother” vessels give rise to capillary sprouts that invade the wound clot.

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Normal Pathophysiology

Steep oxygen gradients, along with the lactate, iron, and acid inherent in wounds, stimulate macrophages to secrete vascular endothelial growth factor (VEGF) and basic fibroblasts growth factor (bFGF) which in turn promote the capillary budding and collagen synthesis of wound healing.

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Pathophysiology

- Radiation effects on normal tissue cells:
  - Incapacitation to produce cells or collagen.
  - Impairment of normal revascularization seen in other tissue injuries.
  - Impaired oxygenation.

The three H tissue- hypovascular, hypocellular and hypoxic

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Pathophysiology

- Impaired Revascularization
  - When tissue is radiated in the treatment of malignancy, normal tissue cells are also damaged.
    - This leads to progressive loss of vascularity and cellularity over time.

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Pathophysiology

- Incapacitation of cell synthesis and collagen
  - Cellular sensitivity to radiation goes from tumors (most sensitive), then endothelium, fibroblasts, muscled and then nerve cells.
  - Highly mitotic cells, such as vascular tissue develops disorganized telengiactic growth that ultimately leads to mutated vessels that are hypoxic and fibrotic when exposed to radiation.
    - This makes tissue much more vulnerable to breakdown.

Soft tissue Radionecrosis can develop 6 month to several years after radiation exposure.

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HBOT Pathophysiology

Mechanism by which HBOT achieves angiogenesis and fibroplasia in radiated tissue is found to be simulated by a similar oxygen gradient phenomenon that Knighton, Silver and Hunt have found to be central in angiogenesis and fibroplasia of normal wound healing.

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HBOT Pathophysiology

- Radiated tissue loses oxygen tension which ultimately leads to a shallow oxygen gradient.
- After exposure to HBOT at 2.4 ATA there is a seven-to tenfold rise in the central oxygen tension, including the non-radiated tissue. Since each area shows increase in oxygen tension, the underlying shallow oxygen gradient is magnified into a steep oxygen gradient.

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Angiogenesis

- Increased VEGF
  - Proliferation of aluminized and functional capillaries
  - Increase capillary density
- New vessels induced by HBOT do not involute after cessation of HBOT any faster than its normal rate of aging.

Angiogenic effect is maintained for up to four years after HBOT.

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HBOT Pathophysiology

- After 10-18 exposures, the oxygen gradient moves centrally, which means that most of the angiogenesis comes from outside of the radiated field.
- After 20-24 exposures, oxygen gradient is eliminated.

HBOT creates steep oxygen gradients in radiated tissue which cannot develop naturally as do other wounds.

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HBOT Pathophysiology

Steep oxygen gradients trigger the recognition of the radiate tissue as a wound and initiates the series of biochemical steps seen in normal tissue angiogenesis.

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Hyperbaric Oxygen Therapy Treatment

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Official Definition

"Hyp**perbaric Oxygen (HBO) Therapy**: A medical treatment in which the patient is entirely enclosed in a pressure chamber breathing 100% oxygen (O2) at greater than one atmosphere (atm) pressure. Either a monoplace chamber pressurized with pure O2 or a larger multiplace chamber pressurized with compressed air where the patient receives pure O2 by mask, head tent, or endotracheal tube may be used. *First Coast LCD for Hyperbaric Oxygen (HBO) Therapy (L36504). (Accessed December 11, 2019)* "

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Pre-requisites

1. History of radiation treatment to the region of the documented injury, terminating at least 6 months prior to onset of signs or symptoms of planned surgical interventions at the site.
2. HBOT in the treatment of Osteoradionecrosis and Soft Tissue Radiation Injury is one part of an overall plan of care that also includes debridement or resection of nonviable tissue in conjunction with antibiotic treatment.

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Common signs and symptoms of Radionecrosis

- Disabling, progressive painful tissue breakdown
- Bleeding
- Bowel or bladder dysfunction
- Wound dehiscence
- Infection
- Tissue loos and graft or flap loss

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Commonly Treated Areas

- Head/Neck
- Breast
- Chest wall
- Pelvic organs (bladder, rectum)

Any tissue exposed to radiation can be treated with HBOT

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HBOT Protocol

- Recommended HBOT Protocol:
  - Hyperbaric treatment is defined as breathing 100% oxygen for 90 minutes at 2.4 ATA with two five minute air breaks.
  - Alternative dosage: 2.0 ATA for 120 minutes.

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HBOT Protocol

- Duration of HBO Therapy is high individualized but is not expected to exceed 4-8 weeks therapy.

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HBOT and Surgery

- Protocols for HBOT when surgery is performed in radiated tissue:
  - Twenty sessions prior to surgical wounding
  - Surgical wounding
  - Ten sessions after surgical wounding

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HBOT and Surgery

- Marx mandibular osteoradionecrosis protocol extends from 30-60 treatments based on stage I-III, adhering to the established principle that all necrotic bone must be derided.
- Soft tissue radio necrosis usually responds with 30-40 treatments followed by reconstruction if deemed necessary.
- An additional 10 treatments is usually followed by reconstruction if deemed necessary.

All treatment is individualized and should be assessed for benefit and outcome each 30 days.

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Patient Workup

- Workup is same as any other patient being evaluated for HBOT:
  - CBC
  - CMP
  - CXR
  - ECHO
  - Pre-albumin
  - Medication Reconciliation
  - Assess for medical devices

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Contraindications

- EF less than 30%- can lead to flash pulmonary edema
- Untreated pneumothorax- spontaneous pneumothorax
- Bleomycin-interstitial pneumonitis
- Cisplatin-impaired wound healing
- Disulfiram-blocks superoxide dismutase, which is protective against oxygen toxicity
- Doxorubicin- cardiotoxicity
- Sulfamylon- impaired wound healing

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Relative Contraindications

- Asthma- air trapping upon ascent leading to pneumothorax
- Claustrophobia- anxiety
- Congenital spherocytosis- severe hemolysis
- COPD- loss of hypoxic drive to breath
- Eustachian tube dysfunction/URI- barotrauma to tympanic membrane

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Relative Contraindications

- High fever- higher risk of seizures
- Pacemakers or epidural pain pump- Malfunction or deformation of device under pressure
- Pregnancy- Unknown effect to fetus
- Seizures- may have lower seizure threshold

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Benefits of HBOT

- Improved Oxygenation
- Angiogenesis stimulation
- Increased elasticity to fibrotic tissue
- Formation of granulation tissue
- Anti-microbial properties
- Increase in VEGF
- Improved neutrophil function
- Arterial vasoconstriction

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Efficacy

- Typically take 20 daily treatment before we start to see clinical evidence of improved angiogenesis and improvement in symptoms.
  - HBOT is the ONLY treatment available that treats the underlying lack of normal microvasculature characteristic of soft tissue radionecrosis.

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Efficacy

- Approximately 80% response rate with improvement in symptoms associated with soft tissue radiation necrosis.

Tissue never recovers to its normal state.

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Conclusion

Treatment of Soft Tissue Radionecrosis requires an inter-professional approach with HBOT done as adjunct therapy and in conjunction with anti-microbial therapy if infection is present, timely surgical debridement, appropriate nutrition, oncology consideration and plastic surgery if warranted.

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Post-Test Questions

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Post-Test Questions

2. True or False: Hyperbaric Oxygen therapy can serve as monotherapy in the treatment of Soft Tissue Radionecrosis.

False

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Post-Test Questions

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References

- Hyperbaric Medicine Practice 4th Edition- Harry T. Whelan, MD, Eric P. Kindwall, MD.
- https://www.ncbi.nlm.nih.gov/books/NBK482261/
- https://www.cms.gov/medicare-coverage-database/license/cpt-license.aspx?from=~/overview-and-quick-search.aspx&npage=/medicare-coverage-database/details/lcd-details.aspx&LCDId=35021&ver=159&name=331*1&UpdatePeriod=859&bc=AAAAEAAAAAAA&
- https://www.medscape.com/answers/1464149-105458/what-are-contraindications-for-the-use-of-hyperbaric-oxygen-therapy-hbot

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THANK YOU!

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