Hyperbaric Oxygen Therapy: Present Indications and Evidence

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**HBOT, A Working Definition**
- Hyperbaric oxygen (HBO₂) is a treatment, in which a patient breathes 100% oxygen intermittently while inside a treatment chamber at a pressure higher than sea-level pressure.
- Must be 1.4 ata or higher to qualify as HBO.
- Administered in monoplace or multiplace chamber.

- Clinical trials in progress re Topical 02
- Hyperbaric Oxygen Therapy Committee Report 2008 (UHMS)

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**MONOPLACE CHAMBERS**

**MULTIPLACE CHAMBER**

- Boyle’s Law
  - For a body of gas at constant temperature, the volume is inversely proportional to the pressure.

- Charles’ Law
  - For a body of gas at constant pressure, the volume is directly proportional to the temperature.
Dalton’s Law

- The sum of the partial pressures of gases in a system = the total pressure in the system

Physiology of HBOT

1) Mechanical effect – reduction of bubble size
   - Boyle’s Law
2) Effect of increased partial pressures of O₂
   - Dalton’s Law

Oxygen behaves like a drug at pressures much higher than atmospheric pressures so, like other drugs, there are specific indications, side effects and adverse effects

Presently Accepted Wound Related Indications

- Diabetic foot wounds, Wagner Grade III and up
- Arterial insufficiency ulcers s/p revascularization
- Failed/failing grafts and flaps
- Gas gangrene
- Necrotizing fasciitis/Fournier’s gangrene
- Delayed radiation soft tissue and bony injuries
- Acute traumatic ischemia – Compartment Syndrome

Presently Accepted Non-Wound Related indications

- Mandibular Osteoradionecrosis
- Carbon Monoxide Poisoning
- Air or gas embolism
- Central retinal artery occlusion (CRAO)
- Chronic refractory osteomyelitis
- Decompression sickness
- Radiation Proctitis

Common Off-Label / Unapproved Uses of HBOT

- Autism
- Cerebral Palsy
- Lyme Disease
- Multiple Sclerosis
- Athletic Injuries
- Rock Stars

Historical Controversy

- Paucity of supporting scientific evidence
- Financial incentive
- Overutilization
- Safety and adverse events
- Cost effectiveness
Scope of Presentation
• Diabetic Foot Ulcer
• Failed flaps and grafts
• Delayed radiation soft tissue necrosis
• Delayed radiation bony necrosis (ORN)

Evidence Based Medicine

Diabetic Foot Ulcer
• Historically – screening criteria poor and anyone with a Wagner III DFU could be treated.
• No requirements to assure adequate vascular supply and wound care ‘best practices’.
• Newer guidelines becoming more stringent
• Need to separate patients for which HBOT will be:
  - Unnecessary
  - Futile
  - Wasteful

How can we reduce unnecessary HBOT?
• Understanding the role of HBOT
  - What it does: Mechanism of action is complex and not simply “oxygenation”
  - What it doesn’t do: There is a reason CMS requires good basic care to be implemented first so HBOT is not to be used in lieu of off-loading, moist wound care etc.

How can we reduce unnecessary HBOT?
TcPO\textsubscript{2} and Healing Prediction
• Can we predict who will heal without HBOT?
  - Because hypoxia is often the final common denominator for wound failure, it is easier to find a value below which a wound will NOT heal than to find a value above which a wound is reliably predicted TO heal.
  - However . . .
  
  Sea level \textit{air} PtCO\textsubscript{2} values can be used to predict which wounds will \textit{not} heal spontaneously.

Factors Affecting HBOT Outcome of Diabetic Foot Ulcers
• Patient age and years of diabetes
• Wagner grade
• Transcutaneous oximetry
• Pack/year smoking history

A history of cigarette smoking >10 pack/years produces a predictable (and linear) increase in the number of hyperbaric treatments needed to achieve improvement

In-Chamber TcPO$_2$:
The best Single Predictor of Healing

- TcPO2 Chamber <100 mmHg: only 18% benefited
- TcPO2 Chamber >200 mmHg: 78.3% benefited
- TcPO2 is 75% accurate at predicting benefit from HBOT in DFUs
- Models incorporating other parameters are better than a single predictors

Cochrane Collaboration 2012

- Authors: Kranke, Bennett, Martyn-St. James, Schnabel, Debus
- Objectives: To assess the benefits and harms of adjunctive HBOT for treating chronic ulcers of the lower limb
- Selection Criteria: RCT’s comparing regimens that included HBOT with those that did not – with or without sham

Bottom Line

- Conclusion: For DFUs, HBOT significantly improved ulcer healing in the short term but not the long term. Trials had various flaws in design and/or reporting. More trials are needed to properly evaluate HBOT in people with chronic wounds; these trials must be adequately powered and designed to minimize all kinds of bias.

Other Evidence Based Review

- Wound Healing Society: 2006 clinical practice guideline states... “hyperbaric oxygen therapy may be of benefit in reducing the amputation rate in patients with ischemic diabetic foot ulcers” (Level I)
- Canadian Diabetes Association: 2006 review states... “Although costly, HBOT is a reasonable, cost-effective adjunct to standard therapy. Prospective studies are needed to assess the long-term success of HBOT” (2006 Technical Review)

CASE 1

- 48 y/o, w/m, presented with 1 yr hx of deep plantar foot ulcers. Positive probe to bone.
- Hx of DM-I since early 20’s

- Immediately debrided soft tissue and bone, intra-op cultures, abx via PICC per I.D.
- 30 HBOs over 6 wks. Complete offloading with 4 wheel scooter
**CASE 2**

- 92 y/o, w/m, referred with gangrenous 3rd toe
- Angiogram/plasty in conjunction with nephrology yielded recanalization of ATA and palpable DP
- Formal ray amputation (after revascularization)
- Silver Hydrogel and gauze dressings
- HBOT 2.0ata 20 treatments
- HBOT D/C’d at 20 tx – 30 had been approved

**Case 3**

57 y/o, w/m, type II DM with large plantar ulcer x 2 yrs. on foot with previous TMA. Debridement, offloading, Apligraf x 3 and 40 HBO tx’s. Healed in 15 weeks.

**HBOT for Failing Grafts/Flaps**

- Used for many years for failed/failing skin grafts and flaps of various types and origins
- Abundance of case reports, series and animal data, however paucity of human trials
- HBOT usually employed pre-operatively to develop granulating wound bed to support split or full-thickness grafts
- CMS presently approves HBOT for grafts and flaps under ICD-9 Code 996.52

**Summary**

- Abundant and significant animal data
- No prospective, randomized clinical trial to validate animal data
- Other measures to promote angiogenesis
- Pharmacologic agents
- Review of available literature regarding efficacy of HBOT for flaps and grafts underscores paucity of supporting clinical information
- Does this mean HBOT should not be used???
“Parachute use to Prevent Death and Major Trauma Related to Gravitational Challenge: Systematic Review of Randomized Controlled Trials”

- Authors argue that there are no prospective, randomized controlled trials available to suggest that the use of a parachute when jumping from a plane yields any better clinical results than free falling without one!
- Would you agree that observational data support the use of a parachute?

Case 1
- 80 y/o, w/m presented with 6-7 month history of non-healing TMA site s/p flap closure 7/14.
- Referred by Interventional Radiology following optimization of flow in ATA to DP.
- TcPO2 values teens to low 30’s on room air and increased to 180’s in chamber at 2 ATA.
- Wound edges separated by 2cm in full length of flap and wound bed 50% slough and 50% gran.
- Initial and serial sharp debridements, collagen, and HBOT.

1/19/15

90% closure by volume

Case 2
Literature References

- Improved survival of split thickness skin grafts (Perins DJD. Lancet 1967;1:868-71.)
- Reversal of distal flap ischemia (Bowersox JC, et al. JHM 1986;1:141-9.)
- Decreased ischemia reperfusion injury (Zamboni WA. Plast Reconstr Surg 1993;91:1110-23.)

Delayed Soft Tissue Radiation Necrosis

- Cutaneous: Head & Neck, Breast, Extremity
- Colon
- Bladder
- Mandible

HBO in the Treatment of Irradiated Wounds

Strategies for treatment of irradiated wounds:

1. High quality standard wound care
2. Negative pressure wound therapy
3. Nutritional repletion
4. Hyperbaric oxygen therapy

Pathophysiology of Delayed Radiation Injury

- Exact causes complex and only partially understood
- Common vascular finding in all organ systems is obliterative endarteritis
- Present model involves the “fibro-atrophic” effect and elaboration of fibrogenetic cytokines
- Vascular damage and stenosis remain consistent finding but not sole cause of damage
- TGF-beta is most frequently studied cytokine

Radiation Therapy

- Impairs vascularity and depletes cell lines
- Impacts all phases of wound healing
- Progressive over time
- Good response to HBOT
- Radiation Proctitis

Clark, Cone et al. 2008

Temporal Nature of Radiation injury

- Acute: due to direct and near immediate cellular toxicity caused by free radical mediated damage to cellular DNA. Subsequent mitosis prevented.
- Sub-acute: Only in a few organ systems, i.e. lungs (radiation pneumonitis), and spinal cord (Lhermitte’s Syndrome).
- Delayed: Usually seen after latent period of at least 6 months, and often many years.
- Consequential effects: Non-resolving acute injuries with no symptom free latent period
Effects of HBOT on Irradiated Tissues

- HBO2 induces neovascularization of previously irradiated tissue.
- Increased vascular density in rabbit mandibles demonstrated by Marx et al in 1990.
- Increased vascularity and resolution of radiation proctitis demonstrated in 2008 by Clarke, et al.
- Mobilization of stem cells by increasing nitric oxide demonstrated by Thom, et al. in ’06 – ’07

Late Effects Of Radiation - Cranial

- 56 y/o, w/f, ref. from Plastics and Neurosurgery for scalp/cranial defect with exposed dura
- S/P resection of multiple meningiomas and with hx of external beam radiation therapy
- Wound dressed with synthetic collagen and gauze cover dressing
- HBOT @ 2.5 ata for 90 min x 30 tx
- Another learning opportunity!

Late Effects of Radiation - Breast

- 69 y/o, w/f, with non-healing left breast wound
- Lumpectomy with post op radiation therapy
- Failed to heal after 15 mos good standard care

L.E.R. Breast

- Debrided in OR to clean granular base

L.E.R. Breast

- 40 HBO2 over 8 weeks.
- NPWT (pump detached for HBO2)
L.E.R. Breast
5 months after initial visit – Healed...

Late Effects Of Radiation - Neck

Osteoradionecrosis
- 2002 literature review by Feldmeier/Hampson reported on a total of 371 cases of ORN.
- Positive outcome reported in 310 (83.6%)
- Some papers report improvement as outcome measure rather than resolution.
- Negative outcomes reported when HBO used alone and not in conjunction with surgery – or – vice-versa.
- TREATMENT OF ORN MUST BE MULTIDISCIPLINARY APPROACH

HBO₂ For Prophylaxis of ORN
- Extraction of teeth from heavily irradiated jaws is a common precipitating factor for ORN.
- Marx published results of randomized prospective trial wherein pts who had received a total radiation dose of at least 6,800 cGy were randomly assigned to pre-extraction HBO₂ or penicillin prophylaxis
- HBO₂ group received 20 daily pre-extraction HBO treatments followed by 10 post-extraction

Mandibular ORN

Thank you!