Hyperbaric Oxygen Utilization in Wound Care

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No relevant disclosures
Diabetes and lower extremity wounds...

- At any time, as many as 1 million diabetics suffer from a lower extremity ulcer
- Constitutes 20% of hospital admissions for diabetics
- And 50-70% of all lower extremity amputations
Diabetes and lower extremity wounds...

- 15-40 fold increase in lower extremity amputation rate than non-diabetics
- Leading cause of non-traumatic amputations
- Accounts for over ½ of all amputations in a subset of only 6% of population
- Accounts for 67,000 limbs lost annually
Lower Extremity Major Amputations in Diabetics

- <50% chance of functional weight-bearing
- $40-$60,000 direct costs
- On average, precedes death by five years
- Serial ascending amputation levels is the norm
Chronic wounds can be explained by the coexistence of...

1. The cellular and systemic effects of aging
2. Bacterial colonization with the resulting inflammatory host response
3. Chronic ischemia, hypoxia, and repeated ischemia-reperfusion injury often in the setting of local ischemia

Hypoxia and Nonhealing
Effect of PO$_2$ < 30 mm Hg

- Decreased neutrophil killing
- Decreased fibroblast growth
- Decreased collagen production
- Impaired capillary growth
PtcO$_2$ As A Predictor of Wound Healing in Diabetic Foot Wounds

PtcO$_2$ < 20 mmHg indicated 39-fold increased risk of early healing failure.

TcPO$_2$ and Prediction of Limb Salvage with HBO$_2$

- $>50$ mm Hg pO$_2$ : Conventional healing
- $40-50$ mm Hg pO$_2$ : $\pm$ conventional healing
- $40-30$ mm Hg pO$_2$ : Mildly Impaired
- $30-20$ mm Hg pO$_2$ : Moderately impaired
- $<20$ mm Hg pO$_2$ : Severely impaired

- 200 mm Hg pO$_2$ at 2 ATA best predictor of healing with HBO$_2$
# Interstitial PO$_2$

Implanted Oxygen Electrodes

<table>
<thead>
<tr>
<th>FiO$_2$</th>
<th>Tissue PO$_2$</th>
<th>O$_2$ Diffusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.21 ATA</td>
<td>30-50 mmHg</td>
<td>100 um</td>
</tr>
<tr>
<td>1.0</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>250</td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>3.0</td>
<td>2000</td>
<td>250 um</td>
</tr>
</tbody>
</table>

Sheffield 1985
Physiology of Hyperbaric Oxygen

- Stimulation of fibroblast replication
- Stimulation of collagen synthesis and cross-linking
- Stimulation of PDGF production
- Down-regulation of ICAM-1 and beta-2-integrins
- Angiogenesis, likely through HIF-1 signal transduction pathway and VEGF
- A steep O2 gradient from the peripheral tissue to the hypoxic wound center is optimal for healing
THE ROLE OF OXYGEN IN WOUND HEALING

- Collagen cross-linking
  
  (Hunt TK. Surg Gynecol Obstet 1972;135:561-7)
A Single HBO2 Treatment Increases Fibroblast Proliferation

Buras and Buras, Harvard Medical School
HBO$_2$ increases PDGFR expression *in vivo*

Before HBO$_2$  

24 hrs after HBO$_2$
# Diabetic Foot Ulcers

## Amputation Rate with HBO₂ vs. No HBO₂

<table>
<thead>
<tr>
<th>Type</th>
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<th>no HBO₂</th>
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<tr>
<td>Stone</td>
<td>501</td>
<td>28%</td>
<td>47%</td>
</tr>
<tr>
<td>Baroni</td>
<td>28</td>
<td>12%</td>
<td>40%</td>
</tr>
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</tr>
<tr>
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<td>18</td>
<td>12%</td>
<td>12%</td>
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</tbody>
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* 1 of 8 amputation each group. 5 of 8 HBO2 healed, 1 of 8 control healed.

R = randomized, P = prospective, C = controlled, Rt = retrospective, B = blinded

Ref: Barnes RC, Clin Infect Dis 2006; 43:188-92
Diabetic Foot Ulcers
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Studies with no heterogeneity. \( RR = 0.31 \) \( NNT = 4 \)

Diabetic Foot Wounds
Randomized Trial of HBO$_2$

- 70 patients randomized to care by standard protocol vs. standard care plus HBO$_2$
- HBO$_2$ at 2.5 atm abs (mean 38±8 treatments)
- Major amputation (BKA or AKA) rate was 9% in HBO$_2$ group and 33% in control group
- Benefit greatest in patients with more severe disease

Faglia E. *Diabetes Care* 1996.
Diabetic Foot Wounds
Londahl RCT, Diab Care 2010

- DFU Wagner 2-4, treated in DFU clinic >2 mo
- Up to 40 treatments at 2.5 ATA, air vs O2
- Outcome: healed ulcer at 1 year f/u

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<tr>
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<th>Control</th>
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<tr>
<td>ITT</td>
<td>25/48 (52%)</td>
<td>12/42 (29%)</td>
</tr>
<tr>
<td>As Treated</td>
<td>23/38 (61%)</td>
<td>10/37 (27%)</td>
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Diabetic Foot Ulcers
Durability of Healing with HBO₂

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Essentially all healed ulcers remained healed at followup (4 years).
Diabetic Foot Wounds
Cost Efficacy of HBO2

- Incremental cost of HBO2 for a nonhealing diabetic wound = $5,166 per qaly at five years

- Drivers are 1) high cost of amputation and rehabilitation and 2) low rate of successful ambulation after BKA

HBO₂ for Diabetic Foot Ulcers
Medicare Coverage

• LE wound due to diabetes (Type I or II)
• > Wagner grade III
• Failed standard wound care for 30 days
Standard Wound Care for Diabetic Foot Ulcers
Medicare Coverage

- Vascular assessment
- Optimize nutrition/glycemic control
- Debridement
- Moist dressing
- Off-loading
- Treat infection
Not all DFU Need Hyperbaric Oxygen Therapy

- TcPO2 > 40
- Contraindications: severe COPD or CHF, spontaneous pneumothorax hx, current chemotherapy, cognitive impairment
- Suboptimal control of glycemia, offloading, infection, necrotic tissue, nutrition
- Surgically correctable arterial disease
1. Acute carbon monoxide intoxication,
2. Decompression illness,
3. Gas embolism,
4. Gas gangrene,
5. **Acute traumatic peripheral ischemia.** HBO therapy is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb, or life is threatened.
6. **Crush injuries and suturing of severed limbs.** As in the previous conditions, HBO therapy would be an adjunctive treatment when loss of function, limb, or life is threatened.
7. **Progressive necrotizing infections** (necrotizing fasciitis),
8. **Acute peripheral arterial insufficiency,**
9. Preparation and preservation of compromised skin grafts (not for primary management of wounds),
10. **Chronic refractory osteomyelitis,** unresponsive to conventional medical and surgical management,
11. Osteoradionecrosis as an adjunct to conventional treatment,
12. Soft tissue radionecrosis as an adjunct to conventional treatment,
13. Cyanide poisoning,
14. Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment,
15. **Diabetic wounds of the lower extremities** in patients who meet the following three criteria:
   a. Patient has a wound classified as Wagner grade III or higher; and
   b. Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes;
   c. Patient has failed an adequate course of standard wound therapy.
Questions?