What is the evidence that hyperbaric oxygen therapy improves wound healing

Robert B. McLafferty, M.D., M.B.A.
Chief of Surgery
Veterans Affairs Portland Health Care System
Professor of Surgery
Division of Vascular Surgery
Oregon Health and Sciences University
Portland, Oregon

Hyperbaric Oxygen Therapy
Disclosures
None

Hyperbaric Oxygen Therapy
Indications
Medicare Reimbursed
- Diabetic lower extremity wounds
- Chronic radiation injury
- Refractory osteomyelitis
- Compromised skin flaps and grafts
- Critical limb ischemia (no options)

UHMS Approved
- Air gas embolism
- Decompression illness
- CO poisoning
- Necrotizing infections
- Crush injury
- Ischemic skin flaps
- Refractory osteomyelitis
- Osteoradionecrosis
- Soft tissue radionecrosis
- Problem wounds
- Severe Blood loss
- Avascular necrosis

Boyle’s Law

Additional O2 Carried by Plasma

Improvement in O2 Diffusion in Tissue
Hyperbaric Oxygen Therapy
HBO Physiologic Changes
- Angiogenesis
- Stem cell mobilization
- Fibroblast proliferation/Collagen Synthesis
- Reduced leukocyte adhesion
- Reduced lipid peroxidation
- Edema reduction
- Enhanced leukocyte antimicrobial activity
- Antibiotic synergy
- Toxin inhibition

Hyperbaric Oxygen Therapy
Diabetic Foot Ulcer Timeline of Data

Hyperbaric Oxygen Therapy
Overview of Results of DFU Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>% Healed at Major Amp</th>
<th>Delay before HBO</th>
<th>Increases Healing Percentage</th>
<th>Decreases Major Infection</th>
<th>Increases Rate of Healing</th>
<th>Increases Duration of Healing</th>
<th>HBO2 after HBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baronti 1997</td>
<td>PCoT</td>
<td>90 x 10</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Maybe</td>
</tr>
<tr>
<td>Chiodi 1996</td>
<td>RCoT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Maybe</td>
</tr>
<tr>
<td>Faglia 1996</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Maybe</td>
<td>Maybe</td>
<td>Maybe</td>
</tr>
<tr>
<td>Faglia 1999</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lin 2001</td>
<td>RCT</td>
<td>90 x 10</td>
<td>No</td>
<td>Yes</td>
<td>Maybe</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pauli 2002</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Attiki 2003</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Maybe</td>
<td>Yes</td>
<td>Yes</td>
<td>Maybe</td>
</tr>
<tr>
<td>Keasler 2003</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Giuggi 2006</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Lindeberg 2009</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Ma 2013</td>
<td>RCT</td>
<td>90 x 10</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Hyperbaric Oxygen Therapy
Diabetic Foot Ulcer and HBO

- 70 subjects enrolled, 68 completed protocol
- Wagner Grade III or >; Outcome: Major Amp
- Groups similar in demographics/variables
- All had multidisc wound therapy
  - with HBO (n=35)
  - without HBO (n=33)

Multivariate analysis confirmed protective role of HBO: OR: 0.084, p = 0.03

Hyperbaric Oxygen Therapy
Chronic/Delayed Radiation Tissue Injury
- Prospective randomized controlled trial
- 74 patients requiring tooth extraction from previously irradiated mandible
- Randomized to perioperative penicillin or 20/10 HBO2 protocol

<table>
<thead>
<tr>
<th>No. Patients</th>
<th>ORN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>37  (135 teeth)</td>
</tr>
<tr>
<td>HBO2</td>
<td>37  (156 teeth)</td>
</tr>
</tbody>
</table>

P = 0.005

Mark RE J Am Dent Assoc 1985
Radiation Proctitis

- Double blinded RCT
- 30-40 HBO₂ at 2.0 ATA versus air at 1.1 ATA
  - Sham patients then crossed over to HBO₂
- 120 completed study protocol
- Healed or improved:
  - 89% HBO₂ group vs. 62% in sham group (p=0.0009)
  - Absolute risk reduction 32%
- Marked improvement in bowel-specific QOL in HBO₂ vs. sham group

Clarke RE. Int J Radiat Oncol Biol Phys 2008

Compromised Flaps and Grafts

- 9 year-old male who ran into a non-tempered sliding glass door
- He sustained a severe laceration of the nose, nearly severing the nose and splitting his upper lip
- HBO₂ consulted at Post-operative Day #3
- The repaired nose did well for a few days but then became ecchymotic and ischemic
- HBO₂ treated for 36 hours post injury
- After 6 HBO₂ treatments no debridement of wound was performed

Plethora of good evidence
- Better to initiate earlier than later
- Keep it in your armamentarium

Summary