Hyperbaric Oxygen: Putting Principles into Practice
Session 245
Sunday, September 11th 2011

Hyperbaric Oxygen Therapy
Putting Principles into Practice
Salvaging Diabetic Foot Wounds

Jeffrey A. Niezgoda, MD, FACHM, MAPWCA

Session Overview
- Statistics & Definitions
  - Non Healing PVD Ulcer
- Oxygen & Wound Healing
- Advanced Modalities for Angiogenesis
- Hyperbaric Oxygen Therapy
  - History, Mechanisms of Action, Brief Literature Review
- HBO DFU Algorithm
- Case Studies

PVD & Non-healing Ulcers

Patients with Non-healing Ulcers

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What do patients with non-healing ulcers have in common?

High Risk for....
Limb Loss

Why are these patients at risk?
Compromised Healing

Why compromised healing?
Many are Obese
Most have Diabetes

Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

1994


2004


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Age-adjusted Percentage of U.S. Adults Who Were Obese or Who Had Diagnosed Diabetes

<table>
<thead>
<tr>
<th>Year</th>
<th>Obesity (BMI ≥ 30 kg/m²)</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>Missing Data</td>
<td>Missing Data</td>
</tr>
<tr>
<td></td>
<td>14.3 - 17.9%</td>
<td>18.8 - 23.9%</td>
</tr>
<tr>
<td></td>
<td>22.0 - 25.9%</td>
<td>7.5 - 9.9%</td>
</tr>
<tr>
<td></td>
<td>≥30.0%</td>
<td>≥9.0%</td>
</tr>
</tbody>
</table>

Diabetic Statistics
- Prevalence of Diabetes (US, All Ages, 2008)
  - 18.2 million people
  - 6.3 percent of the population
- Direct medical costs: $92 billion
- Indirect costs: $40 billion
  - disability, work loss, premature mortality

Source: NIDDK - National Institute of Diabetes & Digestive & Kidney Diseases

The Diabetic Foot Disease
- 82,000 non-traumatic lower limb amputations 2002
- 54,000 diabetic amputations reported in 1992
- $43,000 for minor amputation
- $65,000 for major amputation
- Apelqvist 1995
- $22,000 to $36,000 per diabetic foot ulcer
- Bentkover & Champion, 1993

Source: *2002 Theta Report Advanced Wound Care Biologics Market Analysis

Why compromised healing?
- Obesity
- Diabetes
- PAD - PVD
- Hypoxia

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Wound Healing Compromise
- Tissue Hypoxia
- Infection
- Edema
- Mechanical Forces
- Cellular Dysfunction
- Nutrition

? Common Pathophysiology?
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### Oxygen & Wound Healing
- Angiogenesis is oxygen dependent.
- Antimicrobial activity is oxygen dependent.
- Tissue oxygen tensions above 30mmHg are needed for collagen synthesis.
- The metabolic demands of healing tissue can increase by a factor of 20 or more.

**Advanced Modalities/Therapies**
( Ancillary or Adjunctive Interventions)

**Definition**
Mechanical, Biological or Pharmaceutical modalities that are utilized in addition to standard basic wound care protocols with the intent to promote wound healing and/or limb salvage, via mechanisms which stimulate perfusion or enhance angiogenesis.

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**The Role of the Wound Care Specialist**
- To Initiate the Diagnosis and Treatment of the Factors Compromising Wound Healing
- And then to Utilize Advanced Wound Care Techniques and Adjunctive Modalities to Optimize the Potential for Healing.

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Advanced Modalities
Mechanical
- Pneumatic Compression Therapy
- Pulsed Electromagnetic Field Therapy
- Ultrasonic Guided Debridement
- Negative Pressure Wound Therapy (NPWT)
- Electrical Stimulation Therapy
- Ultraviolet Light Therapy
- Vashe Wound Therapy
- Monochromatic Infrared Energy (MIRE)

Advanced Modalities
Biological
- Bioactive
  - Bioengineered Skin Substitutes
  - Autologous Platelet Grafts
- Biomaterials
  - Autologous Dermal Matrix
  - Acellular Matrices
- Biosynthetic
  - Growth Factors
- Biotechnologies
  - Genetic Transfer
  - Stem Cell Therapies

Advanced Modalities
Pharmaceutical
- Platelet Aggregation Inhibitors
  - Plavix (clostatozol)
  - Pletal (clopidogrel)
  - Prasugrel
- Glycoprotein Platelet Inhibitors
  - Aggrastat (tirofiban)
- Oxygen
  - Hyperbaric Oxygen Therapy

Hyperbaric Oxygen Therapy
Definition
Mechanism of Action

Hyperbaric Oxygen is NOT

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Hyperbaric Oxygen Therapy
Definition: Inhaled 100% Oxygen delivered to the Patient Completely Enclosed in a Pressurized Environment

Hyperbaric Oxygen Therapy
Brief Historical Perspective

D. Jourdanet - 1862

Paul Bert – 1880’s

Notes

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Milwaukee: 1969-2009

Hyperbaric Oxygen Therapy
Mechanism of Action

How is oxygen dosed?

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Hyperbaric Oxygenation

<table>
<thead>
<tr>
<th>Total Pressure</th>
<th>O2 Content w/ HBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATA</td>
<td>mmHg</td>
</tr>
<tr>
<td>1.0</td>
<td>760</td>
</tr>
<tr>
<td>1.5</td>
<td>1140</td>
</tr>
<tr>
<td>2.0</td>
<td>1520</td>
</tr>
<tr>
<td>2.5</td>
<td>1900</td>
</tr>
<tr>
<td>3.0</td>
<td>2280</td>
</tr>
</tbody>
</table>

Normobaric Conditions

1ATA Air

Hyperbaric Conditions

3ATA Oxygen

Normobaric Conditions

Normoxic zone

Hyperbaric Conditions

Normoxic zone

250u

O₂ Diffusion Overlap

64 u

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OXYGEN RESPONSE CURVES (90 min tx)

Hyperbaric Oxygen Therapy
Chamber Types / Oxygen Delivery

Oxygen Delivery
MULTIPLACE MONOPLACE

Hyperbaric Oxygen Therapy
Accepted Indications

Emergent Indications
- Decompression Sickness
- Gas Embolism
- Gas Gangrene
- Acute Ischemia
- Extreme Anemia
- Carbon Monoxide
- Cyanide (Smoke Inhalation)
- Thermal Burns

Elective Indications
- Radiation Injury
- Chronic Osteomyelitis
- Diabetic Wounds
- Problem Wounds

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Approximate distribution for outpatient program. Practice & Hospital variations are common.

- Radiation ~ 30%
- Diabetic ~ 30%
- Flaps & Grafts ~ 15%
- Osteomyelitis ~ 15%
- Anaerobic ~ 5%
- CO / AGE / DCS / Anemia ~ 5%
- Radiation ~ 30%

Barotrauma (Otic, Pulmonary, Odontic)  Hypoglycemia
Hypoglycemia  Hypoglycemia
Claustrophobia  Hypoglycemia
Congestive Heart Failure  Hypoglycemia

ABSOLUTE
- Untreated Pneumothorax
- Relative
- Claustrophobia
- Fever
- CHF, COPD
- High FiO2
- Chemotherapeutic Agents

Tissue Hyperoxygenation
- Salvage marginal tissue
- Satisfy increased demand
- Stimulates Angiogenesis
- Decreases Tissue Edema
- Antimicrobial
- Antioxidant
- Growth Factor Up Regulation

Hyperbaric Oxygen Therapy
Literature Review
Basic Science, Animal & In Vitro Data

Notes
Enhanced Host Resistance

The killing capacity of granulocytes is normal only to the degree that oxygen is available.

Dermal necrosis following $10^7$ E coli

Knighton DR; Archives of Surgery 1986: p191

Regulation of Wound-Healing Angiogenesis

The Effect of Oxygen Gradients

Knighton, Silver & Hunt - Surgery, 1981
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**Conclusions**

- Oxygen gradients govern angiogenesis
- Capillary growth stops when the gradient is flat

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**Experimental Design**

I/R injury and HBO treatment

- 4 hours Hypoxia/Hypoglycemia
- 1.5 hours HBO at 2.5 ATA
- 18.5 hours Normoxia/Normoglycemia
- 20 hours Normoxia/Normoglycemia

**Notes**

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Hyperbaric Oxygen Therapy

Literature Review
Clinical Data and Trials

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**HBO Therapy in a Human Burn Model**

*Niezgoda JA, Plastic Reconstr Surg 1997*

**Study Type:** prospective, randomized, blinded trial

**Methods:** standardized wound model

- Suction cup
- Exposure of dermis
- Ultraviolet Radiation

**Control gp:** 8.75% oxygen at 2.4 ATA bid x 3 days

**HBO gp:** 100% oxygen at 2.4 ATA bid x 3 days

**Measurements:**
- wound size
- hyperemia
- exudation
- epithelialization

**Outcome:**

- **Wound size-** 35% reduction in lesion size (day 2) *p < 0.05*
- **Hyperemia-** 42% reduction in wound hyperemia by laser-doppler (day 2) *p < 0.03*
- **Exudation-** 22% reduction in exudate (day 2) *p < 0.04*
- **Epithelialization-** no difference in time to complete epithelialization *NS*

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**HBO in Diabetic Foot Ulcers**
- Non randomized comparative study
  - 18 patients treated with HBO
  - 10 controls identical wound care only
- Results (p=0.001)
  - 16/18 HBO treated patients healed
  - 1/10 control patients healed

G. Baroni et al., Diabetes Care, 1987; 10:81-86

**HBO in DFU**
- Prospective randomized study of 70 patients using HBO treatment in DFU
  - 35 Patients each group
  - HBOT Group
    - 3 of 35 (8.6%) patients major amputation
    - 1AKA, 2BKA
  - Control Group
    - 11 of 33 (33.3%) patients major amputation
    - 4AKA, 7BKA
  - P=0.016


**HBO in DFU**
- Prospective RCT of 94 patients with DFU
  - Wagner Grade 2, 3, and 4
  - Randomized to HBOT vs Placebo Control
  - HBOT (N=48) Complete Healing
    - 25/48 (52%)
  - Placebo Control Group (N=42)
    - 12/42 (29%) P=0.03
  - Patients completing >35 HBOTxs
    - HBOT Group 23/38 (61%)
    - Control 10/37 (27%) P =0.009


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New CMS Coverage Indication
Diabetic Foot Ulcer

- Lower extremity wound due to Diabetes
  - Type I or Type II DM
- Wagner Grade III or higher
- Failed standard wound care
  - no measurable signs of healing for 30 days
  - Decrease in volume or size
  - Decrease in exudate
  - Decrease in necrotic tissue

Lower Extremity Diabetic Wounds

- Wagner III, IV or V
- Have the 8 elements of Standard Wound Care been met?
- Vascular Status?
- Correction of Vascular Problems?
- Nutritional Status?
- Glycemic Control?
- Debridement?
- Appropriate Dressing?
- Appropriate Off Loading?
- Resolution of Infection?
- NO Decrease in Wound Volume in the past 30 days?
- Begin HBO 2.0-2.4 ATA QD

General Approach

- Wound Care
- Off-loading
- Antibiotics
- Diabetes Control
- Nutrition
- Re-eval for osteo
- Re-eval Nutrition
- Vascular Consult
- Plastic Consult
- Podiatry Consult
- Modify Wound Care
- TCPO2 Mapping

Vascular Consult Reconstructable?
- Yes
- Reconstruct TCOM Adequate?
- No
- TCPO2 - Hypoxia?

Multidisciplinary Team Approach to Extreme Limb Salvage in Patients with DFU Case Studies

Professional Resources

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