The Safe Administration of Hyperbaric Oxygen after Bleomycin

A series of 16 cases with Long Term Follow Up

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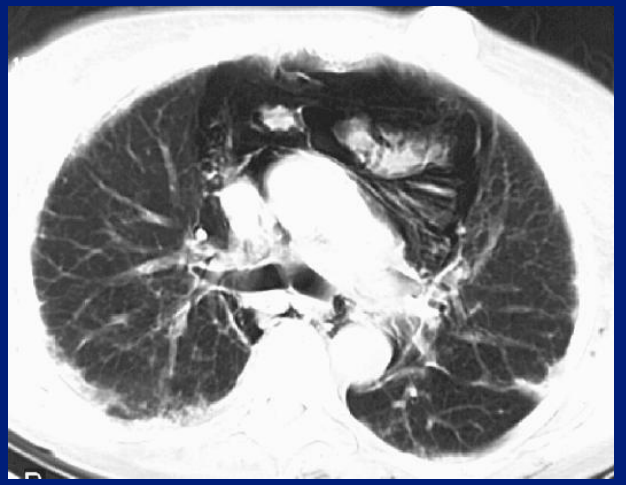
Bleomycin

- Glycopeptide antiobiotic from Streptomyces verticillus
  - Hodgkins lymphomas, head, neck and testis tumors
  - Low myelotoxicity
- Mechanism of Action[1]
  - DNA Binding
  - Chelator of Transition-Metal Ions
  - Bleo hydrolase, low in lungs and skin
  - Renal excretion t ½ 2-4 hrs, longer intra-pleural



- Can cause pulmonary fibrosis (1960s clinical trials)
  - Macrophage /lymphocyte TNF secretion
  - Occurs within hours
  - Risk: dose, smoking, bolus administration, age, reduced GFR, prior lung disease, supplemental O2?

Photo: "Bleomycin Drug Toxicity" University Hospital of Cleveland Department of Radiology http://www.uhrad.com/ctarc/ct120.htm

Perioperative O2 and Bleomycin

- Goldiner et al., 1978- 1979[1,2]
  - 2 studies
    - 1 Retrospective study of 5 patients undergoing surgery 6-12 months after BLM
      - Mean length of 9.6 +/- 0.8 months from treatment
      - Average FiO2 39%
      - All developed ARDS 3-5 days post-op and died of respiratory failure
    - 1 "Prospective" study of 12 patients (case report)
      - Similar profiles to 5 deaths
      - Average FiO2 <25%
      - No respiratory complications noted
- Post Bleomycin O2 restriction incorporated into the medical literature
- By extension incorporated into HBO textbooks
- By extension applied to divers

[1]Goldiner et al. The hazards of anesthesia and surgery in bleomycin-treated surgical patients. Sem Onc 6: 121, 1979
[2]Goldiner et al. Factors influencing postoperative morbidity and mortality in patients treated with bleomycin. BMJ 1:1664-7, 1978

HBO and Bleomycin

- Donat and Levy[1]
  - 77 consecutive testicular cancer patients
  - 97 surgical procedures
  - mean latency time of 6.4 months
  - high dose bleomycin
  - Evaluated wide range of perioperative factors
  - Looked for pulmonary complications causing O2 desaturation
  - No ARDS, No Fatalities

Donat and Levy Conclusion

  - FiO2 > 24% was not a significant independent risk factor for pulmonary mortality

- Peri-operative FIO2 restriction no longer recommended
- Safety of higher PO2 from HBO still questioned

[1]Donat S, Levy D. Bleomycin associated pulmonary toxicity: is perioperative oxygen restriction necessary? J Urol 1998;160: 1347-52

Duke 16 patients who received HBO after BLM

- HBO (with a special-precautions protocol)
  - chest x-ray, spirometry, blood gases, a single 2-ata 120-minutes HBO treatment
- Review of all available follow up records
  - Median follow up was 12.1 months (range 1-259) months
  - Pre-and-post HBO; ABGs, spirometry, xrays and clinical reports were available for 40%, 66%, 72% and 100% of the sample respectively.

Duke Retrospective review 16 patients who received HBO after BLM

- Indications:
  - osteoradionecrosis (11), soft-tissue radionecrosis (3), DCS (1) and a provocative oxygen toxicity test for a military aviator (1)
- BLM dose = 40 to 225u/m2 (range)
- Radiation dose = 63.3 ± 31.72 cGy (mean, SD) none to chest
- Latencies:
  - Radiation to HBO = 24 months (median)
  - BLM to HBO = 32.2 months (median)

Duke Retrospective review 16 patients who received HBO after BLM

- Results:
  - No post-HBO pulmonary complications.
    - One patient experienced pleuritic chest pain that corrected with humidification. She remains well 21 years later
- Conclusions:
  - although BLM and oxygen individually cause acute pulmonary toxicity
  - evidence for increased long-term susceptibility based on their synergy may be over-stated.
- Recommendations:
  - **do not automatically withhold HBO**
  - individually evaluate all candidates and more intensely monitor
  - wait 3 months post-BLM administration