



# Bleomycin and Anaesthesia

## Introduction

Bleomycin is a chemotherapeutic antibiotic isolated from the fungus *Streptomyces verticillus*. It is effective in the treatment of squamous cell, testicular and lymphomatous cancers. Acute interstitial pneumonia and chronic pulmonary fibrosis are the principal therapy-limiting adverse effects of bleomycin. In addition the hyperoxia associated with anaesthesia in patients previously exposed to bleomycin has been implicated to cause rapidly progressive severe pulmonary oxygen toxicity.

Goldiner et al. (1) reported a retrospective series of 5 consecutive patients who received bleomycin 6-12 months prior to undergoing surgery. All developed terminal adult respiratory distress syndrome 3-5 days postoperatively. Autopsy revealed pulmonary changes consistent with pulmonary oxygen toxicity. Bacterial and viral cultures were negative. It was hypothesized that bleomycin had a synergistic effect on inducing pulmonary oxygen toxicity. A subsequent prospective study of 12 similar patients maintained on  $\text{FiO}_2$  22-25% reported no respiratory complications.

Subsequent authors have refuted the recommendation of Goldiner et al. regarding use of low  $\text{FiO}_2$  (2). However the excellent review by Mathes (3) suggests differences in patient risk factors may account for a lack of respiratory complications.

## Risk factors

Mathes concludes the major risk factors for predicting bleomycin induced pulmonary oxygen toxicity with hyperoxia exposure are:

- 1) evidence of pre-existing bleomycin pulmonary damage; or
- 2) bleomycin exposure within previous 1-2 months.

Other factors necessitating consideration on the basis of increasing the possibility of 1) above are:

- a) total bleomycin dose > 450mg
- b) creatinine clearance < 35ml / min

## Current recommendations

- 1) Assess for evidence of bleomycin pulmonary damage. Single breath CO diffusing capacity (DLCO) is the most sensitive indicator of subclinical damage. A fall of 10-15% should be considered significant. Unfortunately a baseline will not always be available for comparison.
- 2) Patients with no major risk factors appear to be at negligible risk from hyperoxia exposure and can be managed accordingly.
- 3) Patients with one or both major risk factors present should be maintained on lowest  $\text{FiO}_2$  to maintain  $\text{SpO}_2 > 90\%$ .
- 4) Although there are no controlled studies to date, case studies suggest pre-treatment with corticosteroids may be of benefit, especially in those cases where  $\text{FiO}_2 > 30\%$  may be required eg. resection of pulmonary metastases<sup>3</sup>.
- 5) Pre-treatment with agents known to amplify defences against oxygen derived free radicals (eg superoxide dismutase, n-acetylcysteine) has not been investigated to date.

## References

- 1) Goldiner PL et al. Factors influencing postoperative morbidity and mortality in patients treated with bleomycin. *BMJ* 1978;1:1664-7
- 2) La Mantia KR et al. Supplemental oxygen does not cause respiratory failure in bleomycin-treated surgical patients. *Anesthesiology* 1984;60:65-7
- 3) Mathes DD. Bleomycin and hyperoxia exposure in the operating room. *Anesth Analg* 1995;81:624-9.

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