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 FiO₂ 22-25% reported no respiratory complications.

Subsequent authors have refuted the recommendation of Goldiner et al. regarding use of low FiO₂ (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 FiO₂ to maintain SpO₂>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 FiO₂>30% may be required eg. resection of pulmonary metastases.

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


Dr Malcolm Thompson. DISCLAIMER: This resource is produced by voluntary contribution as a service to the Australian medical community. This service is provided in good faith and all reasonable care is taken to ensure the information provided is correct, up to date, and that it has been transcribed correctly. None of the authors or contributors can be held responsible for accuracy, and, in consequence, we disclaim any liability arising directly or indirectly from the use of the information conveyed. If you have any doubts as to the validity of any information please email richard@pobox.com and we will attempt to rectify any uncertainty.