Anesthetic management of the surgical patient on bleomycin sulfate

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Postoperative respiratory failure can occur in the postanesthesia patient who had been previously treated with bleomycin sulfate. The author reviews this surgical hazard and presents one technique to prevent complications in the immediate postoperative period. A case is presented to illustrate the principles discussed.

Pharmacokinetics of bleomycin

Bleomycin is a clinically active antitumor agent discovered by Umezawa and his colleagues as a fermentation product of *Streptomyces verticillus*. This chemotherapeutic agent is active in a variety of human tumors including carcinomas of the skin, head, neck and lungs, in addition to testicular tumors.

Bleomycin has minimal myelosuppressive and immunosuppressive activity. The drug appears to concentrate in the pulmonary tissues and squamous epithelium. Major toxic effects of bleomycin include skin lesions and pulmonary fibrosis resulting from an increase in interstitial lung water. The pulmonary fibrosis seen in these patients might mimic the development or recurrence of metastatic pulmonary disease seen on chest roentgenography or computed tomographic (CT) scanning. This drug appears to sensitize the lungs to the effects of oxygen. Therefore, lung damage can occur with concentrations of oxygen (FIO2) normally considered free from toxic effects.

Goldiner and his associates demonstrated that patients who had received bleomycin or who are under current bleomycin therapy are at risk from ARDS after receiving anesthesia. This acute lung damage was manifest within five days postanesthesia. Their first five reported cases experienced a mortality rate of 100%. These patients had all received bleomycin therapy which had been discontinued up to 12 months prior to receiving anesthesia.

At necropsy for each of these patients, Goldiner found abnormal amounts of interstitial fluid in the lungs. The lungs also exhibited interstitial fibrosis, destruction of types I and II pneumocytes,
and alveolar wall and capillary damage as seen in ARDS.²

A greatly increased incidence of ARDS was also shown by Nygaard and his associates.⁵ Five of 12 of their patients developed ARDS; four within three days postanesthesia.

Factors suggested to lessen the risk of developing ARDS postoperatively in these patients include:

1. Reduction of FiO₂ administered during anesthesia and in the immediate postoperative period with inspired oxygen concentrations maintained below 0.3 (preferably 0.25).³,⁴ Continuous monitoring of FiO₂ is imperative at these critical levels.

2. Careful monitoring of fluid therapy and replacement, with emphasis on the use of colloids rather than crystalloids. Crystalloids should be administered at a rate of 3.5 ml/kg/hr or less depending on urine output and central venous pressure (CVP). Goldiner recommends that the volume of colloids replacement (5% PPF and/or whole blood) be based upon cardiac output, pulmonary capillary wedge pressure and hourly urine output.

Goldiner suggested that an FiO₂ not to exceed 0.45 was sufficient to produce a classic oxygen toxicity and that the use of such FiO₂’s along with crystalloids (rather than colloids) increased morbidity and mortality in these patients.¹,² The mortality rate of 12 successive patients in which Goldiner took into account these two factors was reduced to zero.

From previous reports, there appears to be no correlation between preoperative pulmonary function studies and the incidence of ARDS in the postoperative period.⁴ Allen states the possibility of perhaps maintaining the PAO₂ at normal or slightly elevated levels during anesthesia to ensure a favorable shift in the oxygen dissociation curve and to increase oxygen availability to the tissues.⁴

Upon admission to the intensive care unit, the patient should be immediately placed on incentive spirometry to prevent a decrease in the functional residual capacity and vital capacity while on an FiO₂ of 0.24 or less.

A case report

The following case illustrates an anesthetic technique that carefully monitors fluid therapy/replacement and reduces FiO₂ intra- and postoperatively in patients who have previously received bleomycin. Because our patient had received chemotherapy with this agent, this technique was chosen in an effort to prevent the risk of postoperative respiratory failure, a potential lifethreatening hazard.

The patient was an ASA status IV, 30-year-old black male who was initially seen for cancer of the left testis. A left orchiectomy was performed during a previous hospitalization. The patient then underwent combination chemotherapy with vinblastine, cis-diaminedichloroplatinum and bleomycin. Chemotherapy was completed four weeks prior to this admission and the patient’s presentation for anesthesia. The patient was admitted to the hospital at this time for further evaluation and retroperitoneal lymph node dissection.

The patient’s preoperative vital signs were blood pressure 148/78, pulse 84 and regular, and respirations 20. His temperature was 98°F (36.6°C) orally; skin temperature was 36°C. His height was five feet, nine inches and he weighed 145 pounds (66 kg). He was typed and cross-matched for five units of whole blood. The hematocrit was 34.1% and hemoglobin 11.8 gm after previous transfusions.

Urinalysis was normal as were his liver function studies, except for a slightly elevated lactic dehydrogenase (LDH). Potassium was normal. Arterial blood gases were normal on room air: pH 7.39, PAO₂ 91 torr, PACO₂ 40 torr, and 96.9% saturation. The patient’s chest x-ray showed no active pulmonary disease. Pulmonary function studies were essentially normal. The patient was negative for sickle cell anemia or trait. A routine history and physical examination, except for his present illness, proved to be essentially negative. An Allen’s test was performed and was found to be adequate bilaterally.

The patient had no known drug allergies and was presently on no medications. His alcoholic intake was only occasional, and he had smoked one pack of cigarettes per day for the last three years. There were no significant problems with anesthesia experienced by his family. During his previous hospitalization, the patient had undergone his orchiectomy under a subarachnoid block, and the anesthesia administration was without incident or complications.

For the case under discussion, the patient was premedicated with diazepam 10 mg orally (PO) with 30 ml milk of magnesia, promethazine 25 mg intramuscularly (IM) and glycopyrrolate 0.3 mg IM the morning of surgery. He came to the operating room calm and his mouth was dry.

Prior to induction of anesthesia, an arterial line and central venous line were inserted. The following instruments were used intraoperatively:
BP cuff, ECG, esophageal stethoscope, temperature monitor, Foley™ catheter, FIO2 and end-tidal CO2 (ECO2) monitors, endotracheal tube cuff pressure monitor, arterial blood gas monitor, and peripheral nerve stimulator. Sponges were weighed to ascertain an accurate blood loss.

We elected not to insert a Swan-Ganz™ catheter as we would have the benefit of a central venous pressure (CVP) monitor and Foley catheter. We based our colloid therapy on maintenance of a urinary output of at least 1 ml/kg/hr. Crystalloids were given as maintenance at a rate of 4.8 ml/kg/hr to maintain a CVP of 3.5 cm H2O. (Table I summarizes our care plan.)

The patient was not preoxygenated. He was preloaded with butorphanol tartrate (Stadol®) 30 mg intravenously (IV). A routine induction using thiopental sodium (Pentothal®) 375 mg and 100 mg of succinylcholine was administered, preceded by a defasciculating dose of 3 mg d-Tubocurarine (curare). For tracheal anesthesia, a solution of 4% lidocaine (Xylocaine®) 4 ml was given prior to intubation. Stadol® 10 mg IV was given after intubation. The patient was placed on 70% nitrous oxide and 30% oxygen for the operation (FIO2 ≤ 0.30). Curare was used for a muscle relaxant. A total of 40 mg Stadol® and 42 mg curare were given intraoperatively.

Blood pressure was maintained at a steady 130/82 ± 10% from preoperative values. The CVP was maintained at 1.0-3.5 cm H2O during the operation with urine output of 1.5 ml/kg/hr or more. This was accomplished by using a combination of crystalloids and colloids. Total fluids for this seven-hour procedure were: D5RL 150 ml, lactated Ringer’s solution 2100 ml, 5% purified

### Table I.

**Anesthetic management of a patient who previously received bleomycin therapy.**

**Premedication**

- Diazepam 10 mg orally (PO) with 30 ml milk of magnesia
- Promethazine 25 mg IM
- Glycopyrrolate 0.3 mg IM

One hour prior to induction

**Physiologic Monitoring**

- BP-ECG-Temperature monitoring
- Arterial and CVP catheter
- Foley catheter
- ECO2 and FIO2 monitors
- Arterial blood gases
- Peripheral nerve stimulator
- Endotracheal tube cuff pressure monitor
- Circuit pressure
- Sponges weighed for blood loss
- Esophageal stethoscope

**Special Equipment**

- Warming blanket
- Roll (packed under patient’s right hip to give lateral tilt)
- Compressed air cylinder

**Technique**

- No preoxygenation
- Butorphanol tartrate preload IV
- Pentothal induction
- LTA prior to intubation
- Additional butorphanol IV
- Nitrous oxide-oxygen-muscle relaxant
- Patient placed on compressed air and oxygen for emergence (follow arterial blood gases closely and monitor FIO2)

**Postoperative**

- Continued physiologic monitoring as indicated
- Taken to SICU on FIO2 ≤ 0.24
- Incentive spirometry Q15 min x 8, then Q1H while awake

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protein fraction (PPF) 250 ml and 25% albumin 100 ml. The CVP prior to surgery and fluid loading was zero.

Blood loss for this operation was 1000 ml; no blood was given intraoperatively. The patient’s hematocrit during the operation was 32%. Ventilation was controlled with tidal volume and rate adjusted to maintain the P\textsubscript{ACO\textsubscript{2}} at 35-40 torr. The arterial blood gases averaged: pH 7.44; P\textsubscript{AO\textsubscript{2}} 106 torr; P\textsubscript{ACO\textsubscript{2}} 38 torr; BE +1; 97.9% saturation. The FiO\textsubscript{2} was kept between 26-30% intraoperatively.

The patient, upon emergence from anesthesia, was taken off N\textsubscript{2}O and O\textsubscript{2} after reversal from his relaxant with pyridostigmine 20 mg and glycopyrrolate 0.25 mg. He was then placed on compressed air and oxygen at 5 L/min to deliver an FiO\textsubscript{2} of < 0.24.

The patient underwent the following procedures intraoperatively: (1) retroperitoneal lymph node dissection; (2) liver and lung biopsy; (3) ureterolysis with the placement of a catheter; and (4) appendectomy. He was extubated in the operating room and taken to the surgical intensive care unit where he was maintained on an FiO\textsubscript{2} of < 0.24. He tolerated anesthesia well and without complications.

Progress was uneventful with no signs of pulmonary complications five days postoperatively. The patient’s diagnosis was Stage III embryonal-cell carcinoma of the testes.

Conclusion
Exactly why preoperative treatment with bleomycin should complicate the oxygen therapy of the anesthetic patient is not yet known. Bleomycin—both current and previous use—must therefore be considered a potential risk factor in all patients who subsequently require general anesthesia and oxygen therapy.\textsuperscript{1,2,3,7}

REFERENCES
(2) Goldiner PL, et. al. 1978. Factors influencing postoperative morbidity and mortality in bleomycin treated patients. \textit{New York, Memorial Sloan-Kettering Cancer Center}.

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