Supplemental Oxygen Does Not Cause Respiratory Failure in Bleomycin-treated Surgical Patients

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Bleomycin is a chemotherapeutic agent useful in the treatment of selected neoplasms, including nonseminomatous testicular carcinomas.[1,2] An increased incidence of respiratory failure postoperatively in patients previously treated with bleomycin has been reported.[3,4] The clinical picture is consistent with the adult respiratory distress syndrome. Goldiner et al.[4] concluded that the risk of postoperative pulmonary failure in this patient group could be reduced by the use of oxygen concentrations less than 26% perioperatively.

However, the use of gas mixtures containing less than 26% oxygen during anesthesia may lead to hypoxemia. A retrospective study therefore was undertaken of patients treated with bleomycin for testicular neoplasms who subsequently underwent surgical procedures. We sought to determine if postoperative respiratory complications were associated with enriched oxygen mixtures during anesthesia.

METHODS

The hospital records of 16 patients with testicular cancer treated with bleomycin and subsequently undergoing 18 surgical procedures at the Hospital of the University of Pennsylvania between 1976–1982 were analyzed retrospectively. Preoperative evaluation included a chest x-ray as well as pulmonary function tests and blood–gas analysis in most cases. The intraoperative and postoperative management was determined individually by the anesthesiologists and other physicians caring for the patient. Routine monitoring of electrocardiogram, precordial or esophageal stethoscope, and blood pressure by oscillotonometer was employed in all cases. Intraarterial and central venous cannulae were employed in some cases.

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The patients were divided retrospectively into two groups. Group 1 patients (1–13) received a gas mixture containing at least 30% inspired oxygen during surgery and constituted the critical group for observing the incidence of respiratory failure. Group 2 patients (14–16) received a gas mixture with less than 30% oxygen and are included only for completeness. A polarographic oxygen analyzer in the inspiratory limb of a circle anesthetic circuit was used to monitor oxygen content of the gas mixture. Anesthesia was induced with thiopental 3–5 mg/kg with succinylcholine given to facilitate tracheal intubation. Anesthesia was maintained with nitrous oxide supplemented with either an halogenated anesthetic agent or a narcotic.

In nine patients, the total dose of bleomycin administered was 360 units im (30 units weekly for 12 weeks).[2] In seven patients, the total dose exceeded 500 units (two courses of 20 units $\cdot M^{-2} \cdot day^{-1}$ via 24-h continuous intravenous infusion for 7 days each).[5] When a residual mass was detected by clinical or radiologic studies, a restaging surgical procedure was performed to determine whether the mass represented residual tumor, mature teratoma, or necrotic/fibrotic debris.

When available, preoperative vital capacity, single-breath carbon monoxide diffusion capacity, and the alveolar–arterial O_2 gradient were noted. Pre- and postoperative data were compared using Student's t test for paired data. P values less than 0.05 were considered significant.

RESULTS

The patients had a mean age of 27 ± 2* yr in Group 1 and 30 ± 2 yr in Group 2. The mean bleomycin dose was 407 ± 20 units in Group 1 and 534 ± 8 units in Group 2. The interval between the end of bleomycin therapy and surgery was 10.0 ± 0.3 months in Group 1 and 6.3 ± 0.7 months in Group 2. Only three patients had markedly abnormal pulmonary function tests.

The patients received a variety of anesthetic agents (N_2O, morphine, enflurane, halothane, isoflurane). The operations performed were abdominal or lung surgery for excision of a residual mass after chemotherapy. Duration of anesthesia averaged 6.1 ± 0.7 h in Group 1 and

* Data reported as mean ± SE.

6.6 $\pm$ 0.9 h in Group 2. The intraoperative mean $F_{I_{O_2}}$ was 0.41 $\pm$ 0.04 in Group 1 and 0.24 $\pm$ 0.01 in Group 2. Comparison of available $P(A\text{-}a)O_2$ pre- and postoperatively within Group 1 revealed no statistical difference.

Blood loss intraoperatively varied from minimal to 5,000 ml. No patient received more than 10 units of blood replacement. Group 1 received 8.0 $\pm$ 1.4 ml·kg^{-1}·h^{-1} of crystalloid solution and 0.52 $\pm$ 0.26 ml·kg^{-1}·h^{-1} of colloid solution. Group 2 received 2.4 $\pm$ 1.2 ml·kg^{-1}·h^{-1} of crystalloid solution and 1.2 $\pm$ 0.6 ml·kg^{-1}·h^{-1} colloid solution. Both groups received primarily crystalloid fluid replacement.

The postoperative outcome in all patients was satisfactory. Two postoperative pulmonary complications were noted. Pneumonia developed in one patient, which rapidly resolved with antibiotics, while in another postoperative atelectasis developed, which resolved after 3 days. No patient developed respiratory failure. No patient spent more than 3 days in the surgical intensive care unit. All patients left the hospital within 2 weeks of surgery.

DISCUSSION

The most important side effect of bleomycin therapy is pulmonary toxicity.[5] The acute form of pulmonary toxicity may present as a hypersensitivity pneumonitis[6] or a more typical interstitial pneumonitis.[8-12] This may progress to interstitial fibrosis with restrictive pulmonary function. Two groups have reported[3,4] a high incidence of the adult respiratory distress syndrome in patients undergoing surgery after receiving bleomycin.

Nygaard et al.[3] reported on a group of patients undergoing esophageal resection 6 weeks after bleomycin and radiation therapy. Four of eight patients died of respiratory failure within 6 weeks of surgery. Interstitial pneumonitis was demonstrated in all fatal cases. The authors concluded that the surgical trauma triggered a reaction in the lung sensitized by bleomycin and radiation. Goldiner et al.[4] reported five deaths due to respiratory failure in patients who received bleomycin and underwent surgery. Prior to these deaths, 100 patients had undergone similar surgery with no respiratory deaths. Goldiner et al. implicated the oxygen-enriched gas mixtures used perioperatively and possibly large amounts of crystalloid fluids as the cause of respiratory failure. They concluded that these patients should be managed with low inspired $F_{I_{O_2}}$ and colloid fluid replacement. This advice was repeated in three recent reviews.[12-14]

The use of enriched oxygen mixtures is a routine anesthetic practice, except where it is shown to be detrimental to the patient. In the absence of supplemental oxygen, arterial hypoxemia is common during general anesthesia and is multifactorial in origin.[15,16] The use of increased $F_{I_{O_2}}$ and vigilant monitoring is essential in avoiding this complication. This is especially true during one-lung anesthesia for pulmonary surgery.

Analysis of the records of patients treated with bleomycin undergoing surgery at our institution revealed no incidence of adult respiratory distress syndrome. Our Group 1 patients received a mean $F_{I_{O_2}}$ of 0.41, which is virtually identical to the group of patients who died in the Goldiner et al. nonsurvivor group. Our group in fact underwent longer operations and received more crystalloid fluids. The only two minor pulmonary complications noted in our series, pneumonia and atelectasis, are not unexpected sequelae of abdominal surgery. Both these complications resolved quickly with routine care.

There are differences between our patients and those previously reported. Bleomycin doses in our groups were higher than in the Nygaard et al. series but similar to the nonsurvivors in the Goldiner et al. series. Seven of our patients received an identical chemotherapeutic protocol to the Goldiner et al. patients. The interval between drug administration and surgery in our group was comparable to that in the Goldiner et al. nonsurvivors, though longer than that in the Nygaard et al. series. Few of our patients showed abnormal pulmonary function tests as compared with the series of Goldiner et al. The importance of this observation is unknown.

Our data demonstrate that an enriched inspired O_2 concentration (mean $F_{I_{O_2}} = 0.41$) was not hazardous in a testicular cancer population who were exposed to significant doses of bleomycin. Therefore the oxygen concentration administered to such patients during general anesthesia should not be curtailed.

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Antiemetic Efficacy of Droperidol and Metoclopramide

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Postoperative nausea and vomiting occur frequently in outpatients undergoing general anesthesia for therapeutic abortion and may delay discharge from the hospital. Droperidol administered in small doses before anesthesia, or intraoperatively, has been claimed to be an effective antiemetic.[1-5] However, there is concern that droperidol may prolong recovery. Metoclopramide, a drug with antiemetic and other potentially beneficial properties, is not associated with sedation. This study was designed to compare the efficacy and side effects of droperidol with those of metoclopramide, in an ambulatory surgical population.

METHODS

The study population consisted of 87 healthy female outpatients, 6 to 20 weeks pregnant, undergoing general anesthesia for therapeutic abortion (dilation and evacuation). The study was approved by the Committee on the Use of Human Subjects in Research and informed consent was obtained from all participants. Patients were assigned randomly to one of three groups and received, double blind, an iv injection of the study drug 2–10 min before induction of anesthesia. Treatments, which were prepared by a registered nurse with no other involvement in the study, consisted of placebo, i.e., saline, 2 ml, (Group 1, n = 30); metoclopramide, 10 mg (Group 2, n = 28); or droperidol, 1.25 mg (Group 3, n = 29). In Group 3,

saline was added so that all treatments measured 2 ml. Anesthesia was provided with fentanyl, 75–125 μg iv, thiopental 3–4 mg/kg iv, nitrous oxide, 70%, and an iv succinylcholine infusion. Controlled ventilation via a mask was employed.

In the preoperative interview, a history of nausea and vomiting was sought. Intraoperatively, total drug dosage and the duration of anesthesia were recorded for each patient. The occurrence of nausea and vomiting on emergence from anesthesia and in the recovery room was noted. Recovery from anesthesia was assessed by the anesthesiologist in the operating room and by a trained nurse observer in the recovery room. The times from the end of anesthesia until the patient opened her eyes in response to repeated commands, sat up, walked, and was discharged from the recovery room were noted. State of arousal was evaluated at 15-min intervals by both the patient and an observer, each assigning a score of 0 to 5, where 0 reflected a patient who was fully alert and awake and 5 one who was unarousable. All patients received a take-home questionnaire, and an attempt was made to contact them by telephone the next day to determine the incidence of nausea, vomiting, and dizziness after discharge.

Data were analyzed using chi-square analysis and one-way analysis of variance, including Duncan's multiple range test. Differences were considered significant when $P < 0.05$.

RESULTS

Patients in all groups were similar with respect to age, height, gestational age, anesthetic drug dosage, and duration of anesthesia (table 1). Although similar numbers of patients in all groups had reported preoperative nausea, fewer of the patients who subsequently received metoclopramide had actually vomited during their pregnancy (table 2). The overall incidences of postoperative nausea