Title: THE INCIDENCE OF BLEOMYCIN LUNG TOXICITY AFTER ANESTHESIA FOR PULMONARY RESECTION: A COMPARISON BETWEEN HFV AND IPPV

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Introduction. The use of general anesthesia, high concentrations of oxygen, and IV administration of crystaloid solutions were reported to potentiate bleomycin pulmonary toxicity and cause a high incidence of postoperative ARDS with a high mortality rate. The incidence of postoperative ARDS in bleomycin patients was also found to decrease after anesthesia with FIO_2 below 30% and the use of colloid solutions for fluid maintenance. Because our use of conventional anesthesia and IPPV at FIO_2 above 0.5 for the thoracotomy in bleomycin-treated patients was associated with severe postoperative ARDS, we evaluated the incidence of ARDS during the use of HFV and high frequency ventilation at low FIO_2.

Methods and Materials. Thirty patients were studied, ages 13 to 79, undergoing a variety of intrathoracic procedures (lobectomy, segmentectomy, pneumonectomy). The total dose of bleomycin used was between 250 and 750 units. Preoperative pulmonary function tests showed moderate restrictive and obstructive pulmonary changes in each patient. Anesthesia technique of muscle relaxant (pancuronium) and narcotics (fentanyl) was used in all patients. These patients were divided into three groups of 10 patients according to the method of mechanical ventilation received as shown in Table 1:

Table 1

	Ventilation	Gas Mixture
Group A	IPPV	Nitrous oxide + oxygen
Group B	IPPV	Air + oxygen
Group C	HFPPV	Air + oxygen

Patients in Group A received a mean dose of bleomycin of 300 mg (250 to 550 mg). Their mean preoperative PaO_2 was 61 mmHg (59 to 70 mmHg). This group of patients received IPPV at a respiratory rate of 12 breaths/min., V_T 15 ml/kg using a gas mixture of N_2O and O_2.

Patients in Group B received bleomycin at a mean dose of 325 mg (250 - 450 mg). Their mean preoperative PaO_2 was 57 mmHg (52 - 64 mmHg). IPPV was used in this group as in group A but using an air and oxygen gas mixture.

Patients in Group C received bleomycin at a mean dose of 375 mg (250 - 750 mg). These patients' PaO_2 was at a mean of 53 mmHg (49 to 66 mmHg). Two-lung HFV through an ETT was used in these patients with air and oxygen gas mixture at a respiratory rate between 100 to 150 breaths/min, DGP of 15 to 25 PSI, and inspiratory time of .01 to 0.2 seconds.

The parameters of IPPV and HFV were adjusted to maintain $PaCO_2$ at 40 ± 5 mmHg, and all patients were initially ventilated with a 21% oxygen gas mixture. FIO_2 was only increased to maintain PaO_2 within 5% of each patient's preoperative value. Arterial blood gases were analyzed intraoperatively every 10 minutes.

All patients received fluid maintenance of 1 ml/kg/h of Ringer's lactate. Additional volumes were given (100 ml bolus) to maintain CVP above 5 cm H_2O and urine output above 0.5 ml/kg/h. When blood loss exceeded 20% of blood volume, packed cells were given in equal amounts. At completion of surgery, muscle relaxant was reversed with prostigmine and atropine, narcotics by naloxone, and all patients were extubated within one hour.

Respiratory failure during the first three postoperative days (oxygen saturation below 70, and $PaCO_2$ above 70) was treated by intubation and mechanical ventilation with air. FIO_2 was gradually increased to maintain adequate oxygenation. The evaluation of HFV was approved by HIC.

Results. Adequate oxygenation in Group A required the use of a mean FIO_2 of 35% (21 to 50%). Seven patients (70%) required FIO_2 above 21% to maintain adequate oxygenation. In Group B the mean FIO_2 required was 30% (21 to 50%). Six patients in this group required a higher FIO_2 than 21% to maintain adequate oxygenation. In Group C adequate oxygenation was maintained at a mean FIO_2 of 22% (21 to 24%). Three patients in this group required an FIO_2 higher than 21%.

Table 2

	PaO_2 mmHg	
Group	Preoperative	Intraoperative
A (IPPV)	61 (59-70)	57 (51-64)
B (IPPV)	57 (52-64)	51 (50-59)
C (HFV)	53 (49-66)	56 (52-78)

Postoperative acute respiratory failure occurred in four patients in Group A, three of whom died despite maximal respiratory support. In Group B, two patients developed respiratory failure. Short term respiratory support was used for 24 to 48 hours using air and both patients were successfully weaned and extubated. In Group C, all patients maintained adequate postoperative blood gases and FEV_1/FVC within 10% of preoperative value.

Table 3

Group	FIO_2	ARDS	Mortality
A(N_2O+O_2)	35% (21-50%)	4	3
B(Air+O_2)	30% (21-50%)	2	0
C(Air+O_2)	22% (21-24%)	0	0

Discussion. This study shows that the use of two-lung HFV for pulmonary resection achieved adequate oxygenation at lower FIO_2, and significantly reduced the incidence of ARDS compared to IPPV. HFV is associated with a low Qs/Qt, low airway pressure, minimal alveolar trauma, improves surgical access, and minimizes lung retraction and trauma.

The high incidence of ARDS in patients receiving IPPV with N_2O and oxygen suggests a mechanism of interaction between bleomycin, oxygen and nitrous oxide for pulmonary toxicity.