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## An Unusual Cardiovascular Response to PEEP

YOUNG D. KIM, M.D.,\* DENNIS F. DEVEREUX, M.D.,† THOMAS E. MACNAMARA, M.B., CH.B.‡

General agreement holds that positive end-expiratory pressure (PEEP), used in conjunction with controlled ventilation, frequently reduces cardiac output and arterial blood pressure.<sup>1-4</sup> However, there are reports showing no change in cardiac output.<sup>2,4,5</sup> Although varied opinions appear in the literature regarding the effects of PEEP on the cardiovascular system, no one has reported that PEEP is a contributing factor to a hypertensive crisis. The following case represents an unusual response to PEEP.

### REPORT OF A CASE

A 58-year-old white woman with Hodgkin's disease was admitted for evaluation of fever. Past medical history included chronic essential hypertension and hypothyroidism. The patient was taking propranolol for essential hypertension and L-thyroxine for hypothyroidism.

The hospital course was complicated by diffuse pneumonitis. Open lung biopsy confirmed the diagnosis of *Pneumocystis carinii* pneumonitis, and Pentamidine therapy was instituted. Postoperatively, ventilatory support with a volume-limited ventilator (Bennett MA-1) was necessary.  $F_{I_{O_2}}$  0.7 or more was necessary to maintain  $P_{a_{O_2}}$  at 60 torr. With the addition of PEEP, it was possible to decrease  $F_{I_{O_2}}$  to 0.4. PEEP was discontinued by the fourth postoperative day. During this period, hypertension (150/80-170/100 torr) was controlled with methyl dopa administration. On the fifth day, however, the patient became stuporous. At that time vital signs were: pulse rate 100/min, blood pressure 130/70 torr, rectal temperature 38 C. Central venous pressure (CVP) was 7 cm  $H_2O$ . BUN, glucose and electrolytes were normal. Over the next 24 hours, the patient went into a coma, unresponsive to painful stimuli and quadriplegic with no deep tendon reflexes. Neurologic examination indicated an intact brain stem. There was no change in blood pressure, pulse rate, temperature, or blood chemistry. Because analysis of arterial blood revealed  $P_{O_2}$  57 torr,  $P_{CO_2}$  35 torr, and  $pH$  7.45,  $F_{I_{O_2}}$  was increased to 0.5 and 5 cm  $H_2O$  PEEP was added. About 3 minutes after adding PEEP, the first episode of hypertension, tachycardia and rapid ventilator triggering was observed. PEEP was removed, resulting in return of blood pressure and pulse rate to the pre-

existing levels within 5 minutes. Arterial blood-gas values with PEEP were  $P_{O_2}$  121 torr,  $P_{CO_2}$  28 torr, and  $pH$  7.41. Chest x-ray showed no acute change. The second hypertensive crisis occurred in spite of 8 mg morphine and 6 mg pancuronium administered before adding 5 cm  $H_2O$  PEEP. The hypertensive response ensued within one minute and necessitated nitroprusside for control. PEEP was withdrawn, and attempts to reinstitute 5 cm  $H_2O$  PEEP produced similar episodes. The documentation of these events is presented in table 1. Serum catecholamine levels obtained from the radial arterial line before and after PEEP on two separate occasions are shown in table 2. A lumbar puncture was performed with the patient in the lateral horizontal position. The spinal fluid was clear, with an opening pressure of 37 cm  $H_2O$ , which rose to 42 cm  $H_2O$  when 5 cm  $H_2O$  PEEP was added. PEEP of 5 cm  $H_2O$  elevated CVP from 11 to 14 cm  $H_2O$ . Therefore, PEEP was discontinued and  $F_{I_{O_2}}$  was increased to 0.7 to obtain adequate oxygenation. Dexamethasone, furosemide and hyperventilation were used to decrease intracranial pressure (ICP). A Swan-Ganz catheter was inserted. The initial pulmonary arterial pressure was 32/15 torr and pulmonary arterial wedge pressure was 14 torr. PEEP was then gradually reinstated in small titrated increments to 10 cm  $H_2O$  without a hypertensive episode. PEEP of 10 cm  $H_2O$  allowed  $F_{I_{O_2}}$  to decrease to 0.5. The patient died of multiorgan failure four days later.

At autopsy, the findings were: Hodgkin's disease, *Pneumocystis carinii* pneumonitis, anoxic encephalopathy, bilateral cortical infarctions, left ventricular hypertrophy, minimal coronary arteriosclerosis, and renal infarctions.

### DISCUSSION

The addition of PEEP directly precipitated the episodes of hypertension and tachycardia. These events cannot be explained by recognized effects of PEEP on the cardiovascular system.<sup>1-5</sup> "Fighting the ventilator" is not likely to have occurred in this patient, who was given adequate amounts of morphine and pancuronium. Pheochromocytoma was suspected because of the symptoms and elevated serum catecholamines. However, in the absence of demonstrable

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\* Instructor, Department of Anesthesia, Georgetown University School of Medicine; Attending Anesthesiologist, The National Institutes of Health, Bethesda, Maryland.

† Clinical Associate, Surgical Branch, National Cancer Institute, The National Institutes of Health, Bethesda, Maryland.

‡ Professor and Chairman, Department of Anesthesia, Georgetown University School of Medicine; Chief, Anesthesiology Section, The National Institutes of Health, Bethesda, Maryland.

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Address reprint requests to Dr. Kim: Department of Anesthesia, Georgetown University School of Medicine, Georgetown University Hospital, 3800 Reservoir Rd., N.W., Washington, D.C. 20007.

TABLE 1. Arterial Blood Pressure and Pulse Rate Changes upon Adding PEEP

Number of Episodes	Before PEEP		After PEEP	
	Blood Pressure (Torr)	Pulse Rate (Beats/Min)	Blood Pressure (Torr)	Pulse Rate (Beats/Min)
1	120/60	100	240/120	160
2	130/80	109	270/140	145
3	140/70	102	180/100	149
4	130/70	98	230/120	140
5	150/80	110	200/100	150

TABLE 2. Serum Catecholamine Levels before and after PEEP

Number of Episodes	Time	Before PEEP		After PEEP		Remarks
		Epinephrine (pg/ml)*	Norepinephrine (pg/ml)	Epinephrine (pg/ml)	Norepinephrine (pg/ml)	
4		409	428	866	1,222	5 cm H <sub>2</sub> O PEEP
5	1:00 PM	224	1,088	500	1,807	10 cm H <sub>2</sub> O PEEP was maintained during this period; nitroprusside infusion for blood pressure control
	2:55 PM			528	1,523	
	4:15 PM			545	1,356	
	4:25 PM			858	1,455	

\* Pg/ml = picograms, 10<sup>-12</sup> g.

The technique used for the determination of catecholamines in plasma was based on the method described by Weis and Kopin

in 1976.<sup>16</sup> Normal values from Dr. Kopin's laboratory: epinephrine 100 ± 70, norepinephrine 350 ± 100 pg/ml.

evidence at autopsy or in previous investigations, the diagnosis of pheochromocytoma can be considered extremely unlikely.

Because of the close time association between the onset of coma and these events, it was believed that a pathologic change in the brain, aggravated by addition of PEEP, could have caused this unusual response. PEEP may increase ICP.<sup>6,7</sup> The gain in ICP may exceed the highest PEEP applied to the airway, and may occur at any time after adding PEEP.<sup>7</sup> While direct ICP was not monitored in our case, spinal fluid pressure was measured during one of these episodes; the pressure was high, and was increased by adding PEEP. Increased ICP can cause slowing of the pulse and elevation of blood pressure.<sup>6,8,9</sup> However, hypertension and tachycardia can precede or replace the development of the classic Cushing triad.<sup>6</sup> Although the exact mechanism explaining the cardiovascular changes in increased ICP is still unclear,<sup>8,9</sup> one postulated mechanism is that of ischemia of the medullary vasomotor center.<sup>8</sup> There are reports showing hypertension and tachycardia, as well as increased serum catecholamine levels, in patients with a stroke<sup>10</sup> and cerebral infarction.<sup>11</sup> The factor common to all patients with cerebral infarction and hemorrhage may be CNS ischemia, which is believed to be a potent stimulus for the release of catecholamines.<sup>11-13</sup>

In the patient we described, systemic hypoxia, cerebral infarction and increased ICP were additive to threaten CNS oxygen supply. In cases of marginal CNS ischemia, any detrimental factor, such as further increase in ICP with subsequent reduction of cerebral perfusion pressure by adding PEEP, is enough to initiate manifestations of CNS ischemia.<sup>7</sup> CNS ischemia is known to cause hypertension and tachycardia.<sup>14,15</sup> Thus, it is theoretically possible to conclude that CNS ischemia due to increased ICP from PEEP was the most

probable causative factor of this unusual cardiovascular response.

In summary, a hypertensive crisis persistently followed the institution of PEEP in this specific case. Efforts to lower ICP and improve cerebral perfusion, as well as careful titration of PEEP to meet different organ requirements, is necessary in patients in whom the unusual response described here may develop.

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## Responses to Atropine, Glycopyrrolate, and Riopan of Gastric Fluid pH and Volume in Adult Patients

ROBERT K. STOELTING, M.D.\*

Anticholinergic drugs produce dose-related reductions in the acidity and volume of gastric secretions. These drugs could reduce the severity of acid-aspiration pneumonitis should vomiting or regurgitation occur during the operative period. Indeed, atropine (15-20  $\mu\text{g}/\text{kg}$ ) or glycopyrrolate (7.5-10  $\mu\text{g}/\text{kg}$ ) given intramuscularly an hour before anesthetic induction in children increased the incidence of gastric fluid samples with pH values greater than 2.5.<sup>1</sup> Furthermore, glycopyrrolate also reduced gastric fluid volume. However, similar doses of atropine or glycopyrrolate administered to adult patients would exceed the usual preanesthetic medication dose and might introduce undesirable side effects. This report describes gastric fluid pH and volume following more traditional preanesthetic medication doses of atropine (0.4 mg) or glycopyrrolate (0.2 mg) administered to adult patients scheduled for elective operations.

### METHODS

Two hundred and fifty nonobese adult patients scheduled for elective operations were studied. The study protocol was approved by the Indiana University School of Medicine Human Study Committee. No patient had a disease or was receiving a drug known to influence gastric secretion or motility. All had fasted for at least seven hours before induc-

tion of anesthesia. Depending on the preanesthetic medication administered im 60-90 minutes before anesthetic induction, the patients were divided into four groups:

- I, morphine 10-15 mg (75 patients)
- II, morphine-atropine, 0.4 mg (75 patients)
- III, morphine-glycopyrrolate, 0.2 mg (75 patients)
- IV, morphine-atropine-Riopan† (10 ml followed with 10 ml of water 30 minutes before anesthetic induction) (25 patients)

Anesthetic induction was accomplished with galamine (0.3 mg/kg), followed a minute later by thiamylal (4 mg/kg) and succinylcholine (2 mg/kg). iv. A cuffed endotracheal tube was placed and ventilation controlled with 60 per cent nitrous oxide and 40 per cent oxygen. Within 5 minutes after tracheal intubation an 18-French gastric tube (sump-type) was placed in the stomach. Gastric contents were aspirated for pH and volume determination. Gastric fluid pH was measured within 15 minutes after obtaining the sample, using a Corning pH meter and Beckman electrode.

Data were analyzed using the Chi-square test or analysis of variance.  $P < .05$  was considered significant.

### RESULTS

Patient ages and weights were similar in the four groups (table 1). Compared with patients receiving

† Magaldrate (magnesium and aluminum hydroxide as a single molecule), 80 mg/ml.

\* Professor and Chairman, Department of Anesthesia, Indiana University School of Medicine, Indianapolis, Indiana 46202.

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Address reprint requests to Dr. Stoelting.