amine induced consumption of complement. J Immunol 114:120-124, 1975

14. Best N, Sinosich MJ, Teisner B, Grudzinskas JG, Fisher MM: Complement activation during cardiopulmonary bypass by heparin-protamine interaction. Br J Anaesth 56:339-343, 1984

15. Kirklin JK, Chenoweth DE, Naftel DC, Blackstone EH, Kirklin JW, Bitran DD, Curd JG, Reves JG, Samuelson PN: Effects of protamine administration after cardiopulmonary bypass on complement, blood elements, and the hemodynamic state. Ann Thorac Surg 41:193-199, 1986

16. Lakin JD, Blocker TJ, Strong DM, Yocum MW: Anaphylaxis to protamine sulfate mediated by a complement-dependent IgG antibody. J Allergy Clin Immunol 61:102-107, 1978

17. Morel DR, Zapol WM, Thomas SJ, Kitain EM, Robinson DR, Moss J, Chenoweth DE, Lowenstein E: C5a and thromboxane generation associated with pulmonary vaso- and bronchoconstriction during protamine reversal of heparin. ANESTHESIOLOGY 66:597-604, 1987

18. McIntyre RW, Flezzani P, Knopes KD, Reves JG, Watkins WD: Pulmonary hypertension and prostaglandins after protamine. Am J Cardiol 58:857-858, 1986

19. Degges RD, Foster ME, Dang AQ, Read RC: Pulmonary hypertensive effect of heparin and protamine interaction: Evidence for thromboxane $\beta 2$ release from the lung. Am J Surg 154:696-699, 1987

20. Tan F, Jackman H, Skidgel RA, Zsigmond EK, Erdos EG: Protamine inhibits plasma carboxypeptidase N, the inactivator of anaphylatoxins and kinins. ANESTHESIOLOGY 70:267-275, 1989

21. Gottschlich GM, Gravlee GP, Georgitis JW: Adverse reactions to protamine sulfate during cardiac surgery in diabetic and nondiabetic patients. Ann Allergy 61:277-281, 1988

22. Stewart WJ, McSweeney SM, Kellett MA, Faxon DP, Ryan TJ: Increased risk of severe protamine reactions in NPH insulin-dependent diabetics undergoing cardiac catheterization. Circulation 70:788-792, 1984

23. Levy JH, Schwieger IM, Zaidan JR, Faraj BA, Weintraub WS: Evaluation of patients at risk for protamine reactions. J Thorac Cardiovasc Surg 98:200-204, 1989

Anesthesiology
78:372-376, 1993

Acute Right Ventricular Failure after Pulmonary Hypertensive Responses to Airway Instrumentation: Effect of Fentanyl Dose

Paul R. Hickey, M.D., Susan M. Retzack, M.D.†*

ACUTE right ventricular failure and hemodynamic collapse are potential threats in patients with severe pulmonary hypertension undergoing general anesthesia. Pulmonary hypertension and pulmonary hypertensive crises are a known risk factor for mortality in children with congenital heart disease.[1-5] In these patients, pulmonary hypertensive responses as well as systemic hypertensive responses need to be controlled to avoid acute increases in right ventricular afterload, subsequent right ventricular dysfunction, and possible acute right ventricular failure secondary to ischemia.[6,7]

Low-dose fentanyl (8 μg/kg) in combination with thiopental (3 mg/kg) for induction of anesthesia has been shown to blunt circulatory responses to tracheal intubation,[8] but responses of the pulmonary circulation to intubation after this regimen have not been reported. Several studies document the effectiveness of higher-dose fentanyl (25–100 μg/kg) in providing both systemic and pulmonary hemodynamic stability in children undergoing cardiac surgery and preventing pulmonary hypertensive responses to airway stimulation.[9,10] However, little is known about the minimal dose of fentanyl or other opioids required to blunt pulmonary vascular reactivity.

We present a case of documented acute right ventricular failure secondary to a pulmonary hypertensive crisis provoked by upper airway instrumentation. This

* Associate Professor of Anaesthesia.

† Clinical Fellow in Anaesthesia.

Received from Harvard Medical School and The Children's Hospital, Boston, Massachusetts. Accepted for publication October 16, 1992.

Address reprint requests to Dr. Hickey: Department of Anesthesia, The Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115.

Key words: Analgesics, intravenous: fentanyl. Anesthesia: pediatric. Heart: right ventricular failure.

occurred in a lightly anesthetized patient with known pulmonary hypertension despite a supplemental dose of fentanyl prior to airway instrumentation during the course of an interventional cardiac catheterization. After a larger dose of fentanyl, successful airway instrumentation and tracheal intubation were conducted without further pulmonary artery hypertensive responses.

Case Report

A 3-yr-old, 10-kg girl with Shone's syndrome (multiple left heart obstructions: left ventricular inflow, left ventricular outflow, aorta) presented with severe mitral stenosis and pulmonary hypertension for cardiac catheterization and percutaneous balloon mitral valvuloplasty. She had a juxtaductal coarctation of the aorta repaired on day 10 of life with no residual gradient. Subsequent follow-up demonstrated progressive mitral valve stenosis with increased right-sided pulmonary arterial pressures. These were 80–90% of systemic arterial pressures by 2 yr of age when she underwent successful percutaneous balloon mitral valvuloplasty. This reduced the valvular gradient but had no effect on the near systemic pulmonary artery pressures.

Approximately 1 yr later she returned with symptoms of decreased exercise tolerance, tachypnea, and orthopnea. Her medication at this time included 40 μg digoxin twice daily, 6.25 mg captopril three times daily, 20 mg furosemide twice daily, and 6.25 mg spironolactone as needed. Respiratory rate was 28 breaths/min, cuff blood pressure was 100 mmHg (by palpation), and hemoglobin oxygen saturation was 97% on room air as measured by pulse oximetry (Sp_2). The lungs were clear to auscultation, and a II/VI systolic ejection murmur and a II/VI diastolic rumble were heard at the cardiac apex. Chest x-ray showed slight cardiomegaly and increased pulmonary vascularity. Electrocardiography showed sinus rhythm at 80 beats/min with evidence of left atrial enlargement, right ventricular hypertension with strain, incomplete right bundle branch block, and right axis deviation. An echocardiogram showed a 16-mm mitral valve anulus with an estimated mean transvalvar gradient of 18–22 mmHg and peak gradient of 25–30 mmHg. Right ventricular hypertension with estimated peak pressures of 100 mmHg was found by echocardiography when simultaneous upper extremity systemic arterial pressures were 86/43 mmHg. Systolic displacement of the intraventricular septum to the left side indicated right ventricular pressures greater than those in the left ventricle.

A percutaneous balloon mitral valve dilation was planned, and the patient was premedicated with 2.5 mg diazepam orally approximately 1 h before the procedure. Monitoring included a five-lead electrocardiograph, pulse oximetry, automated blood pressure cuff, and capnography. Light general anesthesia for the initial hemodynamic catheterization study was obtained with an initial dose of intravenous ketamine (1 mg/kg) and midazolam (0.15 mg/kg) given in divided doses over 5 min and maintained with a continuous infusion of ketamine and midazolam at a rate of 1–1.5 $mg \cdot kg^{-1} \cdot h^{-1}$ and 0.1–0.15 $mg \cdot kg^{-1} \cdot h^{-1}$, respectively.[11] No substantial cardiovascular changes of heart rate or blood pressure were noted with the initial dose of ketamine. The patient was spontaneously breathing room air throughout the hemodynamic study, and an arterial blood gas measurement showed pH 7.42, Pa_{CO_2} 36.6, Pa_{O_2} 86.5, Hct 28, whereas pressure measurements revealed a peak right ventricular pressure of 120–130 mmHg, right pulmonary artery systolic pressure of 125 mmHg (mean 94), pulmonary capillary wedge pressure of 32 mmHg, pulmonary artery diastolic to left ventricular end diastolic pressure gradient of 14–18 mmHg, and aortic systolic pressure of 94 mmHg (mean 64) as shown in table 1.

After the hemodynamic study was completed, elective tracheal intubation with muscle relaxation was planned for greater control of airway, level of ventilation, and patient movement to facilitate percutaneous balloon dilation of the stenotic mitral valve. At this point, the patient had received a total of approximately 5 mg/kg ketamine and 0.7 mg/kg midazolam over 2 h and was minimally responsive. While the patient breathed 100% oxygen, anesthesia was supplemented with 10 μg/kg fentanyl and muscle relaxation was obtained using 0.1 mg/kg pancuronium without substantial change in heart rate or blood pressure. Ventilation was controlled for 5 min after the fentanyl and pancuronium were given (end tidal CO_2 25 mmHg), and pulmonary artery systolic pressures decreased to less than aortic pressures (table 1).

Table 1. Hemodynamics and Gas Measurements

	Light GA Spontaneous Respiration	10 μg/kg Fentanyl Controlled Ventilation	First Insertion Nasal ETT	After Removal Nasal ETT	15 μg/kg Fentanyl Hyperventilation and Nasotracheal Intubation	10 min after Intubation
Pressures						
Pulmonary arterial systolic pressure (mmHg)	125	85	160	155	75	60
Aortic systolic pressure (mmHg)	94	95	50	95	98	95
ET_{CO_2} (mmHg)	18–24	23–25	25	25	25	32
Pa_{CO_2} (mmHg)	37	—	36	37	37	41
Arterial blood gases						
*p*H	7.24	—	7.39	7.42	7.41	7.34
P_{O_2} (mmHg)	87	—	86	71	71	475
p_{CO_2} (mmHg)	37	—	36	37	37	41
FI_{O_2} (mmHg)	0.21	1.0	1.0	1.0	1.0	1.0

GA = general anesthesia; ETT = endotracheal tube; ET_{CO_2} = end-tidal CO_2.

Five minutes after these drugs were given, an attempt to pass a lubricated, uncuffed 5.0-mm endotracheal tube nasally was met with resistance at 1–1.5 cm depth, and pulmonary artery systolic blood pressure abruptly increased from 85 to 160 mmHg with a resultant decrease in systemic systolic blood pressure from 95 to 50 mmHg and an increase in heart rate from 100 to 120 beats/min (table 1). The endotracheal tube was withdrawn immediately, the lungs ventilated with 100% oxygen, and an additional 15 μg/kg fentanyl was administered. The systemic hypotension rapidly resolved, and systemic arterial pressures returned to baseline, although the pulmonary arterial hypertension persisted for several minutes (table 1).

Once pulmonary arterial pressures decreased to systemic levels, nasotracheal intubation was accomplished uneventfully using a 4.5-mm endotracheal tube. No further increases in pulmonary arterial pressure or decreases in systemic arterial blood pressure occurred, and within several minutes after tracheal intubation, pulmonary arterial pressure had decreased to less than systemic arterial pressure (table 1). By 10 min after the second opioid dose, intubation, and mechanical ventilation, pulmonary arterial pressure was less than two-thirds the systemic arterial pressure. This was the lowest recorded pulmonary arterial pressure at any time during the procedure (table 1).

The balloon valvuloplasty of the mitral valve then proceeded, complicated by transient episodes of varying degrees of atrioventricular conduction block and three episodes of asystole, coinciding with balloon dilation attempts. The patient responded well to resuscitation measures and medications during the periods of asystole. Postdilation measurements showed left atrial pressures of 24/14/21 (systolic/diastolic/mean), and a left ventricular end-diastolic pressure of 14 mmHg, while in 2:1 block. Angiography showed moderate-to-severe mitral regurgitation. The patient was taken to the cardiac intensive care unit, where her course was complicated by fever, right lower lobe pneumonia, and pulmonary artery pressures at systemic levels. She recovered, but remained somewhat listless and irritable. She was discharged to home on the 15th hospital day.

Discussion

Pulmonary hypertension, particularly that seen with some forms of congenital heart disease and with mitral stenosis, remains a poorly understood management problem during anesthesia. Several authors have noted the effective use of ketamine sedation and light general anesthesia in pediatric patients undergoing cardiac catheterization.[11–13] Although ketamine has been associated with increased pulmonary vascular resistance in adults, induction doses of ketamine (2 mg/kg) given as a bolus have been shown in several studies to have little effect on pulmonary vascular resistance in infants and children with normal or elevated baseline pulmonary vascular resistance when effects on the airway and ventilation are controlled,[14,15] although a single report disputes this.[16] When smaller doses of ketamine are given over a prolonged period of time, as in this child, increased pulmonary vascular resistance is unlikely.

Our patient had severe mitral stenosis and pulmonary arterial and right ventricular hypertension documented by echocardiography and previous cardiac catheterizations. During the initial period of light general anesthesia with ketamine and midazolam, while spontaneously breathing she showed no signs of airway compromise, acidosis, hypercarbia, or hypoxia, and pulmonary arterial pressures were slightly suprasystemic (table 1). These measurements were consistent with the echocardiographic evidence of suprasystemic pulmonary arterial pressures (systolic deviation of the ventricular septum to the left) while the patient was awake before the catheterization and show that pulmonary artery pressures were not increased to suprasystemic levels by the ketamine. Furthermore, no clinically significant cardiovascular stimulation was noted when the ketamine was given initially.

After supplementing the anesthesia with the initial dose of fentanyl (10 μg/kg) and pancuronium, ventilation was controlled for 5 min immediately prior to the pulmonary hypertensive event. Neither the heart rate nor the arterial blood pressure increased during this period as a result of the pancuronium, and the pulmonary arterial pressures became slightly subsystemic for the first time during the case (table 1). Instrumentation of the upper airway then provoked severe pulmonary hypertension and systemic hypotension indicative of acute right heart failure. Upon withdrawal of the stimulus, hyperventilation, and increase of the total dose of fentanyl to 25 μg/kg, this resolved. Passage of the smaller nasotracheal tube through the upper airway with subsequent laryngoscopy and endotracheal intubation was then accomplished without another episode of suprasystemic pulmonary hypertension and acute right ventricular failure. In fact, shortly after these events, the pulmonary arterial pressures had decreased to the lowest levels recorded during the catheterization.

It is likely that the dose of fentanyl required to blunt the sympathetic response to instrumentation of the upper airway was underestimated. Low-dose fentanyl (8 μg/kg) when combined with thiopental (3 mg/kg) in adults has been shown to blunt the cardiovascular response to laryngoscopy and tracheal intubation.[8] Higher-dose fentanyl (50–100 μg/kg) appears to be effective in children and adults for blunting vascular responses to surgical stimulation.[17] Doses of 25 μg/kg fentanyl provide stability of both the systemic and pulmonary circulations in infants who have undergone cardiac surgery [10] or are undergoing bronchocarinal

stimulation *via* endotracheal tube suctioning.[11] After a total dose of 25 μg/kg fentanyl had been given, the airway could be instrumented in this patient without a hypertensive reaction in the pulmonary arterial bed. However, because we did not test the reactiveness of the pulmonary vascular bed after intermediate doses of fentanyl, we cannot comment on the minimal dose required to blunt preliminary vascular reactivity in this patient.

Although most studies investigating the ability of a particular anesthetic agent to blunt the circulatory responses to tracheal intubation focus on the stress of laryngoscopy, tracheal intubation, and the systemic circulatory responses, in this case a severe pulmonary response occurred with instrumentation of the upper airway in the nasopharynx. The only part of the airway stimulated at that point was the nasal mucosa, whose innervation is supplied by two branches of the trigeminal nerve (anterior ethmoidal nerve and nasopalatine nerve) and the sympathetic nervous system. Our initial attempts to supplement the level of general anesthesia with fentanyl (10 μg/kg) were inadequate to blunt the sympathetic response to noxious nasal mucosal stimulation. This led to subsequent severe suprasystemic pulmonary artery pressures, acute right ventricular failure, and systemic hypotension. Monitoring the pulmonary artery and aortic pressures enabled us to identify the problem immediately and to document its resolution as stimulus withdrawal, hyperventilation, and an additional 15 μg/kg fentanyl returned pulmonary and aortic arterial blood pressures to baseline. After a total dose of 25 μg/kg fentanyl, no additional pulmonary hypertensive events occurred when nasal intubation, laryngoscopy, and tracheal intubation proceeded 5 min later.

Pulmonary hypertensive crises occurring at various times, including intraoperatively during anesthesia with instrumentation of the airway, postoperatively in the intensive care unit with suctioning of the trachea, or other noxious stimulation, continues to be a management problem for the clinician.[1–5] Some centers use continued postoperative opioid infusions to decrease pulmonary hypertensive and other stress responses in children who have undergone cardiac surgery.[18] Although this is often effective, it is not necessarily consistent with the anesthetic goals for cardiac catheterization procedures, *i.e.*, a short recovery period and minimal hospital stay. Perhaps a shorter-acting opioid such as alfentanil would be useful in this situation. However, dose-response studies of opiates and pulmonary vascular reactivity to noxious stimulation have not been determined in children or adults.

Alternative approaches to prevention of such pulmonary hypertensive events might include local, topical, or regional blockade of upper and lower airway afferent input to the sympathetic vasomotor centers and blockade of the sympathetic efferents to the pulmonary circulation at the level of the stellate ganglion, although these approaches have not been reported in patients. Once pulmonary hypertensive crises have occurred, treatment sometimes requires pressor support to increase perfusion pressure in the coronary arteries supplying the right ventricle to reverse right ventricular ischemia and cardiovascular collapse,[7] although this was not required in our patient. Additional treatments for pulmonary hypertensive crises are directed at selectively decreasing pulmonary vasoconstriction without decreasing systemic perfusion pressure. The use of prostaglandin E1 infusions[19] as well as experimental clinical trials utilizing inhaled nitric oxide[20,21] have met with some success.

This case report illustrates the importance of adequate levels of anesthesia in the prevention of pulmonary hypertensive crises in patients with a reactive pulmonary vasculature. Patients at risk for these problems include those with pulmonary artery pressures approximating 75% or greater of systemic arterial pressures. The mechanism by which anesthesia prevents pulmonary hypertensive crises in these patients is poorly understood, because control of the reactive pulmonary circulation remains to be elucidated. However, for clinicians, this demonstration of the effectiveness of opioids in blunting these responses provides at least one technique for the anesthetic management of such patients.

References

1. Lincoln CR, Rigby ML, Mercanti C, Al Fagih M, Joseph MC, Miller GA, Shinebourne EA: Surgical risk factors in total anomalous pulmonary venous connection. Am J Cardiol 61:608–611, 1988

2. Mavroudis C: Anatomical repair of transposition of the great arteries with intact ventricular septum in the neonate: Guidelines to avoid complications. Ann Thorac Surg 43:495–501, 1987

3. Cullen M, Splittgerber F, Sweezer W, Hakimi M, Arciniegas E, Klein M: Pulmonary hypertension postventricular septal defect repair treated by extracorporeal membrane oxygenation. J Pediatr Surg 21: 675–677, 1986

4. Oelert H, Schafers HJ, Stegmann T, Kallfelz HC, Borst HG: Complete correction of total anomalous pulmonary venous drainage: Experience with 53 patients. Ann Thorac Surg 41:392–394, 1986

5. del Nido PJ, Williams WG, Villamater J: Changes in pericardial surface pressure during pulmonary hypertensive crises after cardiac surgery. Circulation 76(suppl 3):93–96, 1987

6. Belik J, Light RB: Effect of increased afterload on right ventricular function in newborn pigs. J Appl Physiol 66:863–869, 1989

7. Vlahakes GH, Turley K, Hoffman JIE: The pathophysiology of failure in acute right ventricular hypertension: Hemodynamic and biochemical correlations. Circulation 63:87–95, 1981

8. Martin DE, Rosenberg H, Aukburg SJ, Bartkowski RR, Edwards MW, Greenhow DE, Klineberg PL: Low-dose fentanyl blunts circulatory responses to tracheal intubation. Anesth Analg 61:680–684, 1982

9. Hickey PR, Hansen DD, Wessel DL, Lang P, Jonas RA, Elixon EM: Blunting of stress responses in the pulmonary circulation of infants by fentanyl. Anesth Analg 64:1137–1142, 1985

10. Hickey PR, Hansen DD, Wessel DL, Wessel DL, Lang P, Jonas RE: Pulmonary and systemic responses to fentanyl in infants. Anesth Analg 64:483–486, 1985

11. Hickey PR, Wessel DL, Streitz SL, Fox ML, Kern FH, Bridges ND, Hansen DD: Transcatheter closure of atrial septal defects: Hemodynamic complications and anesthetic management. Anesth Analg 74:44–50, 1992

12. Faithfull NS, Haider R. Ketamine for cardiac catheterization. Anaesthesia 26:318–323, 1971

13. Coppel DL, Dunder JW: Ketamine anaesthesia for cardiac catheterization. Anaesthesia 27:25–31, 1972

14. Hickey PR, Hansen DD, Cramolini GM, Vincent RN, Lang P: Pulmonary and systemic hemodynamic responses to ketamine in infants with normal and elevated pulmonary vascular resistance. ANESTHESIOLOGY 62:287–293, 1985

15. Morray JP, Lynn AM, Stamm SJ, Herndon PS, Kawabori I, Stevenson JG: Hemodynamic effects of ketamine in children with congenital heart disease. Anesth Analg 63:895–896, 1984

16. Wolfe RR, Loehr JP, Schaffer MS, Wiggins JW: Hemodynamic effects of ketamine, hypoxia, and hyperoxia in children with surgically treated congenital heart disease residing >1,200 meters above sea level. Am J Cardiol 67:84–87, 1992

17. Hickey PR, Hansen DD: Fentanyl- and sufentanil-oxygen-pancuronium anesthesia for cardiac surgery in infants. Anesth Analg 63: 117–124, 1984

18. Anand KJS, Hickey PR: Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. N Engl J Med 326:1–9, 1992

19. D'Ambra MN, LaRaia PJ, Philbin DM, Watkins WD, Hilgenberg AD, Buckley MJ: Prostaglandin E_1: A new therapy for refractory right heart failure and pulmonary hypertension after mitral valve replacement. J Thorac Cardiovasc Surg 89:567–572, 1985

20. Frostell C, Fratacci M-D, Wain JC, Jones R, Zapol WM: Inhaled nitric oxide: A selective pulmonary vasodilator reversing hypoxic pulmonary vasoconstriction. Circulation 83:2038–2047, 1991

21. Roberts JD, Polaner DM, Todres ID: Inhaled nitric oxide (NO): A selective pulmonary vasodilator for the treatment of persistent pulmonary hypertension of the newborn (PPHN) (abstr). Circulation 84:321, 1991

Anesthesiology
78:376–379, 1993

Intraoperative Pacemaker-mediated Tachycardia: A Complication of Dual-chamber Cardiac Pacemakers

E. Samain, M.D., J. Marty, M.D.,† H. Dupont, M.D.,‡ E. Mouton, M.D.,§ J. M. Desmonts, M.D.†*

PACEMAKER dysfunctions commonly reported during the perioperative period include pulse generator inhibition or reprogramming induced by electromagnetic interference emitted by electrosurgical diathermy units.[1–3] However, more complex or specific complications, such as pacemaker-mediated tachycardia (PMT), may be observed with recently designed dual-chamber pacemakers.[4,5] In this report, we describe an unusually sustained PMT that occurred intraoperatively in a patient with an atrioventricular sequential pacemaker.

* Assistant Professor of Anesthesiology, University of Paris VII.

† Professor of Anesthesiology, University of Paris VII.

‡ Resident in Anesthesiology, Department of Anesthesiology, Bichat Hospital.

§ Staff Cardiologist, Department of Cardiology, Bichat Hospital.

Received from Bichat Hospital and University of Paris VII, Paris France. Accepted for publication October 16, 1992.

Address reprint requests to Dr. Samain: Département d'Anesthésiologie, Hôpital Bichat, 46, rue Henri-Huchard, 75018 Paris, France.

Key words: Complications: tachycardia. Heart: pacemaker.

Case Report

A 71-yr-old, 110-kg man was admitted for elective total knee replacement in October 1990. In January 1989, evaluation of several syncopal episodes had revealed intermittent complete heart block. Consequently, a Telectronics (model Aurora 6291, Sydney, Australia) atrioventricular sequential programmable pacemaker was inserted