placement: 1) preoperative hydration; 2) endotracheal intubation and controlled positive pressure ventilation; 3) skeletal muscle relaxation; 4) maintenance of Trendelenburg's position until after the catheter has been successfully passed through the cannula and the cannula has been removed; and 5) discontinuance of O₂ before instrumentation of the vein. The first measure, adequate preoperative hydration, should be stressed as these patients are frequently dehydrated by the underlying disease process necessitating the placement of the central catheter. Adequate hydration will help prevent entrapment of air by maintaining greater pressure in the central venous system, and furthermore, may make resuscitation more successful should air embolism occur. The second, third, and fourth measures help maintain positive intrathoracic pressure and back-bleeding in the open vein. They insure that the patient does not initiate a spontaneous breath, which would create negative pressure relative to atmospheric pressure. The fifth measure, elimination of O₂ before instrumentation of the vein, is a prophylactic measure in the event air is entrained. Although the use of positive end-expiratory pressure has been promoted to decrease the likelihood of air embolism by also increasing

back-bleeding, its use is not recommended. Recent evidence demonstrates that positive end-expiratory pressure may reverse the pressure gradient between the atria and thereby increase the likelihood of paradoxical air embolism if a patent foramen ovale or atrial septal defect exists. Given that 25–30% of the population may have a probe-patent foramen ovale, the possibility of increased risk of paradoxical air embolism is worrisome.

We present two cases that illustrate the danger of air embolism imposed by the placement of Broviac®/Hickman® catheters in the pediatric patient. Prevention of intraoperative air entrainment should be a major goal in the successful management of these patients. We have outlined several simple measures to prevent air entrainment, which, if followed, should reduce the risk of air embolism.

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Bradycardia and Asystole Following the Rapid Administration of Sufentanil with Vecuronium

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Sufentanil, a fentanyl analogue, has been demonstrated to be five to ten times more potent than fentanyl and to provide similar or greater cardiovascular stability in the clinical setting. The recently released nondepolarizing neuromuscular blocker, vecuronium, has minimal effects on heart rate (HR) and blood pressure (BP) when used with inhaled or narcotic anesthetics. Hemodynamic responses with the simultaneous administration of these two drugs have not been described. We report three patients scheduled for coronary artery bypass grafting (CABG) in whom the association of sufentanil and vecuronium resulted in severe bradycardia or asystole during induction of anesthesia.

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REPORT OF THREE CASES

Case 1: A 61-yr-old man (80 kg) was scheduled for elective, three-vessel CABG. Past medical history included hypertension, hyperlipidemia, obesity, gout, and bilateral internal mammary implantations (Vineberg operation) performed 16 yr before this admission. Cardiac catheterization showed normal left ventricular function. The patient was taking propranolol 40 mg tid, diltiazem 30 mg tid, nitroglycerin patch 5 mg qd, allopurinol 300 mg qd, and probenecid bid. Premedication included diazepam 10 mg orally, scopolamine 0.4 mg im, and nitroglycerin patch 10 mg. The usual dose of propranolol was given on the morning of operation. This patient was monitored via a radial 20-g arterial catheter, an 18-g central venous pressure (CVP)-catheter placed in the internal jugular vein, and ECG, lead V₅ continuously with limb leads intermittently. The following patients were monitored likewise. Baseline hemodynamics were HR = 60 beats/min, BP = 130/76 mmHg, and CVP = 10 mmHg. Breathing 100% oxygen via mask, anesthesia was induced with sufentanil 500 μg and vecuronium 10 mg given iv over approximately 1.5 min. Arterial blood pressure fell to 100/50 mmHg and was accompanied by severe bradycardia and a brief period of asystole, which responded to 0.4 mg iv atropine (fig. 1). The subsequent anesthetic course was uneventful. HR and BP were recorded continuously on a paper strip recorder.

Case 2. A 64-yr-old man (87 kg) was scheduled for elective four-vessel CABG. Past medical history included hypertension, adult onset
diabetes, and peripheral vascular disease. Cardiac catheterization showed the left ventricle to be impaired mildly. The patient was receiving atenolol 50 mg qd, diltiazem 60 mg tid, isosorbide dinitrate 20 mg qid, and Dyazide® qd. Premedication was morphine 7.5 mg and scopolamine 0.4 mg im, with nitroglycerin patch 5 mg. He had received his usual dose of atenolol and diltiazem on the morning of operation. Baseline hemodynamics were HR = 62 beats/min, BP = 146/56 mmHg, and CVP = 8 mmHg.

When the patient was breathing 100% oxygen via mask, anesthesia was induced with sufentanil 750 μg, and vecuronium 8 mg given iv over about 1.5 min. Immediately after drug administration, HR slowed to 55 beats/min with BP = 68/36 mmHg. Acceptable vital signs returned after 0.4 mg iv atropine administration; the subsequent anesthetic course was uneventful.

Case 3. A 55-yr-old man (95.5 kg) was scheduled for elective three-vessel CAGB. Past medical history included hypertension, chronic lung disease, and myocardial infarction occurring 10 months before the operation. Cardiac catheterization showed the left ventricle to be impaired mildly with akinesis of the infraartial portion of the diaphragmatic wall. The patient was receiving metoprolol 50 mg qd, isosorbide dinitrate 5 mg tid, and nitroglycerin patch 5 mg qd. Premedication was morphine 9 mg and scopolamine 0.4 mg im, with nitroglycerin patch 10 mg. He had received his usual dose of metoprolol 2 h before induction. Baseline hemodynamics were HR = 65 beats/min, BP = 148/85 mmHg, and CVP = 10 mmHg.

When the patient was breathing 100% oxygen via mask, anesthesia was induced with diazepam 20 mg, sufentanil 250 μg, and vecuronium 10 mg given iv. Immediately before endotracheal intubation, his BP was 110/60 mmHg with a HR of 55 beats/min. During laryngoscopy, the patient became asystolic (fig 2). Vital signs returned to normal without pharmacologic treatment on completion of intubation; the subsequent anesthetic course was uneventful. HR and BP were recorded continuously on a paper strip recorder.

**DISCUSSION**

All of our patients had preoperative hypertension and had received calcium-entry and/or beta-adrenergic blocking drugs up to the morning of operation. Their baseline HRs were about 60 beats/min. They were not hypovolemic as judged by CVP measurements. Ventricular function was normal or showed mild impairment.

The three cases reported illustrate the undesirable cardiovascular side effects of bradycardia and asystole following the combined use of two newly released drugs. Because the two drugs were given simultaneously, it is not possible to infer the relative contribution of either drug toward the observed cardiovascular effect.

However, there are several potential causes of bradycardia and asystole to be reviewed. These include the rapid administration of a potent opioid; a lack of synergistic interaction between the two drugs involved to achieve desirable hemodynamics; the interaction of either or both drugs with the calcium-entry and/or beta-adrenergic blocking drugs given preoperatively; or vagal stimulation during laryngoscopy under conditions of light anesthesia.

Although rapid injections of fentanyl are well tolerated hemodynamically in patients with good ventricular function, this may not always be the case with sufentanil. The
rates of sufentanil injection in patients 1 and 2 were 4.1 and 5.7 μg·kg⁻¹·min⁻¹, respectively. This is comparable to the 5 μg·kg⁻¹·min⁻¹ rate of sufentanil administration in a similar group of patients receiving beta-adrenergic blocking drugs who did not have resulting bradycardia. However, in that study, the neuromuscular blocker administered simultaneously with sufentanil was pancuronium bromide.

A frequent pharmacologic effect of opioid anesthesia is bradycardia. Studies in animals not receiving atropine have shown reductions in HR to occur with fentanyl or sufentanil. This effect can be countered by atropine or by the vagolytic and indirect sympathomimetic effects of pancuronium when it is used. Because vecuronium does not release histamine and has no autonomic or vagolytic effects, there is no synergistic interaction between drugs to oppose the opioid-induced bradycardia.

The slow baseline HRs (55–62 beats/min) seen in our patients may be reasonably attributed to preoperative beta-adrenergic blocker therapy. Whether these drugs and the preoperative calcium-channel blockers influenced the severe vagotonic responses following the sufentanil-vecuronium injections is not clear.

The electroencephalogram (EEG) effects of sufentanil are very similar to those of fentanyl and probably reflect anesthetic depth. EEG activity representing cortical depression has been observed with sufentanil as low as 2.6–3.7 μg/kg. The sufentanil doses given before the events reported in patients 1 and 2 were 8.6 μg/kg and 6.3 μg/kg, respectively, thus most likely adequate for induction of anesthesia.

In patient 3, decreases in BP and HR occurred with a small dose (2.6 μg/kg) of sufentanil administered after iv diazepam. Some of the hemodynamic instability noted in this patient may have resulted from the combined effects of this drug sequence. Reduction in BP and systemic vascular resistance (SVR) have been shown to occur in a similar drug sequence when fentanyl was used as the opioid. Severe bradycardia, however, has not been reported with this combination. Perhaps the low sufentanil dose in this patient may have been less than adequate narcotic anesthesia, resulting in an accentuated parasympathetic response during laryngoscopy.

In summary, occurrences of bradycardia or transient asystole are described in three patients with slow baseline HRs who received sufentanil and vecuronium for induction of anesthesia. Mechanisms that may have contributed to this effect include the rapid injection of sufentanil in patients receiving beta-adrenergic and/or calcium-channel blockers, or the lack of vagolytic support associated with vecuronium in contrast to pancuronium when used with narcotics in patients not receiving atropine.

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