Clonidine, a centrally acting α blocker used to treat hypertension,1 has been advocated as a preoperative medication because of its ability to reduce sympathetic tone and thus moderate autonomic responses during anesthesia. This reduction in sympathetic tone results in a decreased heart rate, which may be a problem when other drugs are added during the anesthetic.2 In the case reported here, a patient taking guanfacine, a drug related to clonidine, experienced sudden and severe bradycardia during a knee arthroscopy under epidural anesthesia.

CASE REPORT

A 53-yr-old man presented for arthroscopy of his left knee under epidural anesthesia. He was taking 1 mg guanfacine per day for hypertension, but was otherwise in good health. A lumbar laminectomy had been performed under general anesthesia several years previously without incident. There was no history of cardiac disease or diabetes, and an electrocardiogram was normal. Initial blood pressures were 145/85 mmHg with a pulse of 68 beats/min on arrival, and 156/90 mmHg with a pulse of 70 beats/min on entry to the operating room. With the patient in the left lateral decubitus, the tip of an 18-G Tuohy needle was placed in the epidural space at about the L2-3 interspace without difficulty. Twelve milliliters 2% lidocaine with epinephrine plus 50 μg fentanyl and 1 mEq NaHCO₃ were injected, and a catheter was inserted. Seven minutes later, while the patient was sitting and moving himself onto the operating table, an additional injection of 5 ml plain 2% lidocaine was given. There was no response to the tourniquet, but when surgery began, 42 min after the initial injection, he complained of some discomfort. Because of this, he was given an additional injection of 4 ml plain 2% lidocaine with 50 μg fentanyl after aspirating the epidural catheter. At this point, the blood pressure was 142/76 mmHg with a pulse of 57 beats/min. Surgery proceeded and, after 3–5 min, the patient reported complete lack of sensation in the extremity. No premedication had been given, and no intravenous sedatives or opioids were used. Approximately 6 min after the last injection, the pulse rate decreased to 52 beats/min. The blood pressure was 124/67 mmHg, and the patient was comfortable and conversing with the surgeon. When the pulse decreased further to 45 beats/min, 0.8 mg atropine was given intravenously. Before this drug had time to act, the pulse decreased further to 56 and then to 12 beats/min (fig. 1). The blood pressure 1 min previously had been 132/85. At this point, 52 min after the initial injection, the patient complained of slight nausea but was otherwise alert and comfortable. Ephedrine (about 15 mg) and naloxone (0.04 mg) were given. The pulse increased to 104 beats/min with a concomitant increase in the blood pressure to a peak of 218/123 mmHg. After another 15 min, the blood pressure was 161/97 mmHg and the pulse was 85 beats/min. The total duration of the profound bradycardia (pulse <40 beats/min) was less than 2 min. The patient’s nausea cleared rapidly with the increase in his pulse rate, and he remained comfortable and unaware of any problems. Although the pulse oximeter readings were not specifically noted during this episode, the alarm did not sound, indicating a consistent reading above 90%. After the vital signs had stabilized, sensation to light touch was noted to be normal down to at least T3. At the time of discharge, 3 h after the initial epidural injection, the pulse was 72 beats/min and the blood pressure was 128/76 mmHg.

DISCUSSION

Although this patient’s bradycardia did not progress to asystole, some of the observations here may be pertinent to the mechanisms in previous reports of cardiac arrest during spinal anesthesia.3,4 Several factors were present in this patient, each of which may have contributed to the severe bradycardia. Guanfacine is a centrally acting α₂ adrenergic agonist with pharmacologic properties similar to those of clonidine. It has a long half-life, permitting daily dosage, and our patient had taken his medication the morning of surgery. Guanfacine and clonidine act in the central nervous system (CNS) to reduce sympathetic outflow, thus reducing blood pressure and heart rate.5 The use of clonidine as a premedicant is based on its ability to reduce the sympathetic response to stimulation from surgery or induction of anesthesia. The effects of combining clonidine with other drugs that decrease heart rate have not been examined, but it has been shown to exaggerate the reflex bradycardia produced by angiotension.6 Clonidine can produce severe bradycardia,7 and one of the risk factors for this complication is other sympatholytic drugs. Although the exact level of the block in this case was not determined, it was not above T3. Nevertheless, some of the cardiac sympathetics may have been affected.8 Placement of the catheter at L2–3 may have produced a higher block than if the catheter had been inserted at the L3–4 level, and scarring in the epidural space from his previous back surgery may have caused the local anesthetic to move to a slightly higher level. Fentanyl produces bradycardia primarily via the vagus nerve through direct action in the CNS.4 The dose in this case was small (100 μg total), but administration into the epidural space would produce higher spinal fluid concentrations than the same dose given intravenously, thus magnifying any CNS effects. The location of

Medical Director.
Received from the Virginia Beach Ambulatory Surgery Center, Virginia Beach, Virginia. Accepted for publication August 19, 1992.
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Key words: Anesthetic techniques: epidural. Complications: bradycardia. Sympathetic nervous system, α₂ adrenergic agonist: guanfacine.
the epidural catheter (1.2-3) and the slightly head-down position of the patient at the time of the last injection both would favor cephalad spread of the fentanyl within the CNS. The use of intravenous fentanyl is found frequently in case reports of asystole or bradycardia during spinal anesthesia,4,9 and the reduction in heart rate from this source may be a neglected factor. Lidocaine has a direct effect on the cardiac conducting system10 at concentrations that were perhaps present in this case. However, sudden and severe bradycardia is unlikely with this drug alone.

Hypoxia and sedation were definitely not factors. This patient was actively conversing with the surgeon during the entire episode, and a pulse oximeter (with alarm set at 90%) was in place. Although no supplemental oxygen was given, the SpO2 had been 97% prior to the onset of bradycardia. Absorption of epidural medications may produce systemic effects, but the doses in this case were small and spread out over time. Had hypoxia or sedation been present, the episode might have been more difficult to treat, and the outcome might have been different.

The bradycardia in this case might have responded to atropine alone, but given the severity and rapidity of the decrease in pulse rate, other therapy seemed appropriate at the time. Some of the patients reported by Byrd et al.7 did not respond to atropine, although these patients had multiple medical problems and therapy. Naloxone has been shown to reverse the bradycardia produced by clonidine in animals,6 but its effect in humans is unknown. There is also evidence that naloxone can reverse the bradycardia produced by fentanyl.11 If the response to initial therapy had not been adequate, epinephrine would have been a logical next choice.12

Although the entire episode described here lasted less than 2 min, the prior modest decrease in pulse rate from 70 to 58 beats/min served to heighten vigilance and allowed treatment to be given coincident with the onset of severe bradycardia. This finding of a gradual decrease in rate followed by a sudden and severe decrease has been noted in previous reports.3,4,10

Patients frequently present with medications affecting their autonomic nervous system, and these effects must be considered when contemplating anesthetic drugs or techniques that inhibit the sympathetic nervous system. Guanfacine (in this case) or clonidine may represent a special risk, but it seems likely that any drug that can decrease the heart rate places the patient at increased risk for severe bradycardia when another drug is given that decreases heart rate via another mechanism.

The author would like to thank the Computer Resource Center, Dartmouth University, Hanover, New Hampshire, for their assistance with the figure.

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