Asystole and Severe Bradycardia during Epidural Anesthesia in Orthopedic Patients

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IN a number of studies1–3 and case reports,4,5 researchers have described bradycardia and asystole during spinal anesthesia. Proposed physiologic mechanisms have been discussed, and clinical factors that contribute to these events, including hypoxemia6 and lack of vigilance7–9 have been described. Factors associated with the development of bradycardia during spinal anesthesia have been studied by Carpenter et al.2 and Liu and colleagues.10 These include low resting heart rate, use of beta blockers, American Society of Anesthesiologists physical status 1, peak block height, and first degree atrio-ventricular block.

In contrast, there has been little reported on the occurrence of bradycardia and asystole during epidural blockade.11,12 This is a report of 7 cases of severe bradycardia and 5 cases of asystole that occurred during orthopedic surgery under epidural anesthesia during the past 9 yr at our institution. These include one case of asystole and one case of severe bradycardia that occurred in the post anesthesia care unit (PACU). Although this report does not provide data on the incidence of bradycardia, these individual cases provide the greatest experience on patterns of onset of acute bradycardia and asystole during epidural anesthesia yet published, and may provide insight into potential etiologic mechanisms.

Methods

Institution

The Hospital for Special Surgery is an elective orthopedic surgical hospital that currently performs approximately 9,000 operations per year. Since 1987, between 80% and 85% have been performed using regional anesthesia, with 4,000–6,000 operations per year being performed using either spinal or epidural anesthesia. Total knee replacements and total hip replacements (THRs), as well as a variety of arthroscopically assisted knee procedures, are operations commonly performed during epidural anesthesia. Whereas tourniquets are often used for procedures that involve the knee, controlled hypotension is routinely used for THRs. The patients are given an epidural block that extends to the upper thoracic dermatomes, whereas cardiac output and mean arterial pressure (MAP) are maintained using an inotropic agent or vasopressor, usually epinephrine.13,14 If MAP does not decrease to an appropriate level to allow for a dry operative field, a vasodilator such as sodium nitroprusside (SNP) may be added, to augment the hypotension.

Key words: asystole; bradycardia; epidural anesthesia.
CASE REPORTS

Case Identification

Twelve cases of severe bradycardia, defined as a heart rate less than 50 beats/min, or asystole, that occurred in the operating room or PACU in patients who received epidural anesthesia were collected by author NES from cases presented at various conferences. These cases are representative, but not a complete collection of all such events occurring at our institution. Our purpose, with this article, is to discuss the presentation of, and the factors leading to, severe bradycardia and asystole, and not to discuss the incidence of these events in orthopedic patients or with epidural anesthesia. Only cases in which 1-h trend recordings (from Puritan Bennett model 240 monitors, Wilmington, MA) of heart rate were available are presented. When oxygen saturation or pulmonary artery pressure data were available, they are presented as well. Four cases of asystole that represent a variety of procedures and anesthetic events are presented in full case report format. Summary data from the remaining cases are presented in tabular form.

Case Reports

Case 1

A 46-y-old man with rheumatoid arthritis who, apart from moderate obesity (height: 182 cm, weight: 104 kg), was in excellent health. He was scheduled for a total knee replacement. He received 5 mg midazolam intravenously for sedation and had an epidural injection of 20 ml of 0.75% bupivacaine in divided doses via the L3–4 interspace. Thirty minutes after the epidural injection, his MAP decreased from 100 mmHg to 60 mmHg, with no change in heart rate. The tourniquet was inflated at 12.54 (note mark on trend recording), and norepinephrine was administered intravenously at a dosage of 1 μg/min. His MAP increased to 75 mmHg, and his heart rate remained unchanged. During the next 20 min, his heart rate slowly decreased, from 80 beats/min to 60 beats/min, with no significant change in MAP. Oxygen saturation remained 100% throughout, and the patient was awake, breathing oxygen, at 3 L/min via a nasal cannula.

At 13:15, his heart rate acutely decreased to 40 beats/min, and, shortly thereafter, asystole occurred (fig. 1). He was treated with 5 mg ephedrine intravenously and was given a "shock" on the shoulders. His heart rate suddenly increased to 110 beats/min, but the rhythm had changed from normal sinus to atrial fibrillation. He remained conscious throughout. The atrial fibrillation was treated with 0.5 mg digoxin and 5 mg verapamil intravenously. Blood pressure stabilized with 1–3 μg/min norepinephrine. His rhythm reverted to normal sinus at 14:20, and he recovered uneventfully.

Case 3

A 60-y-old man with first-degree atrioventricular block who was post colon resection for adenocarcinoma was scheduled for a left THR while in the lateral decubitus position. He was given 2 mg lorazepam and 4 mg hydromorphone orally for premedication. In the operating room, 1 mg midazolam and 25 μg fentanyl were administered intravenously, and a 17-gauge Tuohy needle was inserted at the L2–3 interspace. We injected 20 ml of 0.75% plain bupivacaine via the needle, in divided doses. The arterial pressure did not decrease, but satisfactory anesthesia was obtained. When 500 ml lactated Ringer's solution had been infused, an SNP infusion was started at 10:11 to decrease arterial pressure to reduce intraoperative bleeding (note mark on trend recording). This resulted in a progressive decrease in MAP from 90 mmHg to 60 mmHg, with an increase in heart rate from 75 beats/min to 95 beats/min. Oxygen saturation was 100% at this time. Shortly thereafter, his heart rate acutely decreased to 60 beats/min and then asystole occurred. The wound was packed, the patient was positioned supine, and external chest massage was begun. We administered 100 μg epinephrine and 0.4 mg atropine intravenously, and the lungs were ventilated with 100% oxygen via a face mask. In 2 min, circulation was restored and the patient regained consciousness. The surgical wound was closed, and an elective THR was performed uneventfully at a later date.

Case 4

A 34-y-old man (height: 180 cm, weight: 68 kg) was scheduled for an arthroscopically assisted anterior cruciate ligament repair. After sedation with 1 mg midazolam and 50 μg fentanyl, an epidural anesthetic was performed at the L3–L4 level by injecting 30 ml of 2% lidocaine with 150 μg epinephrine via a 17-gauge Tuohy needle, in divided doses. Surgery was initiated 60 min later, and a thigh tourniquet was inflated to 350 mmHg, it was deflated after 50 min at 16:05 (note mark on trend recording). At 16:10, 8 ml of 0.5% bupivacaine was injected via the epidural catheter, and 50 μg fentanyl was administered intravenously. The patient was subsequently fully awake. Heart rate slowly decreased from 75 beats/min to 50 beats/min, and then acute asystole occurred at 16:25. Oxygen saturation was 98% when the patient lost consciousness. Thump pacing was instituted, and 0.4 mg glycopyrrolate was administered intravenously. Within 60 s, heart rate and rhythm and blood pressure were restored. The procedure was completed, and the patient recovered uneventfully.

Case 11

A healthy, 42-y-old man had a knee arthroscopy performed as an ambulatory surgical patient. He received 5 mg midazolam and 50 μg fentanyl for sedation and had an epidural inserted at L3–L4 using a total of 25 ml of 2% lidocaine with 150 μg epinephrine. Two hours after the epidural injection, he had return of motor function in his legs, but analgesia remained. Asystole developed acutely at 10:16. He was alert at the time, and there were no apparent precipitating factors. His electrocardiogram strip shortly before the event is shown (fig. 2, line 1). This was recorded as transient slowing of his heart rate developed. His heart rate ranged between 50 beats/min and 60 beats/min, and his blood pressure was 120/70 mmHg.

The asystole is shown on lines 2 and 3 of the electrocardiograph strip and was witnessed. He was treated with thump pacing (see premature ventricular contraction like beats on lines 4, 5, and 6) and 200 μg epinephrine intravenously. Sinus rhythm returned within a minute and he recovered uneventfully.

Anesthesiology, V 86, No 1, Jan 1997
Results

The 12 patients (8 men, 4 women) ranged from age 34–78 yr old (mean age 57). Five, six, and one patient were designated as an ASA physical status 1, 2, and 3, respectively. Table 1 is a summary of the patients’ anesthetic management, intraoperative events, and associated factors taken from chart review. Tracings of heart rate trends from each patient are presented in figure 1. There were five patients in whom asystole developed (cases 1–4, and 11) and seven with severe bradycardia (cases 5–10, and 12). In seven patients (two with asystole and five with bradycardia), the technique of controlled hypotension, as described, was being performed.

All patients were resuscitated successfully with a variety of chronotropic agents, such as epinephrine, atropine, ephedrine, or glycopyrrolate. In addition, thump pacing or cardiopulmonary resuscitation was used with success in two cases. No patient suffered a postoperative myocardial infarction or stroke.

A decline in preload as measured by pulmonary artery pressure was noted in both cases (fig. 3) where a pulmonary artery catheter was used. No patients were hypoxic before the acute bradycardia; the lowest recorded oxygen saturation by pulse oximeter was 92%.

Discussion

History

The occurrence of severe bradycardia during spinal anesthesia was reported by Griffiths and Gillies in

Anesthesiology. V 86, No 1, Jan 1997
1948. During the course of intentional total spinal anesthesia for thoracolumbar sympathectomy, they observed heart rates as low as 30 beats/min. However, Bonica et al. studied the circulatory effects of epidural block, and noted a stable or overall increase in heart rate associated with varying levels of sensory blockade.

In 1988, Caplan et al. published a closed-claims analysis of cardiac arrests during spinal anesthesia. Renewed interest in the development of sudden, severe bradycardia and asystole occurred. Prospective studies have been reported, in which bradycardia was highlighted as one of the more serious complications of conduction blockade. There were no cases of asystole reported in these prospective epidemiologic studies; however, this may reflect a heightened awareness by the anesthesiologists involved, manifest as earlier treatment of bradycardia, thereby limiting the severity or incidence of the bradydysrhythmias.

**Pathophysiology**

Most theories regarding bradycardia and asystole during spinal and epidural anesthesia involve indirect effects of these techniques on the heart. The inhibition of sympathetic efferents during central blockade may lead to decreased venous return to the heart. This, in turn, may activate reflexes that cause bradycardia. At least three such reflexes have been proposed. The first involves collapse-firing of low pressure baroreceptors located in the right atrium and vena cava. A second reflex involves an arc located within the pacemaker cells of the myocardium, in which heart rate is proportional to the degree of stretch. Finally, a paradoxical Bezold-Jarisch response, in which mechanoreceptors located in the interoposterior wall of the left ventricle that, when stimulated, can cause bradycardia, has been proposed and discussed by Mackey et al. The effector arm in each of these mechanisms involves increased vagal tone. In addition to these myocardial reflexes, a high level of sympathetic blockade may alter the balance of autonomic input to the heart, favoring vagal tone, and bradycardia.

Secondary factors, including opioid administration, hypoxemia, sedation, hypercarbia, concurrent medical illness, and use of chronic medications, may contribute to the development or severity of the responses to the mechanisms outlined.

**Patterns of Presentation**

**Pre-event Heart Rate Pattern.** In evaluating the presentation of the development of severe bradycardia or asystole, it would be valuable if a prodromal slowing of the heart rate could be identified. Brown et al., in a letter to the editor, indicated that sudden bradycardia can be associated with a prior gradual decline in heart rate throughout approximately 1 h during spinal anesthesia. If a prodromal slowing could consistently be identified, early intervention could be used, thereby limiting the extent of the bradydysrhythmia. However, after inspection of the individual trends, one can appreciate the great variability in presentation. In our experience, asystole or severe bradycardia may develop after an entire spectrum of pre-event heart rate patterns (see fig. 1, cases 1-12). It is clear, from these cases, that bradycardia or asystole may develop suddenly in seconds or minutes from a stable heart rate (cases 7, 8, and 9), or trend downward more slowly (cases 1 and 4). In several cases, heart rate increased throughout a period before the acute bradycardia or asystole (cases 3 and 10). Although it is important to closely monitor heart rate trends during epidural blockade, prodromal slowing will not always be evident before acute bradycardia and asystole.

**Oxygen Saturation.** The association of bradycardia with severe hypoxemia and hypercarbia has been well established. Caplan’s study indicates that the development of sudden asystole was due to a respiratory mechanism in only half of the cases presented. In case reports, authors described the occurrence of bradycardia during
spinal anesthesia despite measured oxygen saturations of 100%. Our report provides strong evidence for the role of a primary cardiac mechanism for the production of bradycardia or asystole. In all cases, the event occurred while the oxygen saturation by pulse oximeter was greater than 92%. Although hypoxemia may be a contributing event in certain situations, it was not required for bradycardia or asystole to occur during epidural blockade in our patients.

**Volume Status.** A reduction in central blood volume and pressure may predispose to acute bradycardia during conduction blockade. This may occur secondary to the vasodilation from extensive conduction blockade, but is more likely to occur in the presence of volume depletion. In the two cases in which pulmonary artery pressures were measured (fig. 3), a progressive decrease in filling pressures was noted before the onset of bradycardia. In both of these cases, an infusion of SNP was begun shortly before the bradycardia, and mean pulmonary artery pressure decreased from 15 mmHg to 11 mmHg (case 5) and from 17 mmHg to 12 mmHg (case 7) before the acute onset of bradycardia. In an additional 3 cases (cases 2, 3, and 10), infusions of SNP also preceded the onset of bradycardia. Presumably, in these cases as well, the SNP caused a reduction in central blood volume due to vasodilation.

Cases 4 and 8 also lend support to the hypothesis that a sudden decrease in filling pressures may predispose a patient to bradycardia or asystole. In both cases, heart rate began to decrease simultaneously with the deflation of a thigh tourniquet (note the markings on the tracings), although the rate of decrease was much different. The asystolic event occurred 20 min after deflation in case 4, and the lowest heart rate (34 beats/min) occurred 5 min after deflation in case 8. Deflation of a lower limb tourniquet may lead to a reduction in preload, thereby providing conditions favorable for the development of bradydysrhythmias. Kahn et al. observed a decrease in heart rate after deflation of a thigh tourniquet during total knee replacements performed during epidural anesthesia in 42 (11%) of 373 patients. In 15 (4%) of these patients, a reduction in heart rate of 10 beats/min or more occurred. This provides supporting evidence for the risk of acute bradycardia after deflation of a lower limb tourniquet during conduction blockade.

In none of the cases was there evidence for increased or increasing filling pressures. In an interesting analogy, Dickinson notes that fainting does not occur in patients with a history of congestive failure. One can spec-

### Table 1. Patient Intraoperative Events and Anesthetic Management

<table>
<thead>
<tr>
<th>Case No</th>
<th>Procedure</th>
<th>Post Medical History</th>
<th>Prior Headache</th>
<th>Local Anesthesia</th>
<th>Lowest SpO2 (%)</th>
<th>Blocker</th>
<th>Lowest Heart Rate (beats/min)</th>
<th>Onset of Bradycardia (min after epidural injection)</th>
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<tr>
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<td>60</td>
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<tr>
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<td>210</td>
</tr>
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</table>

**Notes:**
- THR: total hip replacement
- ACL: anterior cruciate ligament reconstruction
- A-V: anterograde retrograde

**Abbreviations:**
- TIV: total intravenous
- TIR: total intravenous regional anesthesia
- A-V: anterograde retrograde
- SpO2: oxygen saturation
- L-B: local anesthesia with bupivacaine
- L: lidocaine
- NA: not available

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Anesthesiology. V 86, No 1, Jan 1997
ultimately, these patient's fluid overloaded status may protect them from bradycardia, which may lead to fainting. Although a sudden emptying of the cardiac chambers may not be the sole mechanism involved in the development of bradycardia, evidence seems to indicate that, during epidural anesthesia, a poorly filled heart may be more prone to reflex slowing. 

Age and ASA Physical Status. Carpenter et al. indicate that ASA physical status is a risk factor in the development of bradycardia, with ASA physical status 1 patients having a greater odds ratio of bradycardia developing during spinal anesthesia. Case reports are available in which asystole occurs in patients of varying ASA physical status. Our experience confirms the varied nature of presentation. Five cases occurred in ASA physical status 1 patients, whereas the remaining patients were ASA physical status 2 or 3. Acute bradycardia can occur in patients of any age as well. Our experience confirms this, because our patients varied in age from 54 to 78 yr.

Carpenter et al. also found that preoperative beta blockade increased the risk for the development of bradycardia during spinal anesthesia. Of our 12 patients, 3 were receiving beta blockers chronically (cases 5, 7, and 12). Three of the 12 patients (cases 3, 5, and 9) had first degree atrio-ventricular block, which is consistent with the increased risk of acute bradycardia noted with this condition during spinal anesthesia.

Sedation. The issue of whether sedation is contributory to the development of acute bradycardia or asystole, or is somehow protective, is controversial. In Caplan's study, 12 of the 14 patients received a sedative. However, in several case reports, it was indicated that a lack of sedation may have been involved in the development of the bradycardia. In our series, all patients received some form of sedation, although two patients in the operating room (cases 4 and 9) and both patients in the PACU (cases 11 and 12) were totally alert when acute bradycardia developed.

Timing. In the cases that occurred intraoperatively, bradycardia or asystole occurred from 5 to 90 min after epidural injection, with a cluster of 7 of 10 cases occurring between 50 and 60 min. Of these 7 cases, bupivacaine was the local anesthetic in 5 (cases 1, 2, 3, 5, and 10), and lidocaine was the local anesthetic in one (case 8). Both local anesthetics were used in one case (case 4). The onset and duration of these local anesthetics are very different when used for epidural anesthesia. Although the anesthetic level was not noted, one may infer that the regression of the sensory and sympathetic blockade was at a different stage with the two local anesthetics. This lends support to the hypothesis that acute bradycardia or asystole may occur at any time during an epidural anesthetic. Further support for this observation is supplied by cases 11 and 12, which are instances in which the event occurred in the PACU several hours after initiation of the anesthetic. Figure 2 is the real time tracing for a patient who suffered an asystolic arrest 1 h after being admitted to the post anesthesia care unit. This event occurred 3 h after initiation of the epidural block with lidocaine and epinephrine. Case 12 was a 65-yr-old man recovering from an epidural anesthetic (bupivacaine administered 3.5 h earlier) for a total knee replacement. He had almost full resolution of the block, and this event may have been precipitated by blood loss from the surgical site.

These cases demonstrate that there remains a risk of asystole and bradycardia for several hours after adminis-
tration of an epidural block, even though the sensory and motor modalities have receded considerably. It is clear, from these examples, that the sudden development of asystole or severe bradycardia may occur at any time after initiation of epidural blockade, and an anesthesiologist must be prepared to intervene with appropriate resuscitative measures. This is consistent with prospective studies of spinal anesthesia, which demonstrated that acute bradycardia can occur at any time during conduction blockade as well.

**Treatment and Prophylaxis**

Caplan et al.'s closed claims study demonstrated that there is the potential for a poor outcome when a cardiac arrest occurs during a spinal anesthetic. Of the 14 cases of cardiac arrests presented, there were 6 deaths; in addition, of the 8 survivors, only 1 had sufficient neurologic recovery to carry on activities of daily life. Caplan attributed the poor outcome, in part, to delayed resuscitation with intravenous epinephrine.

Of the five patients in our series in whom asystole developed, all were resuscitated rapidly with atropine, ephedrine, epinephrine, or glycopyrrolate, with no evident end organ damage. In cases 4 and 11, thump pacing was used. This technique was applied successfully by Chester and Ditto in the setting of third-degree heart block during spinal anesthesia. Gibbons and Ditto confirmed the efficacy of thump pacing as a treatment for acute asystole during spinal anesthesia.

It has been suggested that acute bradycardia or asystole can be prevented. Given the proposed mechanisms of the events, one may assume that volume loading, chronotropic support with beta agonists, or attenuation of the effector arm with vagolytics may prevent these occurrences. Sharrock et al. showed that heart rate and pulmonary artery pressures are maintained with epinephrine infusion during THR with extensive epidural blockade. This would suggest that epinephrine may be useful to prevent acute bradycardia or asystole. However, in 6 of the 12 patients in our group, bradycardia or asystole developed while epinephrine was administered. Of these 6 patients, four were concurrently receiving an infusion of SNP. This observation lends support to two theories on the etiology of the bradydysrhythmias. First, in some patients, the added hypodynamic effects of epinephrine may contribute to reflex slowing that has been reported with the Bezold-Jarisch reflex. Second, because epinephrine has no effect on the vagal response, this observation may provide evidence for the importance of the vagal limb of the reflexes involved with the occurrence of bradycardia and asystole during epidural anesthesia.

Our experience confirms the observation that prompt pharmacologic treatment supported by thump pacing is an effective treatment for bradydysrhythmia associated with spinal or epidural anesthesia. Although there may be benefits to prophylactic therapy with atropine, fluids, or epinephrine, bradycardia or asystole may occur despite such measures.

Vigilance on the part of the anesthesiologist is essential. However, given the often instantaneous nature of presentation, vigilance may not be able to prevent this complication in many patients. Heightened awareness of these events will allow the anesthesiologist to promptly and effectively provide optimal treatment of progressing bradycardia or asystole before the development of end organ damage.

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Anesthesiology. V 86, No 1, Jan 1997
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Anesthesiology. V 86, No 1, Jan 1997