Severe Bradycardia after Neostigmine in a Patient Taking Propranolol to Control Paroxysmal Atrial Tachycardia

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Parasympathetic responses predominate during administration of anesthesia to a patient whose beta-adrenergic receptors have been blocked by drugs.[1,2] In this situation, vagal inhibition of the heart, with the possibility of sinus arrest, is a serious hazard. Atropine has been effectively used to avoid this hazard and thereby permit reversal of nondepolarizing neuromuscular blocking agents with neostigmine.[3] The following case history describes the development of severe bradycardia during the reversal of pancuronium with atropine and neostigmine in a patient taking propranolol for the control of paroxysmal atrial tachycardia.

REPORT OF A CASE

A 52-year-old man (weight 82 kg) with a torn meniscus was scheduled for a medial meniscectomy of the left knee. Ten years prior to this admission, the patient had developed paroxysmal atrial tachycardia, which was usually precipitated by excitement or anxiety. For the year prior to admission, propranolol had been used to control the dysrhythmia after vagal stimulating drugs, quinidine, and digitalis had failed to control it. Because of a history of asthma, attempts were made to decrease the dose of propranolol to less than 40 mg twice a day, but these were unsuccessful due to the development of frequent episodes of paroxysmal atrial tachycardia associated with angina. Also elicited in the patient's history were a previous episode of hepatitis, the presence of nasal polyps, and back pain secondary to recently fractured vertebrae. Preoperative urinalysis, complete blood count, chest roentgenogram, and determinations of serum glucose, blood urea nitrogen, and electrolyte values disclosed no abnormality. An electrocardiogram showed nonspecific ST-segment and T-wave changes.

Preanesthetic medication consisted of meperidine, 50 mg, and pentobarbital, 100 mg, given intramuscularly 60 minutes before anesthesia. The last 40-mg dose of propranolol was given ten hours before anesthesia. Immediately prior to the induction of anesthesia, atropine, 0.3 mg, was given intravenously, with an increase in pulse rate from 60 to 85 beats/min and an increase in blood pressure from 120/70 to 135/80 torr. Induction of anesthesia was accomplished by administration in divided doses of meperidine, 60 mg, and thiopental, 250 mg. Pancuronium, 8 mg, facilitated endotracheal intubation. Anesthesia was maintained with divided doses of meperidine, 100 mg, and thiopental, 250 mg, in combination with 70 per cent nitrous oxide, using a total gas flow of 5 l/min with controlled ventilation. Blood pressure, pulse, electrocardiogram, precordial heart sounds, temperature, and muscular response to electrical stimulation of the ulnar nerve were monitored. The patient was placed in a 10-degree head-down position with the knees flexed.

Blood pressure was maintained in the range of 135–100/80–60 torr and pulse rate in the range of 60–85 beats/min during the procedure. Seventy minutes after the induction of anesthesia, reversal of the pancuronium was started with a mixture of atropine, 1.25 mg, and neostigmine, 2.5 mg, given intravenously over five minutes. Following administration of the mixture, the pulse rate decreased from 60 to 30 beats/min with no appreciable change in blood pressure. Atropine, 3 mg, was given intravenously in divided doses, with a gradual increase in pulse rate to 55 beats/min. After vital signs had stabilized, the trachea was extubated. The patient was then given naloxone, 0.2 mg, intravenously and taken to the recovery room after reacting to verbal communication. During the operation, signs of asthma were not present. While in the recovery room, the vital signs and electrocardiogram were similar to the preoperative determinations. The subsequent postoperative course was uneventful.

DISCUSSION

The advisability of discontinuing propranolol prior to anesthesia and operation continues to be controversial. Propranolol through its antagonism of sympathetic activity and its direct effects on the myocardium may produce intraoperative circulatory depression, bronchial constriction, and hypoglycemia,[3–5] Viljoen has proposed that propranolol be withheld for two weeks prior to elective surgery.[6] However, recent evidence suggests that the cardiac effects of propranolol are minimal after the drug has been discontinued for 48 hours.[7] Clinical experience and hemodynamic studies during

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anesthesia have also indicated that patients can be safely anesthetized after receiving propranolol until the evening before operation, so long as parasympathetic predominance is averted by the administration of atropine.[3,8] These studies and the possibility of exacerbation of the primary disease on the discontinuance of propranolol have led to the policy of continuing propranolol during anesthesia and operation if the drug therapy is contributing importantly to the patient's health.[3,4]

Among the various drug interactions that could occur, one might anticipate that beta-adrenergic blockers would interact with nondepolarizing muscle relaxant reversal agents to cause disconcerting clinical problems. By inhibiting the effects of sympathetic activity on the heart, beta blockade produces parasympathetic predominance. Since the chronotropic myocardial response is beta-mediated, this blockade of sympathetic activity explains the failure of atropine to produce sinus tachycardia. However, the effectiveness of atropine as a cardiac cholinergic blocker is not changed; therefore, neostigmine should not produce deleterious effects if vagal blockade is complete. Thus, neostigmine has been safely used to reverse nondepolarizing neuromuscular blocking agents in patients taking propranolol.[3]

In the case discussed here, it was elected to continue propranolol therapy because of a well-documented history of the development of exacerbations of the primary disease when changes in therapy were attempted. Regional anesthesia was thought inadvisable because of the patient's recent vertebral injuries, and halogenated anesthetic agents were avoided because of a history of hepatitis; therefore, a balanced general anesthetic was chosen in order to meet the requirements of the operation while producing minimal cardiovascular depression.

Immediately prior to induction of anesthesia, the patient was given atropine, which produced an increase in the pulse rate of 15 beats/min. Preoperative doses of atropine (to 0.02 mg/kg) supplemented by intravenous administration of atropine during anesthesia have been recommended to offset the cholinergic effects of anesthetic drugs on the heart.[4] However, owing to the chronotropic response to atropine in this patient and the wish to avoid tachycardia that might precipitate dysrhythmia, no more atropine was administered before induction of anesthesia. The course of anesthesia, which had been planned to avoid marked changes in pulse rate, proceeded uneventfully until the conclusion of operation. At that time, the residual effects of pancuronium were reversed by administration of a mixture of atropine and neostigmine. Because it has been shown that the steadiest heart rates are obtained when atropine and neostigmine are injected simultaneously,[9] and because the patient had manifested a chronotropic response to the preanesthetic dose of atropine, the reversal agents were given as a mixture. The subsequent development of severe bradycardia indicates that this patient's cardiac disease and drug therapy had markedly changed the expected response to the atropine–neostigmine mixture. Not until apparent total cholinergic blockade was achieved did the pulse rate stabilize, at a rate which probably reflected the intrinsic heart rate free of most sympathetic and parasympathetic effects. Because this heart rate seemed adequate to maintain perfusion, antagonism of the propranolol with calcium, isoproterenol, or other agents was not considered necessary.

In summary, this case suggests that it may be preferable to avoid the simultaneous administration of atropine and neostigmine for reversal of neuromuscular blockade in a patient who has recently received propranolol. Use of a depolarizing neuromuscular blocking drug such as succinylcholine would allow a patient to initiate spontaneous respiration after discontinuance of the neuromuscular blocker and thereby eliminate the need for reversal agents. However, if a patient has recently received beta blockers, it may be better to avoid the continuous cholinergic stimulation associated with the use of a depolarizing neuromuscular blocking agent. Nondepolarizing neuromuscular blocking agents may be safely used and reversed in a patient taking propranolol if atropine precedes the neostigmine. When it is deemed hazardous to produce complete cholinergic blockade before neostigmine administration,

reliance on mechanical ventilation until neuromuscular function is adequate for respiration would circumvent the possible adverse effects associated with the simultaneous administration of atropine and neostigmine in the patient taking propranolol. However, if in this clinical setting it is elected to reverse a nondepolarizing neuromuscular block by slowly titrating atropine against neostigmine, it should be done with careful monitoring in order to detect quickly possible adverse physiologic responses.

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Impaired Arterial Oxygenation Associated with Use of Bone Cement in the Femoral Shaft

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The use of acrylic (methylmethacrylate) bone cement for fixing prostheses in the femoral shaft has been associated with sudden cardiac arrest.[1–6] The sequence of events leading to these accidents has not been clear. Hypotension produced by the absorption of the volatile methylmethacrylate monomer, a vasodilator,[7] has been suspected to be the cause of the cardiovascular collapse.[5] Recent studies have demonstrated that cement packing produces elevation of femoral medullary pressure, leading to embolization of medullary contents.[8–10] The acute pulmonary fat and bone-marrow embolism resulting from insertion of cement and prosthesis in the femur may interfere with arterial oxygenation. If hypoxemia occurs under these conditions, it may contribute to the occurrence of cardiac arrest, especially when associated with systemic hypotension resulting from monomer absorption.

The present study was designed to determine whether cementing of prostheses into the femur is associated with impairment of arterial oxygenation. Since a decrease in arterial oxygen tension was found in every patient, possible ways of preventing hypoxemia were also studied.

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Materials and Methods

Twenty-four patients, ages 32 to 78 years, free of symptomatic cardiovascular or respiratory disease, were studied while undergoing Charnley total hip replacement. After induction with thiopental and tracheal intu-