Treatment of Chronic Symptomatic Supraventricular Bradycardias with Transdermal Scopolamine*

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The management of symptomatic bradyarrhythmias can be challenging in patients in whom cardiac pacing is not indicated, such as in the terminally ill or severely demented. We applied a transdermal scopolamine patch on one such patient with resultant substantial improvement in his supraventricular bradyarrhythmia.

Chronic persistent or intermittent symptomatic bradyarrhythmias of sinus, atrial or atrioventricular (AV) junctional origin are customarily treated by implantation of a permanent cardiac pacemaker. The management of such arrhythmias can present a challenge in patients in whom permanent pacemaker implantation may not be indicated, such as in the demented or terminally ill. Repeated oral administration of atropine or sublingual administration of isoproterenol may reduce frequency or magnitude of supraventricular bradyarrhythmias, but these therapeutic modalities commonly produce unacceptable side effects and are not without risk. This report describes a demented patient whose supraventricular bradyarrhythmias substantially improved following the application of transdermal scopolamine.

CASE REPORT

The patient was a 94-year-old man with Alzheimer's disease who resided in a nursing home. Until one month prior to admission, he was ambulatory and could feed himself, express basic needs and recognize family members. During the month prior to admission, he became progressively withdrawn with episodes of agitation, became uncommunicative and eventually became bedridden. During this period, aides at the nursing home noted persistently slow pulse rates, sometimes as low as 26 beats per minute. His past medical history was essentially negative. He was receiving hydroxyzine hydrochloride, 20 mg orally every eight hours, but no other medication. The pulse rate on admission was 30 beats per minute, and the blood pressure was 100/60 mm Hg. The remainder of the physical examination was normal except for the neurologic examination which showed disorientation to time, place and situation, diminished cognitive function, and mild diffuse muscle weakness. The resting electrocardiogram showed AV junctional rhythm with AV dissociation at a rate of 30 beats per minute, a QRS duration of 0.11 s, left axis deviation, a 1.7 s period of asystole, and a single premature ventricular beat. The chest x-ray film findings, serum thyroxine level, complete blood count, and serum electrolyte concentrations were normal.

The patient was admitted to the coronary care unit. During cardiac monitoring, the predominant rhythm was AV junctional rhythm (Fig 1A) with and without AV dissociation with an average rate of 32 beats per minute. There were numerous asystolic periods (Fig 1B) lasting up to 4.4 s. There were also frequent multifocal ventricular premature beats (VPBs), numerous VPB couplets, and three 3-4 beat runs of ventricular tachycardia. During a period of slow AV junctional rhythm, a single dose of atropine, 1 mg, was administered intravenously and this produced a brief acceleration of the AV junctional rate from 30 to 60 beats per minute. Temporary transvenous pacemaker insertion was considered to determine whether the patient's mental status would improve with sustained acceleration of the heart rate, but this alternative was refused by the family. Thereafter, a 2.5 cm² transdermal patch containing 1.5 mg of scopolamine (Ciba) was applied. Holter monitoring performed over the ensuing 24 hours showed that by four hours after the application of the scopolamine patch, the average AV junctional rate had increased to about 75 beats per minute (Fig 2). There was a single 2-s period of asystole. There were frequent VPBs, rare pairs and no ventricular tachycardia. Limited improvement in the patient's mental status was noted. He was able to sit up at bedside and assist in his own care. He was returned to the nursing home with instructions for replacement of the transdermal scopolamine patch every three days.

At the nursing home, the patient's neurologic and mental status remained unchanged during the ensuing two months. He then developed bronchopneumonia and died. During those two months, the patient's pulse rate was checked every six hours and never dropped below 50 beats per minute.

DISCUSSION

Scopolamine (hyoscine) is a competitive inhibitor of the muscarinic receptors of acetylcholine and has pharmacologic actions similar to those of atropine. The usefulness of this drug has been limited by its relatively short duration of action and high incidence of side effects when administered orally

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**FIGURE 1A (upper)** Lead 2 rhythm strip showing AV junctional rhythm at a rate of 32 beats per minute. This was the predominant rhythm prior to therapy with scopolamine. 1B (lower). Lead 2 rhythm strip showing a 4.2 s period of asystole. Asystolic periods such as this one punctuated the slow AV junctional rhythm prior to therapy with scopolamine.
or parenterally. The transdermal system of administration is designed to deliver the scopolamine into the systemic circulation over an extended period similar to a slow intravenous infusion. The patch itself is 2.5 cm² in area and has a reservoir layer containing 1.5 mg of scopolamine. About 0.5 mg of the drug passes from this reservoir through a microporous polypropylene membrane and the intact skin to enter the systemic circulation at a steady rate over a period of 72 hours. A continuous controlled release of scopolamine occurs to maintain the plasma concentration at a steady level. The transdermal system of administration of scopolamine is currently used for the prevention of nausea and vomiting associated with motion sickness.¹

The cardiovascular response to antimuscarinic agents depends upon the dose used and the physiologic state of the heart. Atropine, in low doses, may initially produce a decrease in the sinus rate due to central vagal stimulation, but the onset of peripheral muscarinic cholinergic blockade typically causes the sinus rate to rise and the AV conduction time and PR interval to shorten. In patients with second and third degree AV nodal block, atropine may lessen the degree of block and may rarely accelerate the idioventricular rate in patients with trifascicular block. The physiologic state of the heart, in particular the magnitude of vagal tone, seems to be an important determinant of antimuscarinic response. Thus, in the setting of acute myocardial infarction, low doses of atropine are commonly employed to treat sinus and AV junctional bradyarrhythmias without encountering any noticeable worsening of the bradyarrhythmia.¹

Small doses of scopolamine may also cause slowing of the sinus rate in normal individuals and this effect may be more marked than with atropine. In a recent study by Dibner-Dunlap et al.² transdermal scopolamine patches (doses of 0.5, 1 or 1½ patches) were applied to 16 healthy young men. Twenty-four hours after application there was an average increase in cycle length by 13 percent. With higher doses of scopolamine (above 0.2 mg orally or parenterally), cardioacceleration occurs.⁴ Plasma scopolamine levels cannot be directly measured, although a reversed-phase liquid chromatography and radioreceptor assay has recently been developed and may be performed in certain research laboratories.⁴ This assay was not available to us.

The success of transdermal scopolamine in accelerating the heart rate and reducing the frequency and duration of asystolic periods in our patient suggests that it may be useful in the treatment of chronic, symptomatic supraventricular bradyarrhythmias. This may be particularly important in the management of patients who are not candidates for a permanent pacemaker such as those who are terminally ill or severely demented. In our patient, the increase in heart rate was sustained over a period of two months. Since the cardiovascular response to antimuscarinic agents is unpredictable and sometimes paradoxical, the patient should be monitored for some time after application of the patch to determine its effectiveness.

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Neurosarcoidosis Associated with Hypersomnia Treated with Corticosteroids and Brain Irradiation*

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Narcoleptic features developed in a young man with CNS sarcoidosis. This was associated with a structural lesion in the hypothalamus as demonstrated on CT scans of the head. The diagnosis of narcolepsy was established by compatible clinical history and the Multiple Sleep Latency Test. Treatment with high-dose corticosteroids was ineffective, but when the low-dose, whole-brain irradiation was added, complete resolution of the narcoleptic features ensued.

Central nervous system (CNS) involvement in sarcoidosis is well-known.¹ In addition, sarcoidosis may produce psychiatric illness and short-term memory deficits.⁴ However, narcolepsy as a feature of CNS sarcoidosis has never been described to our knowledge. We describe a patient with neuropsychiatric sarcoidosis who presented as having subacute dementia, and who developed laboratory-documented narcoleptic features during the course of the follow-up. This was associated with a hypothalamic nodule demonstrated on the contrast-enhanced CT scan of the head.

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