Paradoxical reflex bradycardia after epinephrine infusion for arrhythmia induction in the electrophysiology laboratory

Timothy R. Larsen, DO,*† Karoly Kaszala, MD, FHRS,*† Alex Y. Tan, MD,*† Kenneth A. Ellenbogen, MD,† Jose F. Huizar, MD, FHRS*†

*From the *Hunter Holmes McGuire VA Medical Center, Richmond, Virginia, and †Virginia Commonwealth University Medical Center, VCU Pauley Heart Center, Richmond, Virginia.*

Introduction

β-Receptor agonists are frequently administered during electrophysiology studies, particularly after radiofrequency ablation to provoke tachyarrhythmias. Isoproterenol, a nonselective β-adrenergic receptor agonist, is the most commonly used agent. Increasing cost and drug shortages have compelled a search for alternative β-adrenergic agonists. One alternative is epinephrine; however, in addition to β-adrenergic receptor stimulation, epinephrine is an α-adrenergic receptor agonist. The nonselective action of β- and α-adrenergic receptors can potentially increase the risk of additional/unwanted side effects. We present a case of epinephrine-induced paradoxical bradycardia and atrioventricular (AV) block after radiofrequency ablation of the slow pathway for the treatment of atrioventricular nodal reentrant tachycardia (AVNRT).

Case report

A 56-year-old man with a history of hypertension presented to the emergency department complaining of palpitations worsening over the past 12 months associated with presyncope. Home medications were hydrochlorothiazide and metoprolol tartrate. The presenting electrocardiogram showed a narrow complex tachycardia at 180 beats/min (Figure 1). This tachycardia terminated with an intravenous push of 6 mg of adenosine. He was subsequently referred for electrophysiology study and radiofrequency ablation.

At presentation to the electrophysiology laboratory, he was in sinus rhythm. Baseline intervals were normal (sinus cycle length 993 ms; AH interval 108 ms; HV interval 50 ms). Right ventricular pacing demonstrated retrograde conduction via the AV node. Para-Hisian and differential right ventricular pacing confirmed the absence of accessory pathway conduction. Ramp atrial pacing induced an AH jump that initiated a supraventricular tachycardia (SVT) with a tachycardia cycle length of 350 ms, concentric atrial activation, and a VA interval of 0 ms. Right ventricular overdrive pacing demonstrated a postpacing interval 150 ms longer than the tachycardia cycle length as well as stimulus to atrial electrogram during pacing minus VA interval during SVT of 142 ms, confirming AVNRT.

During radiofrequency ablation of the slow pathway, accelerated junctional rhythm with 1:1 VA relationship was present. There was no AH prolongation. After ablation, AVNRT was no longer inducible and there was no longer evidence of dual AV node pathways, AV nodal Wenckebach cycle length was reached at 420 ms. Approximately 10 minutes after ablation an epinephrine infusion was initiated

KEY TEACHING POINTS

- Recognize the potential for epinephrine to induce unwanted side effects, including reflex bradycardia and heart block due to heightened parasympathetic tone.
- Understand that these effects are transient and due to normal physiological reflexes and not due to pathological damage to the atrioventricular node. This is especially important after ablation procedures if epinephrine is used to test for arrhythmia induction.
- Understand that the mechanism of increased parasympathetic tone is a response to acute hypertension produced by the α-adrenergic effect of epinephrine. Acute hypertension activates carotid baroreceptors and myocardial stretch receptors.

KEYWORDS Ablation; Baroreceptor reflex; Epinephrine; Pharmacology; Atrioventricular nodal reentry tachycardia
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Address reprint requests and correspondence: Dr Jose F. Huizar, Division of Cardiac Electrophysiology, Hunter Holmes McGuire VA Medical Center, 1201 Broad Rock Blvd, Richmond, VA 23249. E-mail address: Jose.huizar2@va.gov.

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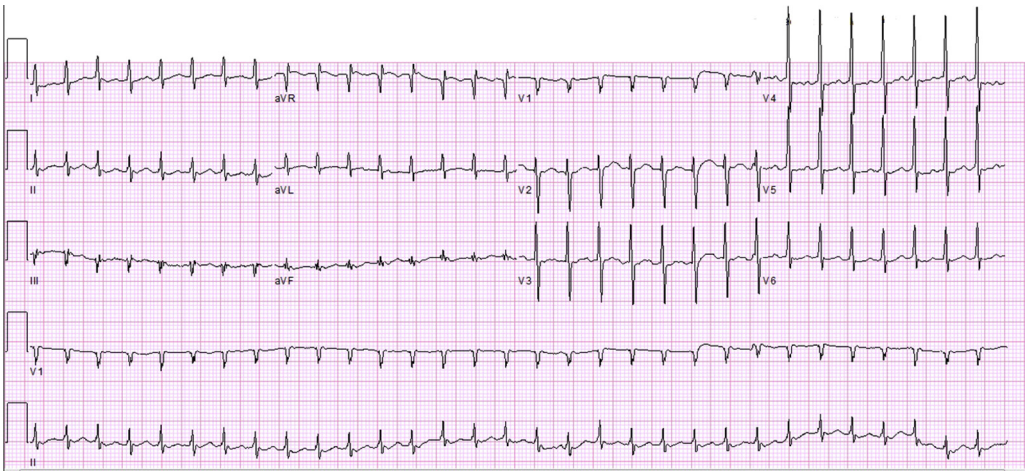

Figure 1 Twelve-lead electrocardiogram demonstrating a narrow complex tachycardia at 187 beats/min.

at 0.2 μg/(kg•min) and titrated up to 0.4 μg/(kg•min) for postablation testing. Shortly after initiating epinephrine, his blood pressure increased from 110/75 to 195/80 mm Hg, sinus rate decreased (Figure 2), and AH interval prolonged until Mobitz I AV block, followed by intermittent complete AV block with junctional escape beat (Figure 3). These changes reversed shortly after cessation of epinephrine infusion, with return of AV nodal Wenckebach cycle length to 420 ms. The patient was observed overnight on telemetry, with no occurrences of arrhythmias. An electrocardiogram the next day showed a stable PR interval.

Discussion

β-Adrenergic receptor agonists are routinely administered in the electrophysiology laboratory to facilitate induction of tachyarrhythmias. These agents can enhance abnormal automaticity and triggered activity and can alter tissue conduction properties, which allows reentrant arrhythmias. In patients with AVNRT, β-agonists enhance both antegrade slow pathway and retrograde fast pathway conduction.[1] These agents are useful for arrhythmia induction, especially after ablation. β-Agonists are particularly important in patients who have evidence of persistent dual AV nodal pathways (ie, nonlinear A1A2-A2H2 curve or AV nodal echo beats during programmed stimulation). Lack of inducibility, despite the presence of dual AV nodal pathways, portends an excellent prognosis, whereas further ablation carries the risk of permanent AV block.[2]

The increasing cost of isoproterenol and drug supply shortages have compelled electrophysiologists to use alternative β-adrenergic receptor agonist agents.[3] Epinephrine has been used as an alternative β-adrenergic receptor agonist when isoproterenol is not available or high cost prohibits use. Both agents elicit potent β_1 and β_2 receptor stimulation; however, epinephrine also stimulates peripheral α receptors.[4] While β_2 receptor activation by isoproterenol often causes hypotension, epinephrine has high affinity to α receptors in the vascular smooth muscle that may result in arteriolar constriction, which increases blood pressure, sometimes dramatically as demonstrated in the present case.

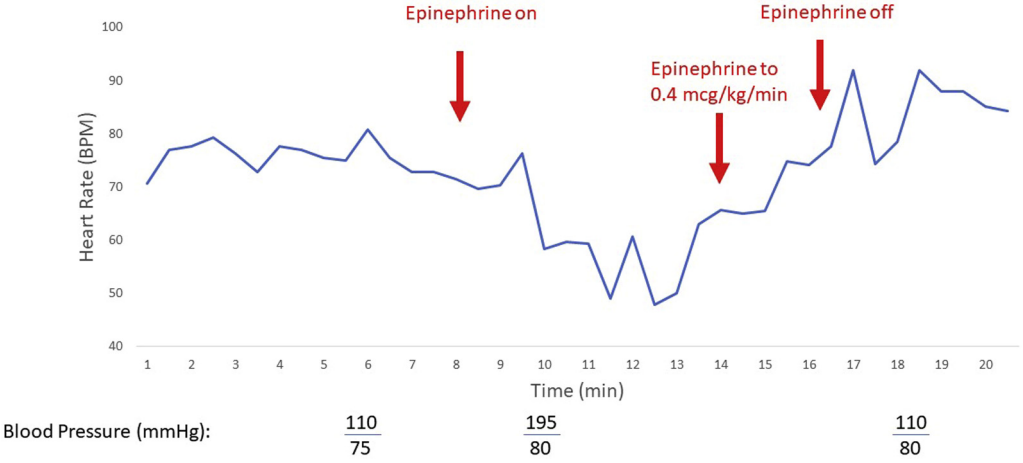

Figure 2 Heart rate trends before, during, and after epinephrine infusion. Epinephrine was initiated at 0.2 μg/(kg•min) and then increased to 0.4 μg/(kg•min). Blood pressure was intermittently recorded using an automated blood pressure cuff on the right upper extremity.

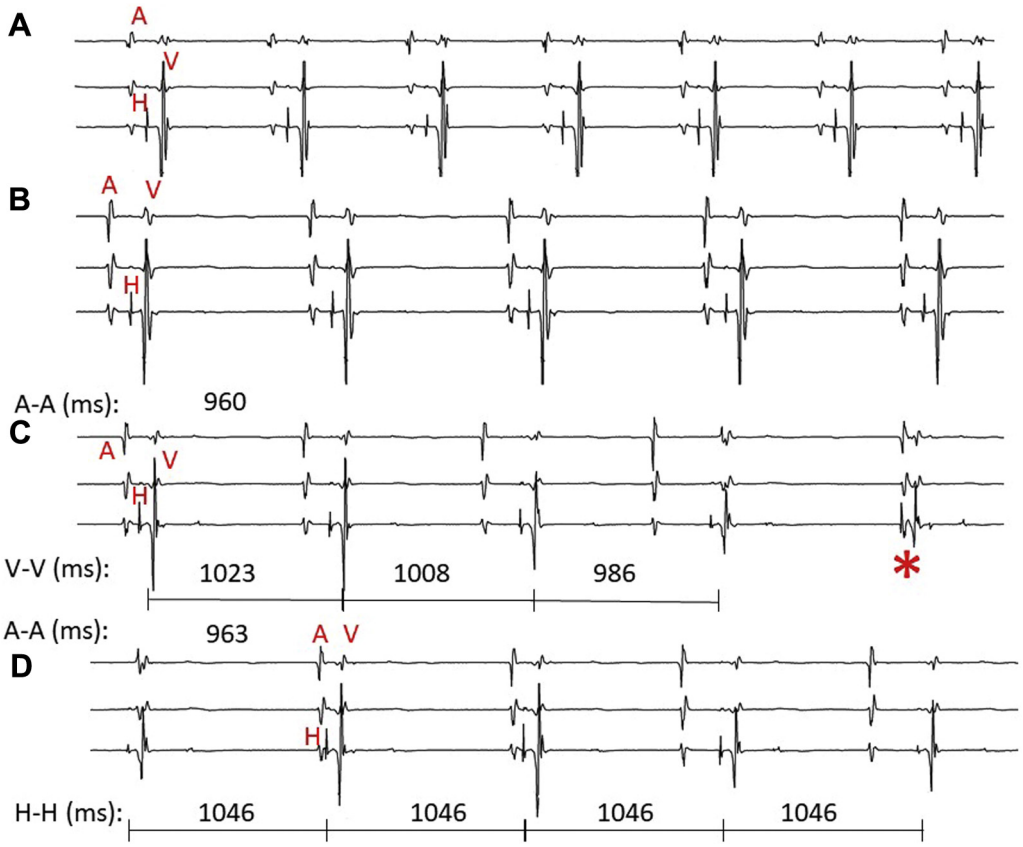

Figure 3 Progression of block in the atrioventricular (AV) node during epinephrine infusion. **A:** Baseline sinus rhythm, sinus rate 68 beats/min, and AH interval 93 ms. **B:** Sinus rate slowing to 62 beats/min and AH interval prolongs to 206 ms. **C:** Mobitz I second-degree AV block, sinus rate 62 beats/min, and AH interval 110, 260, and 390 ms with a junctional escape beat (*asterisk*). **D:** Complete AV block with junctional escape rhythm. Tracings are His proximal, mid, and distal. A = atrial electrogram; H = His electrogram; V = ventricular electrogram.

Acute hypertension can trigger several physiological reflexes. Both the arterial baroreceptor reflex and the Bezold-Jarisch reflex produce bradycardic and hypotensive responses.[5,6] The arterial baroreceptor reflex is triggered by acute stretch of mechanoreceptors located in the aortic arch and carotid sinus.[6] When activated, these baroreceptors trigger an increase in parasympathetic output and decrease in sympathetic tone, which combine to induce bradycardia and hypotension.[6] This reflex is operative when carotid sinus massage is used to diagnose and treat SVTs.[7] The Bezold-Jarisch reflex is stimulated by mechanoreceptors and chemoreceptors located in the myocardium.[8] Activation of these receptors also increases parasympathetic activity and decreases sympathetic activity, which promotes bradycardia and hypotension (similar to the arterial baroreceptor reflex). This reflex has been implicated in vasovagal syncope.[6]

We hypothesize that epinephrine induced acute hypertension and this, in turn, triggered the arterial baroreflex, which resulted in bradycardia and AV node block. Sinus slowing occurring along with AH prolongation, Mobitz I AV block, and intermittent complete AV block (with junctional escape rhythm) are consistent with increased parasympathetic activity and sympathetic withdrawal. This hypothesis is further supported by resolution of bradyarrhythmia and AV block after discontinuation of epinephrine.

As electrophysiologists are increasingly required to find alternatives to isoproterenol, unwanted and unexpected side effects of using agents that lead to stimulation of non-β receptors are likely to occur. It is important to recognize that this type of transient AV block is not pathological (ie, not due to damage to the AV node). The coexistence of progressive sequence of bradycardic events with sinus bradycardia and progressive block within the AV node (AH prolongation, Mobitz I AV block, and intermittent complete AV block with junctional escape rhythm) differentiates transient AV block due to heightened parasympathetic tone from pathological AV block due to injury to the AV node.

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