

A case report of ivabradine used for heart rate control of atrial fibrillation in acute decompensated heart failure

Edward Hardison ^{1*}, Zachary L. Cox ², Katherine Heckman ³,
Patricia A. Kelly⁴, and JoAnn Lindenfeld⁵

¹Department of Internal Medicine and Pediatrics, Vanderbilt University Medical Center and Monroe Carrell Jr. Children's Hospital at Vanderbilt, One Hundred Oaks, 719 Thompson Ln, Suite 20400, Nashville, TN 37204, USA; ²Department of Pharmacy, Lipscomb University College of Pharmacy, 1 University Park Dr, Nashville, TN 37204, USA; ³Department of Internal Medicine, Vanderbilt University Medical Center, 1161 21st Ave S, Nashville, TN 37232, USA; ⁴Missoula Cardiology, 2419 Mullan Road, Suite A, Missoula, MT 59808, USA; and ⁵Department of Cardiovascular Medicine, Vanderbilt University Medical Center, 1161 21st Ave S, Nashville, TN 37232, USA

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Background

Achieving pharmacologic rate control in patients with atrial fibrillation (AF) with rapid ventricular response (RVR) can be tricky when the patient's underlying cardiac function is decreased. We present a case illustrating how ivabradine can be useful in this clinical scenario.

Case summary

A 95-year-old woman with a history of systolic heart failure (HF) presented with acute decompensated HF in AF with RVR. Beta blockade and calcium channel blockade were avoided given her cardiac history, and diuresis with high doses of furosemide was ineffective. Her ventricular response slowed with ivabradine, allowing for rapid decongestion and a safe discharge home.

Discussion

Ivabradine acts on the I_f current of cardiac pacemaker cells to slow heart rate (HR), and it currently carries a class IIa recommendation to reduce the risk of HF hospitalization and cardiac death in patients with left ventricular ejection fraction $\leq 35\%$ and a symptomatic HR ≥ 70 b.p.m. Although current recommendations are for patients in sinus rhythm, ivabradine has a theoretical benefit in patients with AF given its mechanism of action. Because it does not negatively affect inotropy or blood pressure, ivabradine was used in our patient with a good clinical outcome. Our case provides an example of ivabradine's usefulness in patients with AF in RVR with a history of depressed systolic function.

Keywords

Atrial fibrillation • Acute heart failure • Systolic heart failure • Case report • Ivabradine

ESC Curriculum

6.1 Symptoms and signs of heart failure • 6.2 Heart failure with reduced ejection fraction • 6.4 Acute heart failure • 7.3 Critically ill cardiac patient

Learning points

- Ivabradine is currently indicated in select patients with systolic heart failure with sinus tachycardia, but its mechanism suggests its usefulness in atrial fibrillation (AF).
- Ivabradine can be useful in patients with AF who may not tolerate rate control drugs with negative inotropic effects.

* Corresponding author. Tel: +1 615 343 7584, Email: edward.hardison@vmc.org

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Introduction

When patients present with acute decompensated heart failure (ADHF) and atrial fibrillation (AF) with a rapid ventricular response (RVR) there is often concern about using beta blockers or diltiazem to slow the ventricular response due to the risk of exacerbating the heart failure (HF). Amiodarone may be avoided for concern of cardioversion to sinus rhythm before exclusion of a left atrial thrombus. Digoxin may not adequately reduce ventricular rate in high sympathetic states or be appropriate in all patients. While ivabradine's predominant effects are on the sinoatrial node, emerging data suggest ivabradine may effectively reduce atrioventricular node conduction in AF.¹ We report a case in which ivabradine was effective in slowing ventricular rate in a patient who presented with ADHF in AF with RVR.

Timeline

Time	Events
Day of presentation	Patient seen in cardiology clinic with dyspnoea, peripheral oedema, started on furosemide 20 mg daily.
2 days post-presentation	Patient hospitalized with acute decompensated heart failure (HF) in atrial fibrillation (AF) with rapid ventricular response (RVR) (AF with RVR). Started on furosemide 200 mg every 8 h.
4 days post-presentation	Diuresis poor, patient continued with AF with RVR (~110–120 b.p.m.). Digoxin started. Computerized tomography head demonstrated resolved subdural haematoma.
5 days post-presentation	AF with RVR continued (~120–130 b.p.m.), ivabradine started. Apixaban started.
6 days post-presentation	Rate improved (~100 b.p.m.), vigorous diuresis over past 24 h, symptoms improved.
8 days post-presentation	Ivabradine stopped and started on metoprolol. Digoxin stopped. IV diuretics transitioned to oral furosemide 20 mg daily.
9 days post-presentation	Patient discharged home.
13 days post-presentation	Patient followed up with cardiology, heart rate 74, no signs of worsening HF.

Case presentation

A 95-year-old Caucasian woman with heart failure (HF) with reduced left ventricular ejection fraction (LVEF) secondary to ischaemic

cardiomyopathy, aortic stenosis status-post-transcatheter aortic valve replacement, paroxysmal AF, mitral regurgitation, hypertension, and chronic kidney disease presented with progressive dyspnoea on exertion, leg swelling, orthopnoea, and weight gain. Four months previously, she had suffered a subdural haematoma (SDH), with subsequent discontinuation of all HF medications and anticoagulation due to poor prognosis. Two days prior to admission, she was seen in cardiology clinic for routine follow-up and complained of increasing dyspnoea. Despite previous HF medication cessation, she elected admission for dyspnoea management. Furosemide was started and a transthoracic echocardiogram demonstrated an LVEF of 20% (unchanged) and proper function of the prosthetic valve. The electrocardiogram demonstrated sinus rhythm and an unchanged left bundle branch block (Figure 1). On admission, she was severely dyspnoeic. Initial blood pressure was 123/87, respiratory rate was 21 b.p.m., oxygen saturation was 96% on room air, heart rate (HR) ranged from 130 to 160 b.p.m., and she was afebrile. Physical exam revealed rales throughout bilateral lung fields, jugular venous distention to the angle of the mandible at 45°, tachycardia with an irregularly irregular rhythm, strong and equal peripheral pulses, bilateral peripheral oedema to the upper thighs, and cool extremities. An electrocardiogram confirmed AF with RVR (Figure 2). Notable laboratory findings on presentation included an unchanged normocytic anaemia (Hgb 9.6 g/dL) secondary to chronic kidney disease, normal thyroid function testing, and a creatinine of 1.73 mg/dL [creatinine clearance (CrCl) of 16 mL/min].

Differential diagnosis in a patient with hypervolaemia and new onset AF and ADHF includes discontinuation of HF medications, dietary indiscretion, arrhythmia, infection, and ischaemia. Additionally, aetiologies for new AF include HF exacerbation, hyperthyroidism, and pulmonary embolus.

Our patient's presentation was consistent with ADHF and AF with RVR, and her cool extremities were concerning for cardiogenic shock. Given her severe pulmonary congestion and known history of HF with reduced LVEF, as well as a desire to avoid worsening of cardiogenic shock, we avoided beta blockade and calcium channel blockade for rate control. Amiodarone and electrical cardioversion were avoided until a head computerized tomography scan could verify the safety of restarting anticoagulation given recent SDH. Diuresis was begun with 200 mg of intravenous furosemide every 8 h (her home dose was 20 mg of furosemide daily).

Diuresis was poor with this high dose of intravenous furosemide. Digoxin therapy was initiated (0.25 mg of intravenous loading dose, adjusted for weight of 51 kg, and 0.0625 mg every 48 h for a CrCl of 16 mL/min) with slightly decreased ventricular response, but persistent AF with RVR and poor diuretic response with ongoing dyspnoea at rest persisted. Ivabradine 2.5 mg twice daily was started to improve rate control, with subsequent slowing of her HR to 90 b.p.m. and vigorous diuresis. The lower dose was selected based on the patient's weight and renal function according to the package labelling. Figure 3 demonstrates her clinical course. After the patient was decongested, ivabradine was changed to metoprolol to optimize guideline-directed medical therapy, and she was started on maintenance oral furosemide dosing of 20 mg daily. Computerized tomography scan demonstrated complete resolution of SDH, so she was started on apixaban for

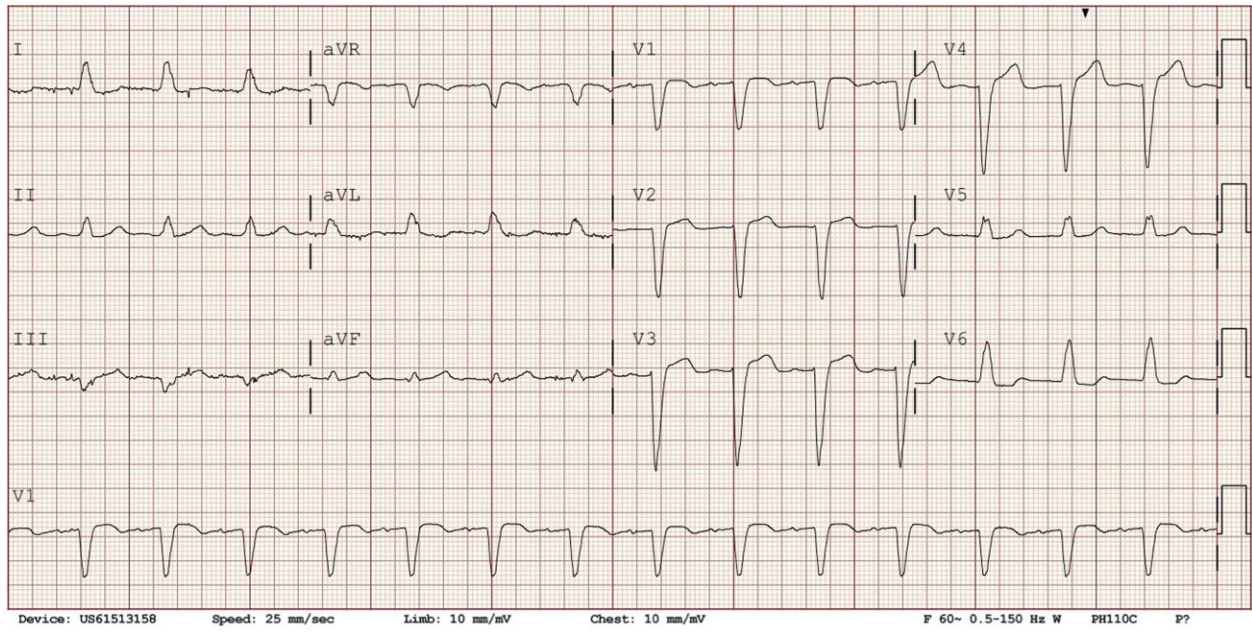


Figure 1 Electrocardiogram prior to presentation demonstrating normal sinus rhythm.

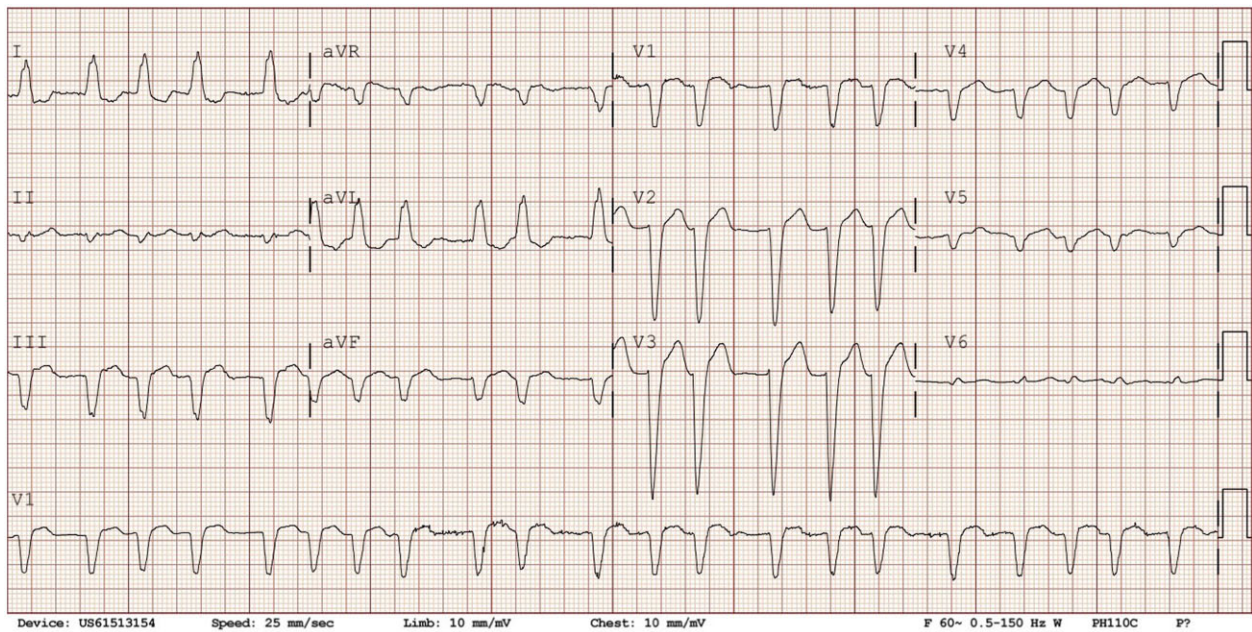


Figure 2 Electrocardiogram on admission demonstrating AF with rapid ventricular response.

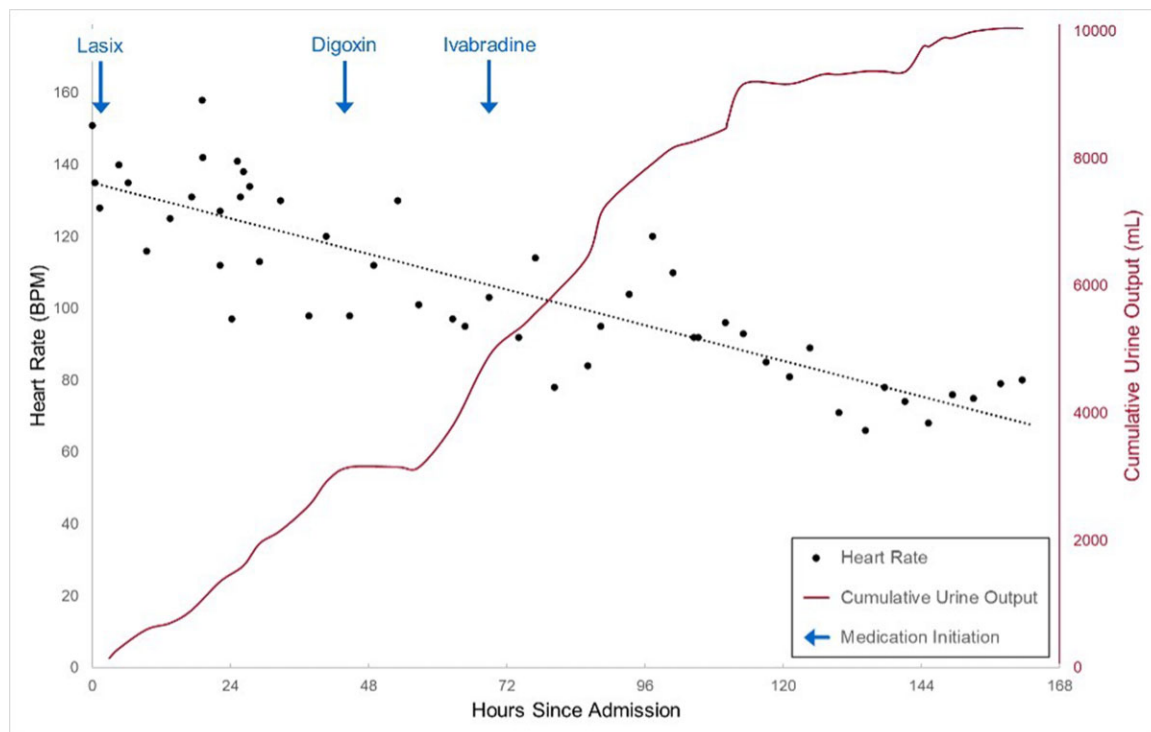


Figure 3 Clinical course including initiation of medications, heart rate trend, and cumulative urine output.

thromboprophylaxis. She was discharged with no jugular venous distension, no peripheral oedema, and clear lungs in AF with a ventricular response of 90 b.p.m.

Discussion

The most recent American and European HF guidelines provide a class IIa recommendation for ivabradine to be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF $\leq 35\%$ in sinus rhythm with a resting HR ≥ 70 b.p.m. who either cannot tolerate or are on maximally tolerated dosages of guideline-directed medical therapy.^{2,3} Clinical trials investigating ivabradine's utility in HF have excluded patients with persistent AF.^{4,5}

Though no guidelines currently indicate the use of ivabradine in patients with AF, emerging data suggest a possible benefit. Ivabradine selectively inhibits the hyperpolarization-activated cyclic nucleotide-gated (HCN) channel, which is responsible for generating the I_f current of cardiac pacemaker cells. Through sympathetic and parasympathetic stimulations, the I_f current determines HR.¹ By inhibiting HCN channels, ivabradine reduces sinus HR. Initially, HCN channels were thought to only be expressed in the sinoatrial node, but recent data suggest expression of HCN channels in loci associated with AF. Ivabradine has been shown in animal models to slow atrioventricular node conduction in AF.⁶ Oral ivabradine acts rapidly, reaching peak concentration in 1 h, with an effective half-life of 11 h.¹ Ivabradine has

no negative inotropic effects or blood pressure reduction, which makes it useful for patients with severe HF.⁷

Ivabradine's mechanism of action suggests a theoretical benefit in patients with AF; however, data supporting its use is limited. One case report demonstrates the utility of ivabradine in slowing HR in a patient in AF with RVR, with coexisting HF with reduced LVEF.⁸ One study demonstrated that ivabradine significantly reduced mean 24 h ventricular rate during AF by an average of 7.7 b.p.m. after 1 month.¹ Another study demonstrated ivabradine's efficacy in slowing HR in patients with permanent AF.⁹ Notably, AF is a reported side effect of ivabradine; however, as suggested by the above studies, it may be beneficial for rate control in AF, which makes further investigation to understand its mechanism of action and clinical use critical.^{5,6}

For our patient, whose pharmacologic options for AF rate control were limited, ivabradine was useful in acutely slowing HR without impairing contractility, allowing for vigorous diuresis, decongestion, and a good clinical outcome.

Follow-up

Two months after discharge, our patient was at a stable dry weight, in AF with an HR of 68 b.p.m. on metoprolol.

Conclusions

Although originally thought to be only beneficial for sinus tachycardia, ivabradine is a potentially useful agent in AF. It has a rapid onset of

action after oral administration. It has no negative inotropic effects, making it effective in patients with reduced contractility, such as ours. Our case adds to the small existing body of literature. Larger trials, such as the ongoing BRAKE-AF trial, are necessary to further discern ivabradine's emerging role in rate control in AF.¹⁰

Lead author biography



Edward (Ned) Hardison, MD is a third-year resident physician in the Internal Medicine and Pediatrics Department of Vanderbilt University Medical Center and Monroe Carell Jr. Children's Hospital at Vanderbilt in Nashville, TN, USA. After graduation, Ned plans to pursue a career in cardiology with a focus on transitions of care in adolescents from paediatric to adult providers.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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