Case Report

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
2018, Vol. 46(11) 4825–4828

DOI: 10.1177/0300060518799566
journals.sagepub.com/home/imr
SAGE

Heart rate reduction after ivabradine might be associated with reverse electrical remodeling in patients with cardiomyopathy and left bundle branch block

Andrea Kučerová, Petr Doškář, Libor Dujka, Veronika Lekešová, Petr Volf, Katarina Koščová, Petr Neužil and Filip Málek

Abstract

Left bundle branch block increases the risk of death in patients with chronic heart failure. We herein report four clinical cases of patients with chronic heart failure caused by nonischemic cardiomyopathy with left bundle branch block that occurred when adding ivabradine to optimal medical therapy, resulting in reverse electrical and mechanical remodeling. This phenomenon might be explained by the effect of ivabradine on reverse remodeling of the left ventricle with improvement of intraventricular conduction.

Keywords

Electrical remodeling, ivabradine, left bundle branch block, cardiomyopathy, chronic heart failure, intraventricular conduction

Date received: 26 June 2018; accepted: 17 August 2018

Introduction

The Ivabradine and Outcomes in Chronic Heart Failure (SHIFT) study showed that the presence of left bundle branch block (LBBB) increased the risk of death in patients with chronic heart failure (CHF) and a heart rate of $\geq$70 beats per minute (bpm) with

Cardiovascular Center, Na Homolce Hospital, Roentgenova 2, Prague, Czech Republic, EU

Corresponding author:
Filip Málek, Cardiovascular Center, Na Homolce Hospital, Roentgenova 2, 150 30 Prague 5, Czech Republic, EU.
Email: filip.malek@centrum.cz

sinus rhythm. Ivabradine was safe in patients with LBBB, and its effect was similar to that in patients without LBBB.[1]

We herein report four clinical cases of patients with CHF characterized by nonischemic cardiomyopathy, sinus rhythm, and LBBB at baseline. The addition of ivabradine to optimal medical therapy was associated with a reduction in the heart rate, narrowing of the QRS complex duration, and loss of the LBBB pattern on electrocardiography (ECG). The aim of this study was to assess the potential indirect effect of ivabradine on intraventricular conduction in patients with cardiomyopathy.

Patients

Four patients (one man, three women; age range, 28–76 years) were followed at a tertiary care heart failure clinic after diagnosis of heart failure with a reduced left ventricular ejection fraction (LVEF) caused by nonischemic cardiomyopathy.

The patients were chosen from the database of the tertiary care heart failure clinic. ECG was recorded at each clinic visit and stored in a personal computer database. Chronic LBBB was defined as a permanent LBBB morphology on 12-lead ECG at each clinic visit before initiation of ivabradine therapy. The heart rate was recorded from the resting 12-lead ECG recorded at each clinic visit.

Three patients had idiopathic cardiomyopathy and one patient had a history of myocarditis. The patients were undergoing optimal medical therapy including maximal tolerated doses of beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and mineralocorticoid receptor antagonists.

Ivabradine was started at a dose of 5 mg twice daily and titrated to 7.5 mg twice daily when the heart rates remained at >75 bpm despite the maximal tolerated beta blocker dose. Heart failure symptoms were mild [New York Heart Association (NYHA) class II in all patients].

Observation

After a mean of 866 days (range, 538–1211 days) of follow-up, a heart rate reduction

Table 1. Effect of ivabradine on parameters of patients with LBBB and CHF.

Case number (sex, age)		Follow-up days	HR, bpm	QRS width, ms	LVEF	LVEDD, mm	NT-proBNP, pmol/l
1 (M, 76 y)	Before IVA	924	87	134	26%	63	224
	After IVA		59	104	46%	52	21
	Change		−28	−30	+20%	−11	−203
2 (F, 45 y)	Before IVA	1211	84	154	25%	57	407
	After IVA		67	106	43%	43	22
	Change		−17	−48	+18%	−12	−415
3 (F, 28 y)	Before IVA	791	86	168	25%	61	139
	After IVA		72	114	44%	55	47
	Change		−14	−54	+19%	−6	−92
4 (F, 44 y)	Before IVA	538	75	140	31%	63	76
	After IVA		58	104	43%	55	11
	Change		−17	−36	+12%	−8	−65

LBBB: left bundle branch block, CHF: chronic heart failure, M: male, F: female, IVA: ivabradine, HR: heart rate, bpm: beats per minute, LVEF: left ventricular ejection fraction, LVEDD: left ventricular end-diastolic diameter, NT-proBNP: N-terminal B-natriuretic peptide.

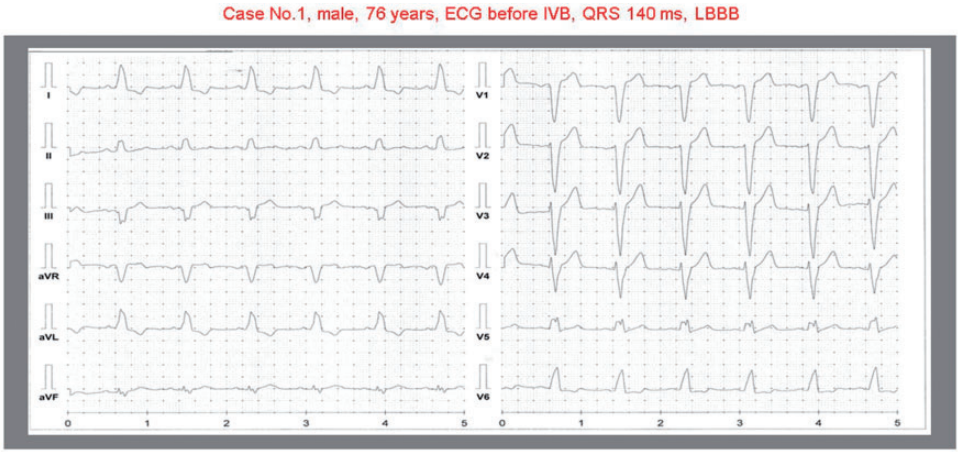

Figure 1. Electrocardiography before ivabradine.

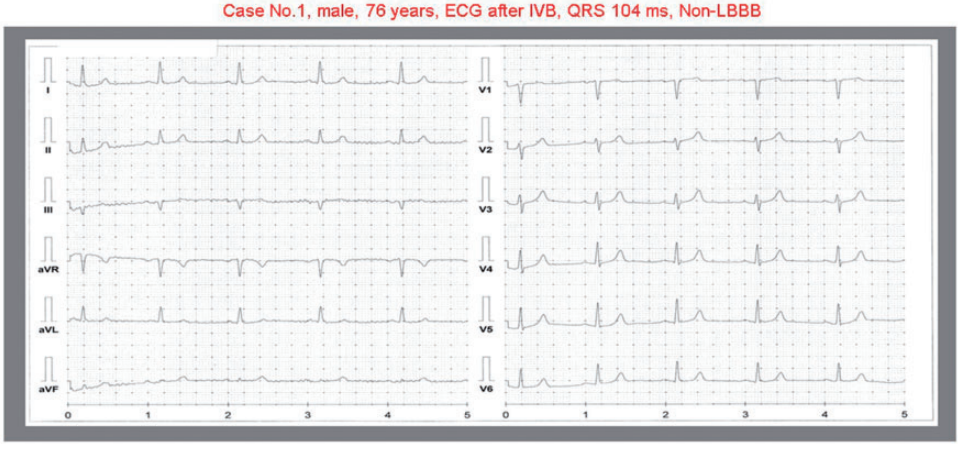

Figure 2. Electrocardiography after ivabradine.

after ivabradine therapy was associated with clinical improvement from NYHA class II to I. We observed an increase in the LVEF, a decrease in the LV end-diastolic diameter, and a reduction in the N-terminal B-natriuretic peptide level. We also observed a reduction in the QRS duration with loss of the LBBB pattern on ECG. The changes in parameters before and after ivabradine are shown in Table 1.

An example of the ECG changes before and after ivabradine is shown in Figures 1 and 2.

This study was approved by the local ethics committee of Na Homolce Hospital (2017). The patients participating in the study provided verbal informed consent.

Discussion

Ivabradine is a selective inhibitor of a specific *If* channel in the sinoatrial node and

causes dose-dependent heart rate reduction. Ivabradine has no effect on conduction, blood pressure, or inotropy of the heart. Experimental studies have shown that ivabradine treatment is associated with reverse mechanical remodeling in animal models of heart failure.[2,3] These experimental results were confirmed in the SHIFT echocardiography substudy.[4] Reverse electrical remodeling as a shortening of the intrinsic QRS interval has been described in patients receiving optimal medical therapy, including beta blockers and angiotensin-converting enzyme inhibitors; in patients receiving cardiac resynchronization therapy; and in patients with LV assist devices.[5–7] Reverse electrical remodeling after ivabradine in humans has not yet been described.

Our study is limited by the fact that it was a retrospective analysis. Holter ECG monitoring and exercise stress tests were not performed in all patients. The LBBB pattern at baseline might be heart rate-dependent. This fact does not decrease the possible indirect role of ivabradine on reverse electrical cardiac remodeling.

Conclusion

Heart rate reduction after ivabradine might be associated with shortening and a change of the morphology of the QRS complex in patients with CHF characterized by non-ischemic cardiomyopathy and LBBB at baseline. This phenomenon might be explained by the effect of ivabradine on reverse remodeling of the left ventricle with improvement of intraventricular conduction.

Declaration of conflicting interest

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: This study was supported by institutional grant MH CZ – DRO (Nemocnice Na Homolce – NNH, 00023884), IG170501.

References

1. Reil JC, Robertson M, Ford I, et al. Impact of left bundle branch block on heart rate and its relationship to treatment with ivabradine in chronic heart failure. *Eur J Heart Fail* 2013; 15: 1044–1052.
2. Navaratnarajah M, Ibrahim M, Siedlecka U, et al. Influence of ivabradine on reverse remodeling during mechanical unloading. *Cardiovasc Res* 2013; 97: 230–239.
3. Milliez P, Messaoudi S, Nehme J, et al. Beneficial effects of delayed ivabradine treatment on cardiac anatomical and electrical remodeling in rat severe chronic heart failure. *Am J Physiol Heart Circ* 2009; 296: H435–H441.
4. Tardif JC, O'Meara E, Komajda M, et al. Effects of selective heart rate reduction with ivabradine on left ventricular remodelling and function: results from the SHIFT echocardiography substudy. *Eur Heart J* 2011; 32: 2507–2515. DOI:10.1093/eurheartj/ehr311
5. Kloosterman M, Riebstra M, Van Gelder IC, et al. Spontaneous resolution of left bundle branch block and biventricular stimulation lead to reverse remodeling in dyssynchronopathy. *J Electrocardiol* 2016; 49: 696–698.
6. Sebag FA, Martins RP, Defaye P, et al. Reverse electrical remodeling by cardiac resynchronization therapy: prevalence and clinical impact. *J Cardiovasc Electrophysiol* 2012; 23: 1219–1227.
7. Drakos SG, Terrovitis JV, Nanas JN, et al. Reverse electrophysiologic remodeling after cardiac mechanical unloading for end-stage nonischemic cardiomyopathy. *Ann Thorac Surg* 2011; 91: 764–769.