Kardiologia Polska
2010; 68, 8: 935–937

ISSN 0022–9032

Inappropriate sinus tachycardia — successful treatment with ivabradine

Nieadekwatna tachykardia zatokowa — skuteczna terapia iwabradyną

Ozlem Ozcan Celebi, Alper Canbay, Savas Celebi, Sinan Aydogdu, Erdem Diker

Department of Cardiology, Ankara Numune Education and Research Hospital, Ankara, Turkey

Abstract

Inappropriate sinus tachycardia (IST) is characterised by an exaggerated increase of heart rate in response to normal physiologic demands. Therapeutic options including medical and radiofrequency ablation interventions are still under debate. Ivabradine inhibits spontaneous pacemaker activity of the sinus node by selectively blocking I_f channels of pacemaker cells. Here we present a case of a patient with IST, who was successfully treated with ivabradine after various ineffective therapeutic approaches.

Key words: inappropriate sinus tachycardia, ivabradine, sinus node blocking

Kardiol Pol 2010; 68, 8: 935–937

CASE REPORT

A 16 year-old female was addmitted to hospital due to tachycardia lasting for a few years. She was complaining of palpitations with minimal exercise during daily activities. Her physical examination was only remarkable for regular tachycardia with a heart rate (HR) of 160 bpm. A 12-lead surface electrocardiogram (ECG) showed tachycardia. Secondary causes of sinus tachycardia was excluded. A 24-hour ECG Holter monitoring revealed that basal HR was between 90 bpm and 180 bpm during daily activities. Heart rate inappropriately increased from 100 bpm to 160 bpm at the first stage of treadmill exercise test. The p wave axis and morphology was similar to that in sinus rhythm. All of these findings were suggestive of inappropriate sinus tachycardia (IST). Accordingly, cardiac electrophysiological study was performed. No other tachycardia was induced by programmed atrial and ventricular stimulation. In order to confirm the diagnosis of IST 1 μg/min isoproterenol infusion was administrated and thereafter HR increased from 90 bpm to 140 bpm. Heart rate response to isoproterenol was brisk. Metoprolol 50 mg daily with a target dose of 200 mg daily was started thereafter. Despite metoprolol at maximal dose, she was still complaining of tachycardia. Repetitive ECG Holter monitoring showed that basal HR was 105 bpm and increased to maximum 164 bpm during daily activities. Because of resistant tachycardia, she underwent sinus node area modification by radiofrequency (RF) ablation. After the procedure HR decreased to 80 bpm and increased to maximum 110 bpm with isoproterenol administration without palpitation. Hovever, she was readmitted to hospital suffering from the same symptoms two months after ablation, which raised concerns about recurrent IST. Subsequent ECG Holter monitoring and treadmill exercise test confirmed the recurrence of IST (Table 1). Since the symptoms were refractory to both metoprolol and RF ablation, we decided to add verapamil at a target dose of 240 mg daily. However, she was still symptomatic and experienced palpitation. Moreover, hypotension impeded additional verapamil use. At that point ivabradine was added to medical therapy with a dose of 5 mg bid and HR slowed down. The ivabradine dose was increased to 7.5 mg bid. One month later, 24-hour ECG Holter monitoring was reperformed and showed that basal HR was 58 bpm and increased to maximal 120 bpm during daily activities (Table 2). She was free from symptoms, howewer, a phosphenes occured after ivabradine. Since it

Address for correspondence:
Ozlem Ozcan Celebi, MD, 381.sokak İdareciler Sitesi B-Blok No: 13 Çiğdem, Ankara, Turkey, tel: +903125084776, fax: +903123110115, e-mail: drozlemoz@mynet.com
Received: 26.11.2009 **Accepted:** 16.12.2009

Table 1. 24-hour ECG monitoring before ivabradine shows increased heart rate during daily activities

INTERVAL	HEART RATE			TOTAL	VPB	VPB	RUNS	SVPB	SVPB	RUNS		TIMES
STARTING	LO	MEAN	HI	BEATS	TOTAL	PAIRS	VT	TOTAL	PAIRS	SVT	PAUSES	ANALYSED
14:02–1	75	131	183	6680	0	0	0	0	0	0	0	0:50
15:00–1	66	99	166	5282	0	0	0	0	0	0	0	0:53
16:00–1	72	97	147	5674	0	0	0	0	0	0	0	0:57
17:00–1	69	100	154	5832	0	0	0	0	0	0	0	0:58
18:00–1	65	91	131	5310	0	0	0	0	0	0	0	0:58
19:00–1	63	89	128	5215	0	0	0	0	0	0	0	0:58
20:00–1	67	92	152	5385	0	0	0	0	0	0	0	0:58
21:00–1	68	93	145	5370	0	0	0	0	0	0	0	0:57
22:00–1	67	112	174	6558	1	0	0	0	0	0	0	0:58
23:00–1	67	94	147	5202	0	0	0	0	0	0	0	0:54
0:00–2	62	91	127	4968	0	0	0	0	0	0	0	0:54
1:00–2	61	81	121	4618	0	0	0	0	0	0	0	0:56
2:00–2	63	74	93	4203	0	0	0	0	0	0	0	0:56
3:00–2	53	68	116	3885	0	0	0	0	0	0	0	0:56
4:00–2	54	63	104	3792	0	0	0	0	0	0	0	1:00
5:00–2	53	60	98	3555	0	0	0	0	0	0	0	0:59
6:00–2	51	61	109	3632	0	0	0	0	0	0	0	0:58
7:00–2	55	67	117	3903	0	0	0	0	0	0	0	0:57
8:00–2	57	67	114	3999	0	0	0	1	0	0	0	0:59
9:00–2	59	71	116	4280	0	0	0	0	0	0	0	0:59
10:00–2	59	75	128	4402	0	0	0	0	0	0	0	0: 58
11:00–2	61	100	166	5490	0	0	0	0	0	0	0	0: 54
12:00–2	72	117	171	6626	1	0	0	0	0	0	0	0:56
13:00–2	90	138	186	7080	0	0	0	0	0	0	0	0:50
14:00–2	128	184	200	1037	0	0	0	0	0	0	0	0:05
SUMMARY	51	89	200	121992	2	0	0	1	0	0	0	22:51

was tolerable and mild, we did not stop the medication. Phosphenes spontaneously disappeared and she improved symptomatically during six months of follow-up.

DISCUSSION

Inappropriate sinus tachycardia is charactarised by an exaggerated increase of HR in response to normal physiologic demands [1]. Increased sympathetic tone and sympathetic receptor sensitivity, blunted parasympathetic tone, and enhanced automaticity by virtue of regional autonomic neuropathy have been proposed to be underlying mechanisms [2]. Clinical features of IST may include palpitation, shortness of breath, chest discomfort, dizziness and fatique [3]. Severe symptoms sometimes may even prevent patients from daily activities. Of note, important diagnostic challenge is to investigate other causes of sinus tachycardia before making a diagnosis of IST.

Medical management of IST usually includes beta-blockers and verapamil [4]. Sinus node modification using RF ablation has been treatment modility of choice in patients with drug refractory IST. However, sinus node modification by catheter-based approach has high recurrence rate and low success rate. A significant proportion of patients who underwent RF ablation of sinus node area or received sinus node blocking agents still suffer symptoms related to tachycardia.

Ivabradine blocks I_f channels of sinus node pacemaker cells. Clinical trials have clearly documented the effectiveness of ivabradine for the treatment of chronic angina pectoris in the setting of contraindication or intolerance for beta-blockers [5, 6]. Blocking I_f channels of pacemaker cells allows HR reduction without affecting myocardial contractility, relaxation and peripheral vascular resistance [7]. This feature is crucial, as hypotensive response to other negative chronotrophic medications such as beta-blockers and verapamil may limit thair widespread use as in our case. Therefore ivabradine, it has been recently suggested a new therapeutic step before invasive sinus node modulation [4].

When ivabradine was administrated to our patient, both the quality of life and symptoms improved. Howe-

Table 2. 24-hour ECG monitoring after ivabradine shows slowered heart rate which is within normal limits at rest and during daily activity

INTERVAL	HEART RATE			TOTAL	VPB	VPB	RUNS	SVPB	SVPB	RUNS		TIMES
STARTING	LO	MEAN	HI	BEATS	TOTAL	PAIRS	VT	TOTAL	PAIRS	SVT	PAUSES	ANALYSED
14:01–1	63	82	121	2682	0	0	0	0	0	0	0	0:32
15:00–1	49	69	104	4063	0	0	0	0	0	0	0	0:58
16:00–1	49	72	110	4275	0	0	0	0	0	0	0	0:58
17:00–1	49	67	97	4015	1	0	0	0	0	0	0	0:59
18:00–1	44	60	89	3619	0	0	0	0	0	0	0	0:59
19:00–1	43	55	85	3327	0	0	0	0	0	0	0	0:59
20:00–1	45	62	84	3718	0	0	0	0	0	0	0	0:59
21:00–1	48	61	82	3659	0	0	0	0	0	0	0	0:59
22:00–1	44	57	77	3415	0	0	0	0	0	0	0	0:59
23:00–1	45	59	85	3492	0	0	0	0	0	0	0	0:58
0:00–2	43	55	80	3259	0	0	0	1	0	0	0	0:59
1:00–2	39	48	71	2894	0	0	0	0	0	0	0	0:59
2:00–2	37	46	65	2760	0	0	0	0	0	0	0	0:59
3:00–2	42	52	78	3137	0	0	0	0	0	0	0	0:59
4:00–2	39	47	76	2854	0	0	0	0	0	0	0	0:59
5:00–2	36	47	79	2849	0	0	0	0	0	0	0	1:00
6:00–2	40	49	83	2351	0	0	0	0	0	0	0	0:47
7:00–2	38	45	80	2746	0	0	0	0	0	0	0	0:59
8:00–2	41	51	87	2891	0	0	0	0	0	0	0	0:56
9:00–2	45	65	101	3944	0	0	0	0	0	0	0	0:59
10:00–2	48	71	117	1298	0	0	0	0	0	0	0	0:18
SUMMARY	36	58	121	67248	1	0	0	1	0	0	0	19:25

ver, there is no established effective dose of ivabradine for the treatment of IST. In our case, initial dose was 5 mg bid but the effective decrease in HR and improvement of symptoms were achieved when the dose was increased to 7.5 mg bid.

Ivabradine is generally well tolerated and only few side effects are known. The most common adverse event is reported to be visual symptoms due to inhibition of h-channels in the eye [7]. Of note, visual symptoms are more likely to occur in a dose dependent fashion (increased by aproximately 14%, 18% and 29% with 5 mg, 7.5 mg and 10 mg of ivabradine respectively). Visual symptoms are usually mild and transient in nature. Besides, phosphenes are previously reported to not be associated with withdrawal of the drug as in the current case [8].

In conclusion, ivabradine seems to be clinically useful for the treatment of IST and should be esperially considered in patients with resistant symptoms.

References

1. Morill CA, Klein GJ, Thakur RK et al. Mechanism of inappropriate sinus tachycardia. Role of sympthovagal balance. Circulation, 1994; 90: 873–877.
2. Shen WK. How to manage patients with inappropriate sinus tachycardia. Heart Rhythm, 2005; 2:1015–1019.
3. Leonelli F, Richey M, Beheiry S et al. Tridimensional mapping: guided modification of sinus node. J Interven Card Electrophysiol, 1998; 9: 1214–1217.
4. Schulze V, Steiner S, Hennersdorf M et al. Ivabradine as an alternative therapeutic trial in the therapy of inappropriate sinus tachycardia: a case report. Cardiology, 2008; 110: 206–208.
5. Borer JS, Fox K, Jaillon P et al. Antianginal and antiischemic effects of ivabradine, an If inhibitor, in stable angina. Circulation, 2003; 107: 817–823.
6. Tardif JC, Ford I, Tendera M et al. Efficacy of ivabradine, a new selective If inhibitor, compared with atenolol in patients with chronic stable angina. Eur Heart J, 2005; 26: 2529–2536.
7. Savelieva I, Camm AJ. If inhibition with ivabradine: electrophysiological effects and safety. Drug Saf, 2008; 31: 95–107.
8. López-Bescós L, Filipova S, Martos R. Long-term safety and efficacy of ivabradine in patients with chronic stable angina. Cardiology, 2007; 108: 387–396.