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Original Article

Association between Electrophysiological and Electrocardiographic Patterns and Recurrence of Bradyarrhythmias in High-Grade Atrioventricular Blocks in Patients Treated with Beta Blockers

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Abstract

Background: Despite the high efficiency of beta blockers in controlling increased blood pressure in hypertensive patients, these types of drugs have clinically remained as one of the main etiologies of atrioventricular (AV) blocks and arrhythmias. The present study aimed to assess the electrophysiological pattern in patients treated with beta blockers after discontinuing the drug use and also to assess the relationship between these electrophysiological findings and the recurrence of bradyarrhythmias in these patients.

Methods: In a prospective cohort study, 159 patients who were treated with different types of beta blockers and referred to Shariati Hospital in 2014 because of the onset of bradyarrhythmias were included into the study. All the participants were followed up for 6 months with respect to the recurrence of bradyarrhythmias.

Results: The rate of the occurrence of different AV blocks ranged between 13.8% and 23.3%, while these blocks also appeared within the follow-up period in the range of 7.5% to 11.3%, indicating a high recurrence rate of these blocks even after electrophysiological study (EPS) or pacemaker implantation. Assessing the relationship between the type of baseline rhythm and baseline characteristics showed a significant difference in the type of rhythm between the young and older patients (P=0.002), between patients with wide and narrow QRS complexes (p<0.001), and between those with normal and reduced left ventricular ejection fractions (P<0.001). Also, the type of baseline rhythm was significantly associated with HV interval in EPS (P<0.001), AV Wenckebach period (P<0.001), AERPAVN (P<0.001), and type of His disorder (P<0.001). The deteriorating effect of beta blockers as AV blocks type II or complete AV block can be more expected in patients with HV>55, AVWP>500, AERPAVN>500, as well as in infra-Hisian disorder.

Conclusion: The recurrence of bradycardia after administrating beta blockers is a common finding. Along with old age, QRS complex widening, and left ventricular dysfunction, the presence of some cut-off points of EPS indices, including HV>55, AVWP>500, and AERPAVN>500, as well as in infra-Hisian disorder can be considered as the main determinants of beta blockers-induced bradyarrhythmias. ***(Iranian Heart Journal 2015; 16(1): 26-33)***

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Keywords: ■Beta blocker; ■Arrhythmia; ■Block; ■Recurrence

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Beta blockers are one of the main groups of cardiovascular drugs in the treatment and control of cardiovascular disorders such as hypertensive disorders, tachy-arrhythmia, cardiac hyperkinetic syndrome, hypertensive circulatory diseases, portal hypertension, and even hyperthyroidism, tremor, migraine headache, anxiety disorder, and psychomotor disorders.[1-5] During the recent years especially in patients with heart failure, the prescription of low dose beta blockers has been very effective on improving clinical condition and long-term prognosis of the affected patients.[6-8] A wide variety of beta blockers are available with the different pharmacokinetic and pharmacodynamic effects. Also, different types of these drugs are now applied regarding their dependency to the receptors, selectivity, partial agonistic action, and pharmachemical components.[9,10] Despite the high efficiency of beta blockers in controlling increased blood pressure in hypertensive patients, these types of drugs have clinically remained as one of the main etiologies of atrioventricular (AV) blocks and bradyarrhythmias.[11,12] The prognosis of patients having experienced blocks and arrhythmias relating to beta blockers has been also uncertain. It has been well demonstrated that the demographic characteristics of patients with AV blocks induced by beta blockers are completely similar to those of patients with the other types of blocks; however, the former group suffer more from hypertension and they tend to have lower rates of structural or ischemic defects.[13-15] Furthermore, the electrocardiographic patterns are not different between the two groups with and without arrhythmias due to the use of beta blockers. In this regard, about half of the patients with AV blocks induced by beta blockers may be affected by syncope induced by deteriorating cardiac block.[16] Moreover, AV blocks may occur more frequently particularly as II or III degrees of blocks following the occurrence of blocks due to beta blockers.[17,18]

According to recent guidelines, some patients with blocks induced by beta blockers may be candidated for pacemakers to relieve their symptoms.[19] However, the efficacy of this modality to treat clinical symptoms remains controversial, which may be due to the type and severity of underlying cardiac diseases.[20,21] Nowadays, the role of underlying diseases as the triggering factors for blocks induced by beta blockers has been questioned and further research in this field is needed.[22] The present study aimed to assess the electrophysiological pattern in patients treated with beta blockers after discontinuing the drug use and also to assess the relationship between these electrophysio-logical findings and the recurrence of bradyarrhythmias in these patients.

Methods

This prospective cohort study included 159 patients who were treated with different types of beta blockers and referred to Shariati Hospital in 2014 because of the onset of bradyarrhythmias. After collecting baseline characteristics and clinical history by

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interviewing, electrocardiography (ECG) was performed from all the participants and the use of beta blockers was discontinued according to the clinical judgment of the cardiologist. In the patients with AV block Mobitz type II or AV block type III and with QRS widening>0.12 second, a pacemaker was implanted. In patients with a narrow QRS complex or without indications for pacemaker implantation, electrophysiology study (EPS) was considered so as to asses the sinus node function or the AV conduction time. All the participants were followed up for 6 months via pacemaker analysis (in the group with implanted pacemakers) or by Holter and clinical assessment for the recurrence of bradyarrhythmias. Finally, the relationship between the electrophysiological and electrocardiographic findings and the recurrence of arrhythmias was assessed.

The results are reported as mean±standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student t-test for the continuous variables and the chi-square test (or the Fisher exact test if required) for the categorical variables. A P value≤0.05 was considered statistically significant. All the statistical analyses were performed using SPSS (version 16.0) (SPSS Inc., Chicago, IL, USA) and SAS (version 9.1) for Windows (SAS Institute Inc., Cary, NC, USA).

Results

Overall, 159 patients, comprised of 85 men and 74 women at a mean age of 65.91±14.46 years (range=34 to 92 years), were included. Regarding the underlying cardiac disorders, 32.7% of the study population had heart failure, 34.6% ischemic disease, 17.6% hypertension, 13.8% cardiac rheumatism disease, and 0.6% palpitation. As regards the underlying arrhythmic abnormalities, 9.4% of the patients had AV type I, 23.3% AV block Mobitz type I, 13.8% AV block Mobitz type II, 18.2% AV block type III, 17.0% sinus bradycardia, 12.6% sinus pulse, and 5.7% atrial fibrillation with a slow ventricular response. The mean QRS widening was 108.57±22.02 msec; 41.5% had widening≥ 120 msec. With respect to the QRS morphological features, 49.7% of the patients had a normal morphology, while 28.9% had left bundle branch block (LBBB), 9.4% had right bundle branch block (RBBB), and 11.9% had bifascicular block. As for the medications, 39.6% of the study samples previously used Atenolol, 20.1% Propranolol, 16.4% Carvedilol, and 23.9% Metoprolol. The mean left ventricular ejection fraction (LVEF) was 46.76±6.71%. In the follow-up study, the recurrence of arrhythmias occurred in 7.5% of the study population as AV block type I, 10.1% as AV block Mobitz type I, 11.3% as AV block Mobitz type II, 11.3% as AV block type III, 7.5% as sinus bradycardia, 6.9% as sinus arrest, 18.9% as atrial fibrillation with a slow ventricular response, and 26.4% as normal sinus rhythm. The mean HV interval was 55.44±16.02, mean AV Wenckebach period was 498.15 ± 161.53, and mean AERPAVN was also 492.99±165.04. Supra-Hisian and infra-Hisian His involvements were also found in 74.2% and 25.8% of the patients, respectively.

All three patterns of HV, AV Wenckebach period, and AERPAVN were adversely associated with the LVEF and they also had a direct association with QRS widening. Assessing the relationship between the type of baseline rhythm and baseline characteristics showed a significant difference in the type of rhythm between the young and older patients (P=0.002), between the patients with wide and narrow QRS complexes (P<0.001), and between those with normal and reduced LVEFs (P<0.001). Also, the type of baseline rhythm was significantly associated with the HV interval (P<0.001), AV Wenckebach period (P<0.001), AERPAVN (P<0.001), and type of His disorder (P<0.001). The present study showed higher AV Wenckebach period,

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higher HV, and higher AERPAVN in AV block Mobitz type II and AV type III when compared to the other types of blocks. In supra-Hisian His level, the prevalence of AV block type I, AV Mobitz type I, atrial fibrillation with a slow ventricular response, and normal sinus rhythm was higher than that in infra-Hisian His level, while AV block Mobitz type II and AV block type III were found more frequently in infra-Hisian His level (Table 1).

Table 1: Association between AV block and electrophysiological pattern at baseline

	HV		AVWP		AERPAVN		His	
	HV<55	HV>55	AVWP<500	AVWP>500	AERPAVN<500	AERPAVN>500	suprahisian	infrahisian
1st degree AVB	14	1	13	2	13	2	14	1
	93.3%	6.7%	86.7%	13.3%	86.7%	13.3%	93.3%	6.7%
type 1 2nd AVB	34	3	32	5	32	5	36	1
	91.9%	8.1%	86.5%	13.5%	86.5%	13.5%	97.3%	2.7%
type2 2nd AVB	3	19	4	17	4	17	2	20
	13.6%	86.4%	19.0%	81.0%	19.0%	81.0%	9.1%	90.9%
3rd AVB	14	14	8	20	8	20	15	14
	50.0%	50.0%	28.6%	71.4%	28.6%	71.4%	51.7%	48.3%
sinus bradycardia	22	5	24	3	24	3	22	5
	81.5%	18.5%	88.9%	11.1%	88.9%	11.1%	81.5%	18.5%
sinus pause	20	0	20	0	20	0	20	0
	100.0%	.0%	100.0%	.0%	100.0%	.0%	100.0%	.0%
AF slow VR	9	0	4	5	4	5	9	0
	100.0%	.0%	44.4%	55.6%	44.4%	55.6%	100.0%	.0%
P-value	< 0.001		< 0.001		< 0.001		< 0.001	

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The deteriorating effect of beta blockers as AV blocks type II or complete AV block could be expected more in the patients with HV>55, AVWP>500, and AERPAVN>500, as well as in those with infra-Hisian disorder. These differential patterns also remained within the follow-up period (Table 2).

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Table 2: Association between AV block and electrophysiological pattern within follow-up time

	HV		AVWP		AERPAVN		His	
	HV<55	HV>55	AVWP<500	AVWP>500	AERPAVN<500	AERPAVN>500	suprahisian	infrahisian
1st degree AVB	10	2	11	1	11	1	11	1
	83.3%	16.7%	91.7%	8.3%	91.7%	8.3%	91.7%	8.3%
type 1 2nd AVB	16	0	12	4	12	4	16	0
	100.0%	.0%	75.0%	25.0%	75.0%	25.0%	100.0%	.0%
type2 2nd AVB	2	16	2	16	2	16	2	16
	11.1%	88.9%	11.1%	88.9%	11.1%	88.9%	11.1%	88.9%
3rd AVB	2	15	1	16	1	16	2	16
	11.8%	88.2%	5.9%	94.1%	5.9%	94.1%	11.1%	88.9%
sinus bradycardia	10	1	9	2	9	2	10	2
	90.9%	9.1%	81.8%	18.2%	81.8%	18.2%	83.3%	16.7%
sinus pause	9	2	9	2	9	2	8	3
	81.8%	18.2%	81.8%	18.2%	81.8%	18.2%	72.7%	27.3%
AF slow VR	26	4	23	7	21	9	27	3
	86.7%	13.3%			70.0%	30.0%	90.0%	10.0%
P-value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

In this study, the relation between electrophysiological and electrocardiographic patterns and the recurrence of arrhythmia in patients who were treated with beta blockers was assessed. Most of these patients experienced various types of arrhythmias, especially AV blocks on admission. Such patients might also experience the recurrence of these arrhythmias after pacemaker implantation or EPS performance. In our survey, the rate of the occurrence of different AV blocks ranged between 13.8% and 23.3%, while these blocks also appeared within the follow-up period within a range of 7.5% to 11.3%, indicating a high recurrence rate of these blocks even after EPS or pacemaker implantation. In this regard, a close relationship is expected between electrophysiological indices after EPS or pacing and the recurrence of arrhythmias.

Regarding the association between the use of beta blockers and EPS findings, the electrophysiological rhythm was significantly associated with HV interval, AV Wenckebach period, AERPAVN, and type of His disorder. On the other hand, the deteriorating effect of beta blockers as AV blocks type II or complete AV block could be expected more in the patients with HV > 55, AVWP > 500, and AERPAVN > 500, as well as in those with infra-Hisian disorder. In fact, along with old age, QRS complex widening, and LV

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dysfunction, the presence of these cut-off points of EPS indices can be considered as the main determinants of beta blockers-induced bradyarrhythmias. Previous reports have found that advanced age, combined drug therapy, the period during the initial 24 hours after the initiation of drug therapy, decreased systolic performance, and female gender are the predictors of proarrhythmias induced by beta blockers.[23,24] Also, it has been previously shown that drug-induced bradycardia usually does not appear in patients with normal sinus node function and normal atrioventricular conduction, which is consistent with our findings.[25,26] Regarding the association between arrhythmias due to beta blockers and QRS widening, it is well known that Na channel blockers can cause ventricular arrhythmias, namely sine-wave-shaped ventricular tachycardia with a wide QRS duration. The QRS width is commonly used as a marker of the magnitude of Na channel-blocking effects.[27] Therefore, we determined the QRS duration as an indicator of the appearance of arrhythmias. Moreover, in our survey, old age was a main factor for the occurrence of drug-induced arrhythmias. It has been previously established that older age is a risk factor for proarrhythmia.[23,24] In our series, most of the patients were categorized as old population. This is probably due to several factors: increased fibrosis and a decrease in pacemaker cells in the nodal area; likelihood of being on multiple drugs; and diminished mental capacity, leading to poor adherence.

Conclusion

The recurrence of bradycardia after administrating beta blockers is a common finding and it may be affected by old age, QRS complex widening, and LV dysfunction, which should be considered as the main predictors of requiring pacemaker implantation in patients treated with beta blockers.

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