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ORIGINAL ARTICLE

Evaluation of Orthostatic Reaction in Patients with Artificial Pacemaker

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ABSTRACT

Background: Normal orthostatic response enables the human being to preserve his blood pressure and organ perfusion with the change in posture. The maintenance of this mechanism is very important for the comfort of the daily life.

Aim of the work: The study aimed to illustrate the orthostatic response of a patient with implanted anti-bradycardia pacing devices compared to normal subjects, aiming at better selection of pacing modality in deferent patient profiles.

Methods: This study was carried out in Pacemaker Follow-up Clinic, Cardiac Electrophysiology Unit, Cardiology Department, Zagazig University, from February 2019 to August 2019. The study included 81 patients with pacemaker implantation [48 with Single ventricular pacing ventricular sensing inhibition (VVI), and 33 with Dual chamber pacing Dual sensing (DDD) pacemakers], and 20 apparently healthy controls.

Results: In the VVI group the heart rate didn't change during the recording period and in the pre-tilt period the heart rate behavior of DDD and control group was the same with no statistically significant difference between the two groups. In the post-tilt period there was a significant increase in heart rate in both groups in nearly the same pattern with no statistically significant difference. In both groups the heart rate didn't drop to the pre-tilt levels until the end of the recording.

Conclusion: Pacing especially VVI mode induce blunting in orthostatic systolic blood pressure response which can be a drawback of pacing. Although a patient with DDD had a much better response than VVI patient.

Keywords: Orthostatic hypotension, pacemaker syndrome, Diastolic dysfunction

INTRODUCTION

Deferent neurohormonal mechanisms contribute to this mechanism including vasoactive and cardio-stimulatory [1], the first mechanism controls the diameters of blood vessels modulating blood pressure and the second mechanism controls the heart rate inducing increase in the heart rate which increases the cardiac output immediately to compensate for the orthostasis of blood to the dependent parts of the body. Many patients have deficiency in any or both the two mechanisms like diabetic patients with autonomic neuropathy resulting in lack of vasopressor response [2].

Patients with single-chamber pacemakers have a fixed escape rate which maintains the heart rate above certain preprogrammed figure, in rate-responsive single-chamber pacemakers the heart rate (HR) can be modulated with a sensor which respond to acceleration or vibration and not to postural changes, thus this group of patients is supposed to have dysfunctional orthostatic response [3].

The aim of the anti-bradycardia pacing is to save the patient's life and to conserve his life quality as well, which was not possible in the early days of pacing, due to technical difficulties [4], although the pacing started with single-chamber pacing, advances in electronics rapidly introduced dual-chamber

pacemakers which bridges the conduction gap and brings the relationship between the atria and the ventricles back to normal. Dual chamber pacing has many advantages over single chamber pacing, and thus used for younger more active patients, and as most of the population in need for pacing are elderly, they have many comorbidities, one of them is orthostatic hypotension. The effect of pacing mode is not known on orthostatic blood pressure control [5].

The study was aimed to illustrate the orthostatic response of a patient with implanted anti-bradycardia pacing devices compared to normal subjects, aiming at better selection of pacing modality in deferent patient profiles.

METHODS

This study was carried out in Pacemaker Follow-up Clinic, Cardiac Electrophysiology Unit, Cardiology Department, Zagazig University and testing for orthostatic response was carried out in the tilt table lab, which is a part of the same unit, during the period from February 2019 to August 2019, The study included 81 patients with pacemaker implantation (48 with VVI, and 33 with DDD pacemakers), the study included 20 apparently healthy controls. The patients and controls were matched in comorbidities (hypertension and DM) patients with comorbidities were minimized as much as possible in VVI group to match DDD and control groups. Medical research and ethics committee approved the study. All patients gave an informed consent to participate in the study.

The patients were classified into three groups: Group (A): VVI patients, Group (B): DDD patients, Group (C): Normal healthy control.

Methods of Assessment:

Patients were selected consecutively from patients attending pacemaker clinic follow-up if they fulfill the inclusion criteria and have none of the exclusion criteria and willing to participate in the study.

Demographic data and full history and clinical examination are recorded in a specially designed patient sheet concentrating on the presence of comorbidities and the presence of symptoms suggesting orthostatic hypotension and history of medications.

Pacemaker data is collected based on programmer interrogation data to insure proper pacemaker parameters and function.

In the post absorptive state patients are allowed to lie for 6 minutes on the tilt table (brand: Kondak, model: KD-ZLC-01A, Shanghai, China), while recording ECG, and blood pressure every minute (Hewlett Packard Viridia 26c Modular Patient Monitor, California, USA), then the table is elevated to 80 degrees and the blood pressure and heart rate are recorded every minute for another 6 more minutes.

The presence of orthostatic hypotension is considered if there is a reduction in either the systolic blood pressure by 20mmHg or more or reduction in the diastolic blood pressure by 10 mmHg or more.

Inclusion criteria

Age between 45 and 60 years, no orthostatic symptoms (e.g. postural syncope, presyncope, blurring of vission or nausea), Device interrogation using the suitable programmer to confirm 95% or more pacing of the device, Device pacing during the test for orthostatic hypotension using the tilt table should be 100%.

Exclusion criteria

Less than 100% pacing during the test in groups A and B., Pregnancy, or lactation., Patients on medications inducing orthostatic hypotension., Patients with known neurological or musculoskeletal abnormalities that affect balance., Patients with autonomic neuropathy due to any cause., We tried to minimize the numbers of diabetic and hypertensive patients as much as we can in group A and we matched the numbers in groups B and C accordingly.

Written informed consent was obtained from all participants. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans

All participants were subjected to:

Complete history taking with special emphasis on [Age, Sex, Risk factors including (hypertension, diabetes mellitus), Pregnancy or lactation, Drug History, Neurological or musculoskeletal abnormalities, Type of device VVI, DDD.

Tilt table test: Each patient was positioned supine then upright at a 60 and 80-degree angle to horizontal on an atilt table with a footboard for weight bearing. The electrocardiogram was monitored continuously. Blood pressure was measured every minute using an automatic blood pressure device. The blood pressure was measured on the right arm in supine and then standing position. Supine blood pressure was measured every minute for 6 minutes.

Statistical Analysis:

Data were analyzed using (SPSS version 16.0, IBM SPSS Collaboration and Deployment Services, New York, USA.) data were expressed as mean± SD. comparative analysis of curves using one way ANOVA and unpaired samples t test. p-value was considered significant as P > 0.05: Non-significant (NS), P < 0.05: Significant (S), P < 0.01: Highly significant (HS)

RESULTS

The study population mean age was 53.4±3.87 (45-60) years, patients in VVI group was significantly older than the other two groups (Table 1). The study showed that the percentage of males was significantly higher in pacemaker groups when compared to the control group (Table 2). Regarding comorbidities there was no statistically significant difference between the studied groups (Table 3). The rate of systolic blood pressure drop between the 1st and second minute was the highest in the control group followed by DDD group and the least in VVI group (3±2.6, 2.66±1.5 and 2.0±1.45 respectively) the difference was only significant between controls and VVI groups (p=0.045) while was no statistically significant difference between the other groups. Between the 2nd and the 6th minutes of recording there was no significant change within and between groups (Table 4). During the 6th minute (immediately after tilt) there was a drop in systolic blood pressure in all groups the drop was significantly higher and faster in the VVI versus. DDD groups only. From the 7th minute until the end of recording the following happened, In VVI group the systolic blood pressure went progressively down and didn't pick up until the end of recording, In DDD group the systolic blood pressure went down until the 9th minute and started to pick up but didn't reach the pre tilt levels, In control group the systolic blood pressure started to pick up immediately and progressively until the end of recording but didn't reach the pre tilt levels, All the previous changes were statistically significant between all the groups. From 1st to 6th minute (pre-tilt) there was no significant change in diastolic blood pressure between groups except a significant fluctuation in diastolic pressure in the control group during the last two minutes (Table 5). After tilt there was no significant change in diastolic pressure in control group, while in both VVI and DDD groups there was a drop in the diastolic pressure, which reached its bottom in VVI group at the 9th minute and reached its bottom in DDD group at the 8th minute then progressively increased until the end of recording but didn't reach the level of the initial diastolic readings for each two groups. In the VVI group the heart rate didn't change during the recording period. In the pre-tilt period, the heart rate behavior of DDD and control group was the same with no statistically significant difference between the two groups. In the post-tilt period, there was a statistically significant increase in heart rate in both groups in nearly the same pattern, in both groups the heart rate didn't drop to the pre-tilt levels until the end of the recording (Table 6).

Table 1: Mean age distribution between studied groups.

	Mean ± SD	Minimum	Maximum	P
VVI	54.75±3	50	60	0.003
DDD	52.36±4.415	45	59	
control	51.95±3.859	46	59	
Total	53.42±3.866	45	60	
VVI	54.75±3	50	60	

VVI: Single ventricular pacing ventricular sensing inhibition. DDD: Dual chamber pacing Dual sensing

Table 2: Sex distribution between studied groups.

			Sex		Total	p
			Female	Male		
Group	**VVI**	**N**	6	42	48	
		%	12.5%	53.2%	100.0%	
	DDD	**N**	5	28	33	

			Sex		Total	p
			Female	Male		
		%	15.2%	35.4%	100.0%	<0.001
	control	N	11	9	20	
		%	55.0%	11.4%	100.0%	
Total		N	22	79	101	
		%	21.8%	78.2%	100.0%	

VVI: Single ventricular pacing ventricular sensing inhibition. DDD: Dual chamber pacing Dual sensing

Table 3: Comorbidities distribution between studied groups.

			HTN		Total	p
			Normotensive	Hypertensive		
Group	VVI	N	42	6	48	0.95
		%	87.5%	12.5%	100.0%	
	DDD	N	29	4	33	
		%	87.9%	12.1%	100.0%	
	Control	N	17	3	20	
		%	85.0%	15.0%	100.0%	
Total		N	88	13	101	
		%	87.1%	12.9%	100.0%	
Diabetes		VVI	DDD	Control		0.98
		5(10.4%)	3(9.1%),	2(10%)		

VVI: Single ventricular pacing ventricular sensing inhibition. DDD: Dual chamber pacing Dual sensing

Table 4: Comparison of the systolic blood pressure between the studied groups.

Mean ±SD mmHg change	VVI	DDD	Control	P
2-3 minute	-0.39±3.03	0.181±2.48	0.8±2.89	0.271
3-4 minute	-0.125±2.7	-0.42±2.7	-1.60±3.5	0.151
4-5 minute	0.12±4.4	-0.81±2.1	-0.45±3.3	0.505
5-6 minute	0.06±3.1	0.0±2.1	1.2±3.8	0.310
6-7 minute	-9.8±3.0*	-7.87±4.3*	8.45±3.0	0.038
7-8 minute	-2.27±1.2	-5.54±2.9	+0.8±0.83	<0.001
8-9 minute	-0.89±0.7	-2.0±1.35	+0.8±0.61	<0.001
9-10 minute	-1.25±0.7	+2.15±1.58	+0.6±0.75	<0.001
10-11 minute	-1.06±0.7	+2.69±1.57	+1.15±0.81	<0.001
11-12 minute	-1.04±0.71	+2.48±1.6	+0.95±0.6	<0.001

VVI: Single ventricular pacing ventricular sensing inhibition. DDD: Dual chamber pacing Dual sensing

Table 5: Comparison of the diastolic blood pressure between the studied groups.

Mean ±SD mmHg change	VVI	DDD	Control	P
1-2minute	-0.10±1.85	-0.30±3.19	-0.6±3.8	0.79
2-3 minute	+0.02±1.7	+0.18±2.7	+1.15±6.7	0.48
3-4 minute	-0.22±1.9	+0.181±2.2	-1.15±5.0	0.26
4-5 minute	-0.187±1.88	+0.06±2.4	+2.15±5.96	0.024
5-6 minute	+0.12±1.9	-0.45±3.2	-2.5±6.56	0.031
6-7minute	-5.58±2.7	-3.27±2.22	+0.181±2.2	0.124
7-8minute	-2.54±1.28	-1.66±0.98	+0.06±2.4	0.046
8-9minute	-2.66±1.4	+1.06±0.78	-0.45±3.2	<0.001
9-10minute	+1.68±0.92	+0.9±0.68	-3.27±2.22	0.006
10-11minute	+1.437±0.89	+1.00±0.701	-1.66±0.98	0.007
11-12minute	+1.33±0.97	+0.93±0.60	-2.66±1.4	<0.001

VVI: Single ventricular pacing ventricular sensing inhibition. DDD: Dual chamber pacing Dual sensing

Table 6: Comparison of the heart rate between the studied groups

Mean ±SD mmHg change	DDD	Control	P
1st minute	73.73±8.460	71.85±7.975	0.51
2nd minute	73.85±8.337	71.95±8.049	0.53
3rd minute	73.42±8.537	71.45±7.817	0.62
4th minute	73.39±9.017	71.35±8.561	0.71
5th minute	73.58±9.364	72.75±9.824	0.96
6th minute	73.30±9.136	71.70±8.548	0.55
7th minute	82.00±11.297	81.10±8.902	0.34
8th minute	85.64±11.586	82.00±8.675	0.27
9th minute	86.94±11.592	82.95±8.300	0.25
10th minute	86.09±11.482	83.80±8.501	0.27
11th minute	85.94±11.906	84.60±8.580	0.31

DDD: Dual chamber pacing Dual sensing

DISCUSSION

Anti-bradycardia pacing started as a lifesaving intervention, through years, and with the rapid technological advances the devices became smaller and more energy efficient. Lifesaving besides quality of life became the targets for the anti-bradycardia pacing. Guidelines included sections describing which device is the best for which patient [6]. Studies also showed higher overall complication rates with dual-chamber pacing as compared with single-chamber ventricular pacing systems. Nevertheless, the consensus group concluded: "While implant complications are more frequent for dual-chamber than single-chamber pacemakers, the higher risk of complications for dual-chamber pacemakers is offset over time by the need to reoperate on a number of patients with single-chamber pacemakers for [atrioventricular] block or pacemaker syndrome." The VVI pacemaker being the simplest and the easiest to implant was the most implanted device [7].

Physiological pacing was best provided by the DDD pacemakers, regarding the chronotropic response of the patients, and AV synchronization. Thus, was provided to younger more active patients, it's not known wither the DDD pacemakers can make a difference for patients with abnormal orthostatic blood pressure response, the current study is considered the first to address that issue [8].

We collected our patients from the pacemaker follow-up clinic. Majority of the patients under follow-up were VVI patients with the VVI patients being significantly older than patients with DDD pacemakers that agreed with the recently published international registries like the study of *Pombo Jimenez et al.* [9]. Velten et al., [10] reported that age being a factor affecting the orthostatic response was controlled by narrowing the selected sample age groups. Although we tried, the best but patients in VVI group were older by a mean of 2 years, which can be neglected as a factor affecting the accuracy of the study.

Males represented most of the pacemaker group, while the majority of the control group were females, as during risk factors matching the female population of the hospital co-workers were a bigger pool for selection than males, and that also wasn't considered as a factor that affect the results as gender is not considered as a factor affecting the orthostatic response [10].

Comorbidities such as hypertension and diabetes mellitus (DM) is considered as an important factor in determining the orthostatic response [10], thus we successfully matched the three groups regarding hypertension and DM.

After the first minute of recording, it was interesting to notice a small drop of the systolic blood pressure in all groups that can be explained by the time taken by the subjects to be familiar with the surroundings and to get the sympathetic firing to the resting state as explained by *Zhang et al.* [11].

Although we excluded patients with symptomatic orthostatic hypotension, none of our patients developed symptoms during the tilt or achieved the target of 20mmHg drop in systolic or 10mmHg drop in diastolic blood pressure.

The most significant finding of this study was the systolic blood pressure response in the VVI and DDD patients compared to controls. These changes reflect the great role played by heart rate change in controlling orthostatic blood pressure which was demonstrated in different studies of *Fanciulli et al.* [12] and study of *Oksanen et al.* [13].

Although none of the groups were able to return to pre tilt blood pressure by the end of the 6 minutes of tilt but patients with VVI pacemakers didn't even show any pickup of the systolic blood pressure during the tilt and the pressure continue to drop, on the other hand patients with DDD pacemakers systolic blood pressure started to pick up during the 6 minutes of tilting, but they did so later than the control group, which demonstrates probably the difference in cardiac output between controls and DDD pacemaker patients which can be attributed to mechanical asynchronization on the inter and intraventricular levels which occur during RV apical pacing as demonstrated by Akbarzadeh and Toufan, [14] who demonstrated the wide range of systolic and diastolic dysfunction which can be induced even with dual chamber pacing on echo Doppler based study. Also, Atrioventricular (AV) interval optimization which enhances the cardiac output is considered inferior in the pacing group as demonstrated by Crystal and Ovsyshcher, [15] who stated that "In patients with dual chamber pacemakers due to AV block and otherwise normal hearts, empirically selected AV intervals may lead to compromise of cardiac hemodynamics. Optimal AV intervals may be selected by serial cardiac output measurements" which is not easily performed during every implantation procedure.

Although diastolic blood pressure depends mainly on venous tone [10] but the pacing group especially the VVI patients showed a significant tilt associated drop but unlike systolic blood pressure it picked up rapidly may be because of cardiac output on the diastolic blood pressure which is less that its effect in systolic blood pressure.

CONCLUSION

Pacing especially VVI mode induce blunting in orthostatic systolic blood pressure response which can be a drawback of pacing. Although a patient with DDD had a much better response than VVI patient.

Conflict of Interest

The authors of this manuscript declare no relevant conflicts of interest, and no relationships with any companies, whose products or services may be related to the subject matter of the article.

Financial Disclosures

None.

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