Investigation of the BNP Level Changes in Blood Stream in Different Modes and Lead Locations after Pacemaker Implementation

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Submission: 13-07-2011 Accepted: 18-01-2012

ABSTRACT

As has been proven, increase of mechanical strain could result in an increase of brain natriuretic peptide (BNP) in the blood stream of implanted patient pacemakers. We measured the BNP concentration in blood due to different mode and lead implantation location of pacemaker in the time period of 3 months. The aim of this study was to investigate the changing trend of BNP level after pacemaker implantation. One hundred and three pacemaker implanted patients were monitored. Patients were in the age span of 54±12 years, including 48 men and 55 women. A group of 44 were programmed in Dual Chamber Rate Adaptive (DDDR) Pacemaker mode and a group of 59 were programmed in Ventricular Rate Modulated Pacing (VVIR) mode by the recommendation of the cardiologist. Between these two groups, the pacing levels of pacemakers was divided to under and above 50%. Some of these pacemaker leads were located at the apex of the right ventricle and the others were located in the septum wall in the right ventricle. To evaluate BNP changes during a period of 3 months, the BNPs were measured in pg/ml within 24 h of implantation (BNP1) and after 3 months (BNP2). For different classes of pacemaker implantations, the ratio of final measurement (BNP2) is divided to after implantation measurements (BNP1). Results showed that in VVIR mode, the ratio is 1.54±0.3 and in DDDR mode, the ratio is 0.38±0.17, with acceptable standard error means (<0.04). Also, comparisons are made for lead location at two modes of DDDR and VVIR separately. In the DDDR mode, the ratio for apex location is 0.49±0.12 and for septum location is 0.22±0.34, with acceptable standard error means (<0.02). In the VVIR mode, the ratio for apex location is 1.71±0.27 and for septum location is 1.28±0.09, with acceptable standard error means (<0.04). Therefore, BNP decrease in DDDR mode is more than in VVIR mode programming. In both cases of DDDR and VVIR modes, the septum location of the leads would result in a greater decrease of BNP.

Key words: *Pacemaker, BNP, mode, implantation position*

INTRODUCTION

Pacemaker implantation is one of the most modern treatment techniques used in most heart diseases. More than 250,000 pacemakers (cardiovascular implantable electronic device) are implanted annually. On the other hand, a great number of patients under cardiac pacemaker treatment suffer heart failure with the passage of time. This is a progressive and malignant disease. Gradually, it is progressing to chronic case, such that 300,000 people annually lose their lives due to this disease. The major source of brain natriuretic peptide (BNP) is ventricle muscles during systolic malfunctioning of the heart. The human myocardium undergoes a period of hypertrophic growth without cell division during postnatal maturation. This growth could occur in a diverse form in response to prolonged mechanical load, hemodynamic, hormonal and pathologic stimuli. It intensifies during ischemic heart disease, valvular insufficiency and cardiomyopathy, increases wall thickness and results in concentric hypertrophy.[1,2] At the cellular level, cardiac myocytes respond to diverse types of biomechanical stress by initiating several different processes that, via activation of transcription factors, lead to hypertrophic gene expression and growth of individual myocytes.[3] This is followed by release of certain proteins such as BNP. Therefore, BNP release is in response to increase in the volume and pressure of the ventricle. Nowadays, BNP level has become a good measure of ventricle failure. The most important diagnostic symptom for this disease is the increasing levels of BNP existent in the blood. There were intensive studies on the relation between heart failure and increment of the sodium levels in blood.[4]

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Electric impulse trigger of the heart begins from the sino–atrial node on the right atrium and, after arterial compression, is transferred to the atrio–ventricular node and transmission through Purkinje fibers, leading to ventricle contraction. It could be concluded that the Dual Chamber Rate Adaptive (DDDR) pacemaker is the most suitable type of pacemaker that could synchronize and adapt to physiological function of the heart. In DDDR pacing mode, the heart performs much better than in Ventricular Rate Modulated Pacing (VVIR), which is respiration demand sensitive. In the VVIR pacing mode, the contraction of the ventricles is independent from atria; therefore, stresses due to the lake of synchronization of upper chambers and lower chambers results in increase of BNP level in the blood stream. Kurum *et al.* in their study on 22 patients with implanted pacemakers, including 11 in DDDR mode and 11 in VVIR mode, found that the BNP level at the blood stream of patients in DDDR mode is significantly lower than that of those in VVIR mode.[5] In another study on 105 patients with implanted pacemakers including 32 in DDDR mode, 30 in ventricular rate modulated pacing (AAIR) pacemaker mode and 73 in VVIR mode, the BNP level of patients in the blood stream were investigated. The BNP level of the blood stream of all patients had been measured on the day of the implantation and after 1 month of implantation. The BNP level had changed differently within different groups so that the level changes were lowest in the AAIR mode group, medium in the DDDR mode group and highest within the VVIR mode group.[6] In another study by Sadowski *et al.* on 28 patients under treatment by two modes of DDDR and AAIR pacing, it had found that there is not significant difference in changes of the BNP between them.[7] The present research project makes an attempt to establish a relationship between the pacing mode of the cardiac pacemaker and the BNP changes in patient's blood. It proposed to determine an appropriate method for the application of the pacemaker procedure, leading to the reduction of BNP level. We measured the BNP concentration in blood due to different mode and lead implantation location of pacemaker in the time period of 3 months.

MATERIALS AND METHODS

In this study, 109 patients including 59 females and 50 males were selected. Only those patients were chosen who were suffering from heart pacing failure. The age range of these patients was distributed within the 54±12 years age bracket. At the end of the study, we end up with only 103 patients. For all of these 103 patients (including 48 men and 55 women), pacemaker implantation were recommended. The recommended modes of pacemakers were DDDR and VVIR. The pacing levels of pacemakers were divided to under and above 50%. It is known that the pacing level is dependent on different wave shapes, pulse energy level, pulse raise time, duration and amplitude.[8,9] Subsequent to the analysis of the pacemaker set, specific to each patient, the operation mode of the set and the lead configuration (location including on the septum or apex) were investigated. In this study, Demand pacemaker from Medtronic and S T Jude were used for implantation on patients. Pacemaker configurations in the point of pacing percentage, mode and lead position are listed in Table 1.

By discrimination of implanted pacemakers based on the aforementioned categories, there would be eight groups of implanted pacemakers, as divided in Table 2.

These pacemakers were programmed and monitored by their counterparts Medtronic 2090 Programmer and S T Jude Medical's Merlin programmers, respectively.

Patients were monitored for 24–48 h after pacemaker implantation. During monitoring, if the patient was stable, his blood sample was taken and blood serum was centrifuged at 3000 rpm (15°C for 10 min) and separated plasma was immediately assayed and frozen to -20 to 40°C. Samples are transferred to the laboratory for BNP measurements.

The BNP level of blood samples was measured by the electrochemiluminescent method with the Elecsys 2010. All samples were measured with a specific immunoradiometric assay for human BNP using a highly sensitive, commercially available, enzyme-linked immunoassay (Biomedica Gruppe, Austria) and reported in pg/ml.

The BNP protein levels of each patient were undertaken on two occasions; simultaneous after pacemaker implantation and 3 months after the pacemaker implantation. Patients were monitored regularly after pacemaker implants and with pacemaker analyzers after 3 months of the implantation.

Table 1: Pacemaker mode, lead position and pacing percentage

Pacing mode		Lead position		Pacing (%)	
DDDR	VVIR	Septum	Apex	≤50%	<50%
44	59	42	61	42	61

DDDR – Dual chamber rate adaptive pacemaker; VVIR – Ventricular rate modulated pacing

Table 2: Distribution of patients on different groups for different categories

Groups	No. of patients	Pacing mode	Lead position	Pacing (%)
G1	7	DDDR	Septum	≤50
G2	12	DDDR	Septum	<50
G3	10	DDDR	Apex	≤50
G4	15	DDDR	Apex	<50
G5	12	VVIR	Septum	≤50
G6	11	VVIR	Septum	<50
G7	13	VVIR	Apex	≤50
G8	23	VVIR	Apex	<50

DDDR – Dual chamber rate adaptive pacemaker; VVIR – Ventricular rate modulated pacing

The ratios of BNP level of the second round of sampling to first round are worked out for each patient individually.

RESULTS

For different classes of pacemaker implantations, the ratio of final measurement (BNP2) was divided to after implantation measurements (BNP1). The mean value and standard deviation plus standard errors of the eight groups' BNP ratios are given in Table 3. As shown in Figure 1, BNP ratios (BNP2/BNP1) for DDDR mode of pacemaker implantation "G1, G2, G3 and G4" are less than 0.6 and therefore BNP levels are decreasing, but in the VVIR mode "G5, G6, G7 and G8" are more than 1.2 and therefore BNP levels are increasing.

In the point of view of the percentage, there is a difference between BNP changes of pacing percentage of above and under 50%. As shown in the odd groups "G1, G3, G5 and G7," where the pacing percentage was above 50%, the BNP ratio was lesser than their counterparts in the even groups "G2, G4, G6 and G8," where the pacing percentage were less than 50%.

If the patients are classified on the basis of pacing mode, including DDDR and VVIR, we would end up with results like those in Table 3. As shown in Table 4, in the VVIR mode, the ratio is 1.54±0.3 and in the DDDR mode, the ratio is 0.38±0.17, with acceptable standard error means (<0.04).

In a detailed consideration, we could have a close look at pace location leads in different modes as brought in Table 5. Also, comparisons are made for lead location at two modes of DDDR and VVIR separately; in the DDDR mode, the BNP ratio for apex location is 0.49±0.12 and for septum location is 0.22±0.34 with acceptable standard error means (<0.02). In the VVIR mode, the BNP ratio for apex location is 1.71±0.27 and for septum location is 1.28±0.09 with acceptable standard error of means (<0.04).

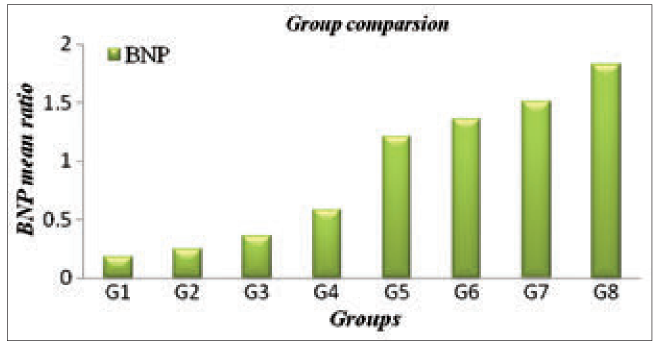

Figure 1: Brain natriuretic peptide (BNP) ratio in the different groups

Table 3: Mean ratio of BNP2/BNP1 in the different groups

	G1	G2	G3	G4	G5	G6	G7	G8
BNP2/BNP1	0.178	0.243	0.358	0.584	1.204	1.358	1.504	1.826
Std. deviation	0.015	0.006	0.036	0.059	0.043	0.019	0.059	0.274
Std. error of mean	0.006	0.002	0.059	0.015	0.012	0.006	0.016	0.057

Table 4: Group statistics for different modes of lead configuration

Mode	*N*	Mean ratio±STD	Std. error of mean
DDDR	44 (G1, G2, G3, G4)	0.38±0.17	0.02
VVIR	59 (G5, G6, G7, G8)	1.54±0.30	0.04

DDDR – Dual chamber rate adaptive pacemaker; VVIR – Ventricular rate modulated pacing

Table 5: Group statistics of mean ratio for the lead position

Mode	Position	*N*	Mean ratio±STD	Std. error of mean
DDDR	Septum	19 (G1, G2)	0.22±0.34	0.01
	Apex	25 (G3, G4)	0.49±0.12	0.02
VVIR	Septum	23 (G5, G6)	1.28±0.09	0.02
	Apex	36 (G7, G8)	1.71±0.27	0.04

DDDR – Dual chamber rate adaptive pacemaker; VVIR – Ventricular rate modulated pacing

DISCUSSION

The BNP decrease in the DDDR mode is more than that in the VVIR mode programming. In both cases of DDDR and VVIR modes, the septum location of the leads would result in a higher more decrease of BNP. The results indicate that the most useful application of the pacemaker is the DDDR style and the setting of the lead on the wall between the septum (inter-septum walls) where the pacing percentage is at a minimum. As the pacing percentage of the pacemaker increases, the BNP protein levels existing in the patient's blood under pacemaker treatment decrease inversely.

CONCLUSION

In this study, we found that the DDDR mode is much better than the VVIR mode of pacing according to the increase in BNP level in blood stream after pacemaker implantation. As experienced on our cases after 3 months of implantation, the BNP level had reduced significantly in the DDDR mode of implant. The implantation of the pacemaker interventricle septa is significantly better than interapex implantation, but the difference is not as significant as the difference between DDDR in comparison with VVIR mode. Also, there is a slight difference in BNP ratio changes between pacing percentage of above and under 50%, which is the decrease of ratio with the increase of pacing percentage. There should be an extremum in the decrease of BNP ratio to the increase of pacing percentage. Finally, we are suggesting to extract 12 standard ECG lead signals and vectorcardigrams of patients with right ventricular septal versus apical pacing to find out the time sequence functionality of the heart.[10,11] In expectation, in reference to normal heart function, there would be close correlation with either of these modalities.

ACKNOWLEDGMENT

Authors are hereby acknowledge the financial and spiritual support of the Vice Chancellery of Research of the Isfahan University of Medical Sciences for this research work.

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How to cite this article: ***

Source of Support: Nil, **Conflict of Interest:** None declared

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