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The influence of permanent cardiac pacing on plasma levels of B-type natriuretic peptide in patients with sick sinus syndrome

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Abstract

Background: *Unequivocal data presenting the impact of different pacing modes on B-type natriuretic peptide levels has never been published. The aim of the study was to assess changes of plasma B-type natriuretic peptide (BNP) during permanent cardiac pacing in patients with sick sinus syndrome (SSS).*

Methods: *Patients with SSS undergoing routine pacemaker implantation were enrolled. Each subject underwent medical history and examination, echocardiography and blood sampling. Analysis was performed on 12 females (42.9%) and 16 males (57.1%), mean age 71.3 ± 9.03 years, range 49–90 years. There were 11 pacemakers with AAIR pacing mode (39.3%; AAI group) and 17 with DDDR mode (60.7%; DDD group) implanted. There were no significant differences in age, concomitant diseases or echocardiographic parameters between the groups in baseline characteristics or plasma BNP levels (94.05 ± 54.1* vs. *73.57 ± 70.13 pg/mL; p > 0.2).*

Results: *During six months follow-up no significant changes in plasma BNP levels in AAI group (94.05 ± 54.1* vs. *94.05 ± 54.1 pg/mL; p > 0.5) as well as in DDD group (73.57 ± 70.1* vs. *82.39 ± 58.9 pg/mL; p > 0.5) were noticed.*

Conclusions: *Atrial (AAIR) and dual chamber (DDDR) pacing did not influence plasma BNP levels in patients with SSS and preserved left ventricular systolic function.* (Cardiol J 2008; 15: 39–42)

Key words: sick sinus syndrome, BNP, permanent cardiac pacing

Introduction

Permanent cardiac pacing is a well-established method of sick sinus syndrome (SSS) management. Several studies are taking place to assess the influence of permanent pacing on cardiac hemodynamics and its monitoring with natriuretic peptides [1]. The results of certain trials concerning the impact of different pacing modes in SSS on natriuretic peptides concentration are equivocal or even divergent. The aim of this study was to assess changes of plasma B-type natriuretic peptide (BNP) levels during permanent cardiac pacing in patients with sick sinus syndrome.

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Methods

The patients

The study group consisted of 12 females (42.9%) and 16 males (57.1%) with SSS, aged 49–90 years

Table 1. Baseline characteristics.

	Total (n = 28)	AAI (n = 11)	DDD (n = 17)
Age (years)	71.3 ± 9.03	72.4 ± 10.1	70.5 ± 8.53
Females	12 (42.9%)	6 (54.5%)	6 (35.3%)
Males	16 (57.1%)	5 (45.5%)	11 (64.7%)
AH	25 (89.3%)	10 (90.9%)	15 (88.2%)
PAF	15 (53.6%)	5 (45.5%)	10 (58.8%)
IHD	18 (64.3%)	5 (45.5%)	13 (76.5%)
LVEDD [mm]	51 ± 12	54 ± 6,1	49 ± 15
LVESD [mm]	34 ± 4.9	35 ± 4.9	34 ± 5
LA [mm]	37 ± 5.2	35 ± 5	38 ± 5.3
LVEF (%)	55 ± 8	55 ± 8	54 ± 9

AH — arterial hypertension, PAF — paroxysmal atrial fibrillation, IHD — ischemic heart disease, LVEDD — left ventricular end-diastolic diameter, LVESD — left ventricular end-systolic diameter, LA — left atrial area in M-mode, LVEF — left ventricular ejection fraction; differences between groups are insignificant

(mean 71.3 ± 9.03). They underwent cardiac pacemaker implantation according to current guidelines [2]. The exclusion criteria were permanent atrial fibrillation, complete heart block, acute coronary syndrome six weeks prior to implantation, the presence of inflammation, stroke three months prior to implantation, hepatic or renal failure, heart failure in II NYHA class or higher, neoplasia, respiratory insufficiency regardless of cause, structural heart disease, connective tissue disease, storage disease, muscular dystrophy and hemoglobin concentration less than 10 g/dL. All participants were administered beta-adrenolytics and angiotensine converting enzyme inhibitors due to ischemic heart disease and/or arterial hypertension. Single- or dual-chamber pacemakers were implanted (Axios, Biotronik) with respect to atrio-ventricular conduction competence rated by the measurement of the Wenckebach point (atrial rhythm with atrio-ventricular block of second degree) during the implantation procedure. According to the guidelines of the Polish Cardiac Society [2], a dual-chamber pacemaker was implanted if the Wenckebach rate was lower than 130 beats per minute. The available algorithms of right ventricular pacing minimization were activated. The pacing sites were the right atrial auricle and right ventricular apex. The basic clinical characteristics of the study group are presented in Table 1. During six months follow-up all subjects underwent physical examination, echocardiographic evaluation, blood sampling for BNP level measurements and pacing trend assessment.

The local ethics committee approved the study and informed consent was obtained from each subject.

Echocardiographic evaluation

Prior to device implantation all subjects underwent standard transthoracic echocardiographic evaluation of the atria and ventricles with left ventricular function assessment. Additional echocardiographic exams were performed three and six months after implantation to obtain the left atrial size. Echocardiography was performed with an ACUSON Sequoia C 256 system using a 3.5 MHz transducer in the second harmonic mode. Measurements were performed in parasternal long axis projection in M-mode. Left ventricular ejection fraction was obtained by the Simpson method.

Plasma BNP level measurements

Plasma BNP levels were assessed three times in each subject (prior to implantation and three and six months after the procedure) with a AxSYM BNP microparticle enzyme immunoassay (Abbott Laboratories). Venous blood sample for a single BNP measurement was taken after a 15 minute rest in supine position and stored in a cooled test-tube with EDTA.

Statistical analysis

Continuous variables are presented as mean ± ± standard deviation. The significance of the differences between means was tested with the t-Student test. Categorical variables were assessed with the chi-square test. A p value of less than 0.05 was considered significant.

Results

Patients were divided into two groups according to pacing mode. The AAIR mode was applied in 11 subjects (39.3%; AAI group), and the DDDR mode in 17 subjects (60.7%; DDD group). There were no significant differences in age (72.4 ± 10.1 *vs*. 70.5 ± 8.53; $p > 0.5$), arterial hypertension: 10 (90.9%) in the AAI group *vs.* 15 (88.2%) in the DDD group ($p > 0.6$) or paroxysmal atrial fibrillation: 5 (45.5%) in the AAI group *vs*. 10 (58.8%) in the DDD group ($p > 0.6$). There was a borderline significance in ischemic heart disease occurrence: 5 (45.5%) in the AAI group *vs*. 13 (76.5%) in the DDD group ($p > 0.05$). There were no significant differences between groups in echocardiographic parameters of left ventricular function or dimensions of the atria and ventricles. The mean plasma BNP level prior to implantation in the AAI group did not differ significantly from the level in the DDD group (94.05 ± 54.1 *vs*. 73.57 ± 70.13 pg/mL; $p > 0.2$). There were no significant changes in plasma BNP

Table 2. Changes in plasma BNP levels in the AAI group and DDD group during six-month follow-up.

	AAI	DDD
BNP_0 [pg/mL]	94.05 ± 54.1	73.57 ± 70.1
BNP_3 [pg/mL]	111.81 ± 29.2	90.75 ± 78.1
p — BNP_{0-3}	> 0.5 (NS)	> 0.5 (NS)
BNP_6 [pg/mL]	82.94 ± 79.9	82.39 ± 58.9
p — BNP_{0-6}	> 0.5 (NS)	> 0.5 (NS)

BNP_0, BNP_3, BNP_6 — plasma BNP levels before, three and six months after implantation

levels in the six months follow-up in the AAI group (94.05 ± 54.1 *vs*. 82.94 ± 79.9 pg/mL; p > 0.5) or in the DDD group (73.57 ± 70.1 *vs*. 82.39 ± ± 58.9 pg/mL; p > 0.5) (Table 2). The baseline left atrial size was 35.1 ± 4.9 mm in the AAI group and 37.9 ± 5.3 mm in the DDD group. No significant changes were observed after six months (39.2 ± ± 3.1 mm and 41.1 ± 10.5, respectively). The percentage of pacing in the AAI group was from 3% to 97% (mean 52 ± 50.9). In the DDD group the percentage of atrial pacing was from 34% to 74% (mean 59.8 ± 13.9), and the percentage of ventricular pacing was from 19% to 100% (mean 60.8 ± 34.5). There was no significant difference between the percentages of atrial pacing between the groups (p > 0.5).

Discussion

Natriuretic peptides are neurohormones that play an important role in fluid homeostasis and vasoconstriction due to their antagonistic action towards the renin-angiotensin-aldosterone system. They are also crucial to vascular function and remodelling by enhancement of the influence of nitric oxide and the prevention from lipid insudation into the vascular wall. Synthesis and release of BNP is stimulated by mechanical stretching of the heart chambers. A 134-amino acid prepropeptide is cut into a precursor proBNP108, which is divided into 76-amino acid inactive NT-proBNP (plasma half-life 90–120 min) and BNP (plasma half-life 18 min). Its biological activity is realised by binding with cell receptors. It is eliminated via glomerular filtration and endopeptidases. The elimination of NT-proBNP has not been completely investigated [3].

In many cases, permanent cardiac pacing leads to some side effects despite significant clinical improvement. One of the most explored aspects is the development or aggravation of congestive heart failure (CHF) due to long-lasting right ventricular apex pacing and the pathologic pathway of depolarisation and intraventricular dyssynchrony [1, 4, 5]. Plasma BNP measurement is a well-established diagnostic and risk stratification tool in patients with CHF [6–8]. It is also very helpful in the monitoring of stable patients. Assessment of BNP plasma levels in patients with permanent cardiac pacing has not been widely explored, whereas in patients without pacemakers it has.

The available publications on the influence of permanent cardiac pacing on plasma BNP levels consider comparisons of ventricular pacing mode (VVI) to atrial (AAI) and dual-chamber pacing-mode (DDD) [9–11]. In the last 10–15 years, the VVI mode has become rare in patients with SSS as they receive dual-chamber or atrial pacemakers. Therefore, the assessment of plasma BNP during AAIR or DDDR pacing modes in patients with SSS seems to be reasonable.

Wang et al. [9] reported a significant increase in BNP concentration during VVIR pacing in patients with SSS being in III or IV functional NYHA class and with diminished left ventricular ejection fraction. In contrast, dual-chamber pacing (DDDR) in patients with SSS and impaired left ventricular systolic function significantly decreased BNP levels due to the restoration of atrio-ventricular synchrony and an improvement in hemodynamics. However, there were no significant changes in BNP levels in patients with preserved left ventricular function during both DDDR and VVIR pacing modes in the nine-month follow-up. The results of the study presented are convergent. There were no significant changes in plasma BNP levels in patients with preserved systolic left ventricular function during the six-month follow-up. However, three months after implantation an upward trend in BNP levels with a tendency to decrease after the next three months was noticed. An interesting observation is that in the DDD group BNP levels after six months were slightly higher than the baseline. The most probable reason for this finding is the prolonged pacing of the right ventricular apex and depolarisation pattern imitating left bundle branch block resulting in ventricular dyssynchrony. A similar tendency was noticed by Wang et al. in patients with preserved systolic left ventricular function and VVIR pacing mode. A favourable, but not significant, tendency in the neurohormonal profile in the AAI group (decrease of BNP level to baseline) resulted from the lack of right ventricular pacing.

The results of the presented study indicate that in patients with SSS and preserved systolic left ventricular function AAIR as well as DDDR pacing

mode did not influence plasma BNP levels or left atrial diameter. Despite activation of the available algorithms of right ventricular pacing minimization, the mean percentage of ventricular pacing reached almost 60%. Surprisingly, there was no significant increase in BNP levels. This finding may explain the insignificant influence of permanent cardiac pacing on long-term prognosis in patients with SSS [12–14].

An important clinical implication of research on the influence of cardiac pacing on BNP release may be its application for screening in patients with risk factors of CHF (i.e. advanced age, atrial fibrillation, prior myocardial infarction) including right ventricular pacing [1, 4, 11, 15–18]. Some authors claim that BNP measurement during pacemaker follow-up is justified for monitoring the severity of CHF [19], and increased levels of BNP may indicate the need of pharmacotherapy optimisation or upgrading the pacing to the biventricular mode.

Limitations of the study

Small sample size, lack of randomization (due to strict indications to definite pacing mode, frequently established during procedure) and a limited length of follow-up do not really entitle us to extrapolate trends in the general population.

Conclusions

Atrial (AAIR) and dual-chamber (DDDR) permanent cardiac pacing in patients with sick sinus syndrome and preserved left ventricular systolic function did not provoke any significant changes in BNP plasma levels.

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The authors do not report any conflict of interest regarding this work.

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