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Does permanent cardiac stimulation through atrial natriuretic peptide secretion influence the basic parameters of renal function?

Janusz Sielski[1], Marianna Janion[1], Zenon Gawor[2], Jerzy Bobiarski[3] and Katarzyna Ciuraszkiewicz[1]

[1]Department of Cardiology, Regional District Hospital, Kielce, Poland
[2]Department of Internal Medicine, Nephrology and Dialysis Therapy, Medical University, Łódz, Poland
[3]Department of Cardiac Surgery, Medical University, Łódz, Poland

Abstract

Background: *The aim of this study was to evaluate atrial humoral function and renal function after pacemaker implantation due to atrioventricular conduction disturbances. We analyzed blood atrial natriuretic peptide (ANP) concentration and basic parameters of renal function within 1 month of implantation of VVI and DDD pacemakers. We evaluated correlations between blood ANP values and basic renal function parameters.*

Methods: *We studied two groups of patients with atrioventricular (AV) conduction disturbances: second-degree AV block and third-degree AV block. Group I comprised 20 patients aged 71–90 years (median 77.5 ± 5.9 years) in whom permanent VVI pacing was applied, and group II consisted of 20 subjects aged 49–81 years (median 68.9 ± 11.9 years) in whom DDD/ /VDD pacemakers were implanted. The control group consisted of 15 healthy volunteers aged 58–80 years (median 72.7 ± 2.8 years). Plasma concentration of ANP was determined by radioimmunoassay. The parameters of renal function we analyzed with Jaffe's colorimetric and kinetic test.*

Results: *Patients in group I showed a significant decrease in blood concentration of ANP from 168.1 ± 81.9 pg/1000 μL to 118.0 ± 61.1 pg/1000 μL ($p < 0.01$) 7 days after implantation. At 30 days, ANP was 121.4 ± 71.9 pg/1000 μL. In group II, plasma concentration of ANP decreased significantly from 134.9 ± 8.1 pg/1000 μL to 104.9 ± 6.1 pg/1000 μL ($p < 0.01$) 7 days after implantation and to 110.8 ± 53.3 pg/1000 μL at 30 days. Patients in group I had elevated, albeit insignificantly, clearance of creatinine to 76.1 ± 17.8 ml/min at 7 days ($p > 0.05$) which increased significantly to 85.0 ± 17.9 ml/min at 30 days. In group II, clearance of creatinine increased insignificantly to 84.6 ± 13.2 ml/min ($p < 0.05$) at 7 days and was significantly elevated to 96.9 ± 18.2 ml/min ($p < 0.05$) at 30 days. In group I, plasma concentration of creatinine decreased significantly ($p < 0.05$) to 1.15 ± 0.30 mg/dl at 7 days and to 1.01 ± ± 0.21 mg/dl at 30 days. In group II, there was a significant decrease ($p < 0.05$) to 1.15 ± 0.24 mg/dl at 7 days and to 1.08 ± 0.27 mg/dl at 30 days. There was a positive correlation between creatinine clearance and plasma ANP concentration in groups I and II ($r = 0.301$; $p < 0.05$).*

Address for correspondence: Janusz Sielski, MD
Grunwaldzka 45, 25–736 Kielce, Poland
e-mail: jsielski7@interia.pl
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Conclusions: *In patients with a pacemaker implanted due to atrioventricular disturbances, blood concentration of ANP was decreased. Renal function was improved after pacemaker implantation.* (Cardiol J 2007; 14: 568–572)

Key words: atrial natriuretic peptide, VVI and DDD pacemaker, renal dysfunction

Introduction

Natriuretic peptides play a very important role in the regulation of the cardiovascular system [1]. The first reports on endocrine function of the heart date back to 1956, when Kish [2] described osmophilic granules in the atrial muscle cells of guinea pigs. Later in 1981, de Bold et al. [3] observed significant renal natriuretic excretion after intravenous injection of atrial myocardial extract in rats. Subsequent studies demonstrated the existence of the natriuretic peptide family. The group includes, generally: atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), C — type natriuretic peptide (CNP) and urodilatin [4, 5]. Te increased stretch of the atrial muscle is the main mechanism stimulating ANP release [6]. This is according to Laplace's law which says that the cavity wall tension depends on its dimension and the pressure gradient across the wall. Therefore atrial pressure elevation results in increased atrial stretch and increased ANP secretion [7]. Animal experiments showed that atrial and ventricular rates are independent factors stimulating ANP secretion [8]. It was emphasized that mechanical stretch of atrial cardiomyocytes can also influence ANP release.

Atrial secretion of natriuretic peptides proves that they have a double role to play: mechanical and endocrine [9].

In renal failure, elevated concentration of natriuretic peptides causes intense sodium secretion by suppressing tubular sodium reabsorption [10].

Arterial hypertension, ischemic heart disease, pericarditis is the most common cardiovascular disease coexisting with renal failure [11, 12]. On the other hand, in chronic cardiovascular diseases such as hypertension, ischemic heart disease or heart failure, renal function parameters are increased. In patients qualified for permanent pacing, changes in levels of renal function parameters are possible before, during and after longer procedures. The above considerations inspired us to evaluate blood ANP concentration and renal function within one month of permanent pacemaker implantation. We also analyzed the correlations between blood ANP values and renal function parameters after implantation.

Methods

The study group comprised 55 patients without clinical symptoms of renal failure, with sinus heart rate, including 40 patients with II and III degree atrioventricular (AV) conduction disturbances. Group I consisted of 20 patients aged 71–90 years, mean age 77.5 ± 5.9 years, with VVI pacemakers implanted due to AV conduction disturbances. Group II comprised 20 patients aged 49–81 years old, mean age 68.9 ± 11.9 years, with DDD or VDD systems. Group III, the control group, included 15 healthy volunteers, aged 58–80 years old, mean age 72.6 ± 2.8 years.

We examined three groups of patients. Blood samples were drawn for the determination of plasma αANP before, 7 days and 30 days after pacemaker implantation, and only once in the control group. αANP concentration of the blood was measured by double-antibody radioimmunoassay kit (Human αANP-RIA system RPA 512, Amersham) [13].

Creatinine clearance was analyzed with Jaffe's calorimetric and kinetic test. Creatinine, when treated with picric acid in alkaline solution, forms a coloured complex. Increase in absorption was measured at 500 nm, which is proportional to creatinine concentration in material. We analyzed samples of plasma and urine from 24-hour urine collection. Reference values for daily creatinine excretion were 1.0–2.5 g/24 h, and for creatinine clearance 75–110 ml/min. We used Technicon Ra 1000 automated analyzer for measurements [14].

Results

In patients before pacemaker implantation, blood concentration of ANP achieved its highest level in group I (168.6 ± 81.9 pg/1000 μL) and was statistically higher ($p < 0.05$) compared to the control group III (47.6 ± 12.9 pg/1000 μL). In group II, ANP plasma level was 134.9 ± 83.1 pg/1000 μL (Fig. 1). In patients with an implanted pacemaker in group I, blood concentration of ANP decreased significantly ($p < 0.05$) to 118.0 ± 61.1 pg/1000 μL 7 days after implantation and to 121.4 ± 71.9 pg/1000 μL at 30 days (Fig. 1). In group II, ANP levels decreased

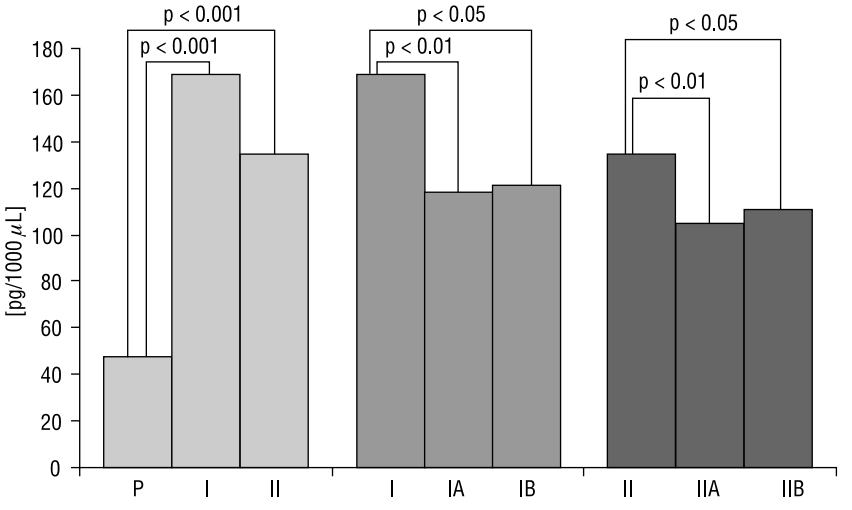

Figure 1. Plasma concentration of atriall natriuretic peptide; P — control group, I — VVI group before pacing, II — DDD/VDD group before pacing, IA — VVI group 7 days after implantation, IB — VVI group 30 days after implantation, IIA — DDD/VDD group 7 days after implantation, IIB — DDD/VDD group 30 days after implantation.

significantly ($p < 0.05$) to 105.0 ± 57.1 pg/1000 μL at 7 days and to 110.8 ± 53.3 pg/1000 μL at 30 days after pacemaker implantation (Fig. 1).

In patients before pacemaker implantation, urine creatinine clearance based on measurement of 24-hour urine reached its peak value in the control group III (96.4 ± 35.8 ml/min) and was significantly higher ($p < 0.05$) than in group I (72.1 ± 19.3 ml/ /min) and group II (82.3 ± 15.9 ml/min) (Fig. 2).

After pacemaker implantation, in group I, creatinine clearance increased significantly ($p < 0.05$) to 76.1 ± 17.8 ml/min at 7 days and to 85.0 ± ± 17.9 ml/min at 30 days after the procedure (Fig. 2). In group II, creatinine clearance increased significantly ($p < 0.05$) to 84.6 ± 13.2 ml/min at 7 days and to 96.9 ± 18.2 ml/min at 30 days after implantation (Fig. 2).

Creatinine concentrations in patients before pacemaker implantation reached the level of 1.19 ± ± 0.43 mg/1000 μL in group I, which was significantly higher ($p < 0.05$) compared to the control group III (0.91 ± 0.17 mg/1000 μL). In group II, before pacemaker implantation, the level of creatinine in blood increased to 1.21 ± 0.24 mg/1000 μL being also statistically higher in comparison to the control group (Fig. 3).

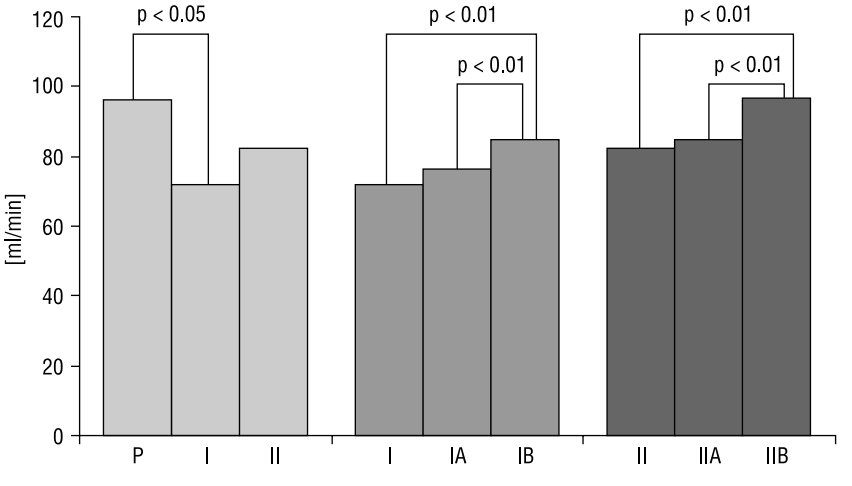

Figure 2. Creatinine clearance level; P — control group, I — VVI group before pacing, II — DDD/VDD group before pacing, IA — VVI group 7 days after implantation, IB — VVI group 30 days after implantation, IIA — DDD/VDD group 7 days after implantation, IIB — DDD/VDD group 30 days after implantation.

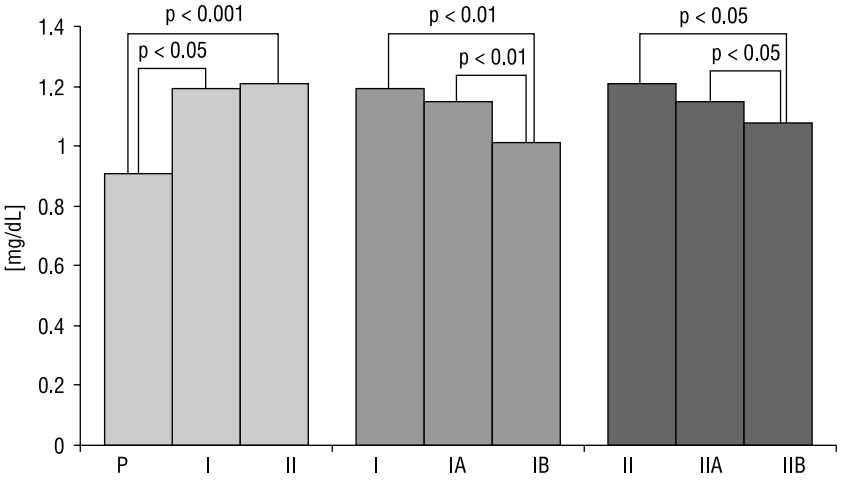

Figure 3. Blood creatinine concentration; P — control group, I — VVI group before pacing, II — DDD/VDD group before pacing, IA — VVI group 7 days after implantation, IB — VVI group 30 days after implantation, IIA — DDD/VDD group 7 days after implantation, IIB — DDD/VDD group 30 days after implantation.

In group I, in patients with a permanent pacemaker, blood creatinine concentration decreased to 1.15 ± 0.30 mg/1000 μL 7 days after the procedure and to 1.01 ± 0.21 mg/1000 μL 30 days after implantation, which was significantly lower ($p < 0.05$) than blood creatinine levels in this group before implantation of the pacemaker (Fig. 3). In group II, in patients after implantation of the pacemaker, creatinine concentration in blood samples decreased after 7 days to 1.15 ± 0.24 mg/1000 μL and at 30 days to 1.08 ± 0.27 mg/1000 μL (Fig. 3).

Moreover, we observed a positive correlation between plasma ANP and the increase in creatinine clearance in groups I and II. This correlation was found to be $r = 0.301$ ($p < 0.05$).

Discussion

All data obtained from patients qualified for permanent pacemaker implantation indicate an increase in atrial natriuretic peptide secretion. Compared to the control group, blood ANP levels were higher in both groups of patients.

At follow-up, ANP levels decreased in patients with VVI mode pacemakers. Seven days after implantation, ANP reached its mean and at 30 days, its lowest value.

In patients after implantation of DDD/VDD mode pacemakers, ANP blood concentration decreased during follow-up. The lowest value was attained 7 days after the procedure and increased slightly after 30 days.

In patients with VVI mode pacemakers compared to the group with DDD/VDD pacemakers, initial blood concentration of ANP was higher. We also noticed higher dynamics of blood ANP decrease after the implantation in this group of patients, with the lowest value at 7 days after the procedure.

Initially, in all patients before implantation of permanent stimulating systems, renal function parameters (plasma creatinine concentration and creatinine clearance) were significantly worse in comparison to the control group.

In both groups of patients, with VVI and with DDD/VDD mode pacemakers, during 30-day follow-up, there was a significant improvement of renal function expressed as increased creatinine clearance and lower blood creatinine concentration. Changes in basic, measurable renal function parameters in patients with different stimulating system modes are strongly dependent on renal activity of natriuretic peptides. Natriuretic peptides affecting kidney function increase glomerular filtration and inhibit sodium reabsorption in the collecting tubuli [15, 16].

Initial parameters of renal function during different types of stimulation have been investigated in animal experiments and clinical trials. Yoneda et al. [17] reported that during ventricular stimulation in anesthetized dogs (pacing with increasing frequencies 200–250 beats/min), no significant increase of maximal urinary excretion of sodium was observed. Seymour et al. [18] in their experimental studies in conscious, unstressed dogs observed a decrease of renal filtration from 168 ± 19 ml/min to 96 ± 9 ml/min and reduced sodium excretion from 36 ± 5 to 10 ± 4 mEq/d, after rapid ventricular pacing (260 beats/min). In subsequent experiments,

Williams et al. [19] observed that rapid ventricular pacing produced a fall in both plasma vasopressin and plasma renin activity, and a rise in urine flow rate associated with an increase in free water but not sodium clearance.

Analysis of renal function parameters in the three groups of patients revealed that creatinine clearance increased, whereas plasma creatinine concentration decreased, after implantation of a permanent pacemaker.

In conclusion, in patients with permanent stimulation, blood ANP levels decrease after the implantation, but greater dynamics of this fall can be observed in the group with ventricular mode pacemakers. Therefore, pacemaker implantation in patients with advanced atrioventricular conduction disturbances significantly influences the improvement of selected renal function parameters. Numerous correlations between ANP values and renal function parameters confirm this fact.

Permanent pacemaker implantation in patients with advanced atrioventricular conduction disturbances, apart from direct therapeutic improvement, influences indices of long-term cardiovascular recovery. This is expressed as a decrease in ANP blood concentration and improvement in basic parameters of renal function.

Conclusions

1. In patients with severe atrioventricular conduction disturbances and permanent pacing, plasma ANP concentration decreases.
2. During follow-up, in patients after pacemaker implantation, there are numerous correlations between blood ANP levels and renal function parameters. These correlations are found mainly in patients with DDD/VDD mode.
3. In patients with advanced atrioventricular conduction disturbances, after pacemaker implantation, there is permanent improvement of renal function parameters.
4. Atrial natriuretic peptide can be used to monitor changes in the cardiovascular system and renal function after pacemaker implantation.

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