Facilitating influence of procainamide on conversion of atrial flutter by rapid atrial pacing

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In a prospective, double-blind, randomized, placebo-controlled study we investigated the facilitating influence of intravenous procainamide on conversion of atrial flutter by rapid atrial pacing.

Fifty consecutive patients with spontaneous sustained atrial flutter were 1:1 randomized into two homogenous groups: group A received 10 mg kg⁻¹ procainamide intravenously, group B placebo. After infusion there was a significant (P<0.01) lengthening of the flutter cycle with respect to baseline in group A, exceeding the flutter cycle length of the control group (P<0.05). The overall success rate of rapid atrial pacing in restoring sinus rhythm was significantly higher after pre-treatment with procainamide compared to placebo (100% vs 76%; P<0.05): 20 patients of group A reverted immediately after pacing to sinus rhythm, the remaining five after a brief episode of atrial fibrillation. In the placebo group, 16 patients showed a prompt conversion to sinus rhythm and three after transient atrial fibrillation. In the remaining six patients, due to sustained pacing-induced atrial fibrillation, direct current cardioversion was necessary. After administration of procainamide a less aggressive stimulation protocol with significantly (P<0.01) longer paced cycles to interrupt atrial flutter was achievable.

In conclusion, intravenous procainamide augments the efficacy of atrial pacing to convert atrial flutter to sinus rhythm.

Key Words: Atrial flutter, pacing, procainamide.

Introduction

Since its first description in 1967[1] transvenous rapid atrial pacing has become an accepted simple and safe method for the prompt termination of atrial flutter. The reported rate of successful restoration of sinus rhythm is variable. Whereas in patients suffering from this arrhythmia in the early phase after cardiac surgery sinus rhythm could be restored in almost all cases[2], the efficacy of this therapeutic option in other populations has been limited and a variable rate of pacing-induced sustained atrial fibrillation has been reported[3-7]. Thus, if sinus rhythm is the desired endpoint, further therapy such as direct current cardioversion may still be required. There have been many studies[6-13] questioning whether the acute administration of a type IA antiarrhythmic agent could increase the success rate of atrial pacing in restoring sinus rhythm, with controversial results[6,7,12]. Controlled trials and definitive studies on this topic in a larger cohort of patients are surprisingly scarce. So we performed a prospective, randomized, placebo-controlled, double-blind study in 50 patients to assess the value of acute intravenous procainamide in facilitating the conversion of atrial flutter to sinus rhythm by rapid atrial pacing.

Methods

Study population

Consecutive patients with sustained atrial flutter who were referred to our institution for conversion of the arrhythmia were included in the study if they fulfilled the following criteria: informed consent to the study protocol, spontaneously occurring stable atrial flutter of the common type (continuous sawtoothed flutter waves with a rapid positive and a slow negative deflection in lead II, III, aVF)[14], duration of the arrhythmia ≥ 24 h, documented sinus rhythm ≤ 3 months. Exclusion criteria were: New York Heart Association functional class of heart failure IV, open heart surgery ≤ 1 month previously, systolic blood pressure < 100 mmHg, bundle branch block, ingestion of class I antiarrhythmic drugs or sotalol ≤ 24 h or ingestion of amiodarone ≤ 3 months previously.

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Study protocol

Before the commencement of the study, routine demographic data, patients' history, clinical evaluation, a surface ECG (measurements of QRS duration, atrial and ventricular rate, and the ratio of atrioventricular conduction) and a M mode echocardiogram (determination of left atrial size by measuring the distance between the left atrial wall and the posterior aortic root) were obtained. A 6 F quadripolar electrode catheter was inserted percutaneously through an antecubital or femoral vein by investigator I (J.J.) and positioned against the lateral wall of the high right atrium. The mean atrial cycle length was measured by intraatrial ECG recordings. Then all patients were 1:1 randomized into two groups: group A received 10 mg . kg⁻¹ body weight procainamide in 250 ml 5% dextrose within 15 min intravenously, group B received only 5% dextrose solution. Fifteen minutes after completion of the infusion blood pressure measurement, surface ECG and intraatrial ECG-recordings were repeated. Then rapid atrial pacing was performed by investigator II (A.H.) who had no information concerning drug administration. Bipolar atrial pacing at twice the stimulus threshold (pulse duration: 1·5 ms) was performed in the high right atrium using a programmable stimulator (UHS 20, Biotronik, Berlin, Germany). Pacing was initiated at a cycle length 10 ms shorter than the atrial flutter cycle length at the end of infusion and continued for ≥15 s after establishing atrial capture. On cessation of pacing, if atrial flutter persisted, the pacing cycle length was decreased stepwise by 10 ms and pacing was again performed in the same manner until termination of atrial flutter or induction of atrial fibrillation. If atrial flutter was not interrupted by pacing the high right atrium, pacing was performed from other sites (low right atrium, medium paraseptal or posterior right atrium). During stimulation simultaneous recordings of 5 surface electrocardiographic and 1 intraatrial lead were registered at a paper speed of 50 mm . s⁻¹.

Statistical analysis

Values are reported as mean ± SD. Comparison between groups was performed by Student’s t-test for continuous variables with normal distribution, non-parametric analysis was performed by Mann–Whitney U-test. Differences in values before and after treatment within the same group were evaluated with Student’s t-test for paired data. Dichotomous variables were compared by using chi-square analysis. The level of statistical significance was set at a P-value <0·05.

Results

Fifty out of 120 consecutive patients who were referred to our laboratory for pace termination of atrial flutter were eligible for the study. They were 1:1 randomized in two groups, homogenous for age, gender, duration of atrial flutter, underlying heart disease, diameter of the left atrium, cycle length of atrial flutter and all other acquired data (Table 1).

There was a significant (P<0·01) lengthening of the flutter cycle with respect to baseline in patients after administration of procainamide. After infusion they revealed a significantly longer flutter cycle length than patients in the control group (Table 2). After drug administration a slight decrease of the atrioventricular ratio was registered, but no abrupt increase of the ventricular rate due to changes of atrioventricular conduction was observed (Table 3). Procainamide led to a significant decrease of systolic and diastolic blood pressure without causing any major symptoms or necessitating discontinuation of drug delivery (Table 3). Reversion to sinus rhythm following rapid atrial pacing occurred immediately in 20 patients in group A and after a brief (3 s to 10 min) episode of atrial fibrillation in the remaining five patients. In the control group, 16 patients reverted to sinus rhythm immediately after pacing and three further patients after transient atrial fibrillation (10 s to 2 h). Six patients in group B and no patient in group A persisted in atrial fibrillation after atrial pacing and were referred to successful direct current
cardioversion the following day (Fig 1). Thus, the overall success rate of rapid atrial pacing in restoring sinus rhythm was significantly higher after pre-treatment with acute intravenous procainamide (100% vs 76%; P<0.05). The minimal paced cycle length needed to interrupt atrial flutter was significantly longer in patients receiving procainamide than in those without adjunctive therapy. There was no significant difference concerning the minimal paced cycle length assessed as percentage of the atrial flutter cycle length at the beginning of pacing in both groups (Table 4). Six patients of group A and eight patients of group B (P=ns) required pacing from sites other than the high right atrium. The pacing site did not influence the rate of pacing induced atrial fibrillation. There were no significant pauses observed in either group before the first sinus beat was registered after cessation of pacing (group A: 1.4 ± 0.8 s; group B: 1.1 ± 0.4 s; P=ns).

Discussion

In recent years several investigations have been published using different study designs to analyse a potential benefit of pre-treatment with class I antiarrhythmic drugs on the efficacy of rapid atrial pacing in converting atrial flutter to sinus rhythm. Most former studies included only smaller patient populations and their results were not uniform. Intravenously given disopyramide in patients with induced atrial flutter of short duration[10] or intravenous procainamide in spontaneously occurring atrial flutter[9] resulted in a high success rate of rapid atrial pacing in those patients in whom pacing failed before drug administration. In contrast, a recently published study showed no beneficial effect of intravenous procainamide after a primary unsuccessful pacing attempt[6]. Retrospective non-randomized studies showed a higher success rate of overdrive pacing in patients with spontaneous atrial flutter after acute intravenous application of disopyramide or procainamide[9] and flecainide given orally or intravenously[4,19] in comparison to patients not receiving antiarrhythmic drugs. Two prospective[6,7] and two retrospective[4,12] studies showed no influence of previous long-term administration of antiarrhythmic drugs on the pacing result. In a prospective study in a small cohort of patients[4,13], pre-treatment with intravenous disopyramide significantly augmented the rate of sinus rhythm after rapid pacing for atrial flutter in comparison to a placebo group, whereas the same drug given orally during several days before pacing showed only an insignificant increase of the success rate. The results of a recently published double-blind, randomized, placebo-controlled trial[12] showed that the use of intravenous ibutilide, a class III antiarrhythmic agent, enhances the termination of atrial flutter by atrial overdrive pacing. In this study a further but non-randomized group of patients received procainamide intravenously. It was shown that both ibutilide and procainamide facilitated pacing induced termination of atrial flutter.

Our prospective, randomized, placebo-controlled study demonstrated in a large cohort of patients the facilitating influence of an acute pretreatment with intravenous procainamide on the efficacy of rapid atrial pacing in restoring sinus rhythm in sustained atrial flutter. The conversion rate in our control group is well within the range of the reported success rate of former studies dealing with similar patients[8,11], whereas pacing after intravenous administration of procainamide resulted in all our patients, directly or after transient atrial fibrillation, in sinus rhythm. Experimental[9,17] and clinical studies[11,18,19] have shown that class IA drugs prolong the atrial flutter cycle length mainly by reducing conduction velocity within the reentry circuit. The resulting wider excitable gap allows the stimulus to penetrate the reentry circuit more easily[9,19]. The relationship between paced and spontaneous cycles was not affected by the drug in our investigation. But as former studies[6,11,13,19] have shown, due to the significant longer atrial flutter cycle length after infusion of

Table 3 Effects of procainamide on surface ECG and blood pressure

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After procainamide</th>
<th>P</th>
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<tbody>
<tr>
<td>Atrial rate</td>
<td>262 ± 37</td>
<td>221 ± 29</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AV ratio</td>
<td>2.8 ± 0.9</td>
<td>2.5 ± 0.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Ventricular rate</td>
<td>101 ± 31</td>
<td>96 ± 26</td>
<td>ns</td>
</tr>
<tr>
<td>RR systolic</td>
<td>136 ± 23</td>
<td>117 ± 21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RR diastolic</td>
<td>85 ± 12</td>
<td>78 ± 12</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

AV=atrioventricular, RR=Riva Rocci blood pressure, ns=not significant.

Figure 1 Results of rapid atrial pacing. ■=immediate sinus rhythm; □=sinus rhythm after atrial fibrillation; ▪=persistent atrial fibrillation.

Table 4 Effects of procainamide on pacing intervals

<table>
<thead>
<tr>
<th></th>
<th>Group A (Procainamide)</th>
<th>Group B (Placebo)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL (ms)</td>
<td>277 ± 40</td>
<td>247 ± 40</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PCL (ms)</td>
<td>198 ± 19</td>
<td>175 ± 22</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>PCL as % of CL</td>
<td>72 ± 8</td>
<td>71 ± 6</td>
<td>ns</td>
</tr>
</tbody>
</table>

CL=cycle length 15 min after infusion, PCL=minimal paced cycle length, ns=not significant.
procainamide, atrial stimulation could be performed at a rate less likely to precipitate atrial fibrillation. The well known efficacy of intravenous procainamide in converting acute atrial fibrillation to sinus rhythm could be a further possible explanation for the beneficial effects observed in our study.

In conclusion, the adjunctive therapy of intravenous procainamide is a safe method of augmenting the efficacy of transvenous rapid atrial pacing in restoring sinus rhythm in patients with sustained atrial flutter. This therapy can be recommended for clinical use in an appropriate patient population to reduce the incidence of persistent pacing induced atrial fibrillation which might need further treatment, such as direct current cardioversion.

References