A Study of the Effect of Procaine Amide Hydrochloride in Supraventricular Arrhythmias

By Malcolm C. McCord, M.D., and James T. Taguchi, M.D.

The effect of the intravenous administration of procaine amide in 25 patients with supraventricular arrhythmias is reported. The data, including six conversions of auricular fibrillation, indicate a pronounced effect of this drug on the auricles as well as on the heart as a whole. Special attention is directed to the finding of frequent and undesirable electrocardiographic and hypotensive effects of this drug.

Procaine amide hydrochloride has been reported to be of value in the management of cardiac arrhythmias of ventricular origin. It has been considered as having little effect on the auricles. The present report describes the results of the intravenous administration of procaine amide in 25 patients with cardiac arrhythmias of supraventricular origin.

Material and Methods

The effect of procaine amide on 25 patients with supraventricular arrhythmias was studied. There were 16 patients with auricular fibrillation, 4 with auricular flutter, 3 with paroxysmal supraventricular tachycardia, and 2 with frequent premature auricular contractions.

All of the cases were men in the older age group with an age range of 45 to 77 years. The majority had arteriosclerotic heart disease, hypertensive heart disease, or both. Three patients had rheumatic valvular heart disease; 2, aortic insufficiency due to syphilitic aortitis; and one each, pericarditis, cor pulmonale, and thyrotoxicosis. In 2 cases there was no evidence of heart disease.

The drug, which comes in 10 cc. vials, was diluted to 30 cc. with normal saline and administered intravenously in all cases. The dose of procaine amide given intravenously ranged from 300 mg. to 2000 mg. or from 3 to 33.3 mg. per Kg. of body weight. The rate of administration varied from 50 to 100 mg. per minute. Of 27 administrations 22 were given at the rate of 50 mg. per minute.

Additional oral doses were given in only 6 cases. The oral dosage varied from 0.5 Gm. to 1.5 Gm. every four hours.

Electrocardiographic control was maintained continuously during and for variable periods following administration. Lead II was usually employed but occasionally precordial or esophageal leads were obtained in an attempt to accentuate the auricular complexes. Where possible, auricular and ventricular rates, P-R, QRS, and Q-T intervals were measured. Pertinent changes of the P or f waves, QRS complexes, S-T segments, and T waves were carefully noted.

Blood pressure determinations were made frequently during and following administration in most cases and subjective symptoms were recorded.

Results

Auricular Fibrillation

Of 16 patients (table 1) with auricular fibrillation to whom procaine amide was administered intravenously, restoration to normal sinus rhythm was effected in 6 (cases 1, 2, 3, 4, 5, 6a). However, in one patient (case 6a) this was of momentary duration and could not be maintained or re-established. To date prophylactic oral administration was necessary in only one case in whom auricular fibrillation recurred. In this patient reversion to sinus rhythm followed 1 Gm. of procaine amide orally every four hours for six doses and was maintained by 0.5 Gm. twice a day.

Of the 16 patients, 7 (cases 1, 2, 3, 4, 5, 8, 15) could be considered to have developed
### Table 1.—Clinical and Electrocardiographic Data in 25 Patients with Supraventricular Arrhythmias

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Type of arrhythmia</th>
<th>Duration of arrhythmia</th>
<th>Digitalization</th>
<th>Total dose of procaaine amide (mg.)</th>
<th>Rate mg. per min. l. V.</th>
<th>Effect of therapy on auricular mechanisms</th>
<th>Effect of therapy on ventricular mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aur. fib.</td>
<td>3 hrs.</td>
<td>0</td>
<td>500 6.3 50</td>
<td></td>
<td>Conversion to sinus tachycardia</td>
<td>Marked tachycardia</td>
</tr>
<tr>
<td>2</td>
<td>Aur. fib.</td>
<td>2 mo.</td>
<td>+</td>
<td>650 10.0 50</td>
<td></td>
<td>Conversion to sinus rhythm</td>
<td>Elimination of occasional premature ventricular systoles</td>
</tr>
<tr>
<td>3</td>
<td>Aur. fib.</td>
<td>4 days</td>
<td>0</td>
<td>700 8.5 50</td>
<td></td>
<td>Conversion to sinus rhythm</td>
<td>Intraventricular block</td>
</tr>
<tr>
<td>4</td>
<td>Aur. fib.</td>
<td>3 days</td>
<td>+</td>
<td>750 10.0 50</td>
<td></td>
<td>Conversion to auricular flutter then to sinus rhythm</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Aur. fib.</td>
<td>10 days</td>
<td>+</td>
<td>1000 13.0 50</td>
<td></td>
<td>Conversion to auricular flutter then to sinus rhythm</td>
<td></td>
</tr>
<tr>
<td>6a</td>
<td>Aur. fib.</td>
<td>15 years</td>
<td>0</td>
<td>1000 10.3 100</td>
<td></td>
<td>Temporary conversion to aur. flutter then sinus rhythm</td>
<td>Short runs of ventricular tachycardia</td>
</tr>
<tr>
<td>6b</td>
<td>Aur. fib.</td>
<td>15 years</td>
<td>0</td>
<td>1000 10.3 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td>Short runs of ventricular tachycardia</td>
</tr>
<tr>
<td>7</td>
<td>Aur. fib.</td>
<td>3 years</td>
<td>+</td>
<td>400 7.0 50</td>
<td></td>
<td>No detectable change</td>
<td>Intermittent right bundle branch block</td>
</tr>
<tr>
<td>8</td>
<td>Aur. fib.</td>
<td>48 hrs.</td>
<td>0</td>
<td>1000 9.9 50</td>
<td></td>
<td>No detectable change</td>
<td>Marked tachycardia</td>
</tr>
<tr>
<td>9</td>
<td>Aur. fib.</td>
<td>Long standing</td>
<td>+</td>
<td>1000 10.0 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Aur. fib.</td>
<td>Long standing</td>
<td>+</td>
<td>1000 15.0 50</td>
<td></td>
<td>No detectable change</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Aur. fib.</td>
<td>Long standing</td>
<td>+</td>
<td>1000 14.5 50</td>
<td></td>
<td>No detectable change</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Aur. fib.</td>
<td>Long standing</td>
<td>+</td>
<td>1000 15.2 50</td>
<td></td>
<td>No significant change</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Aur. fib.</td>
<td>4 years</td>
<td>+</td>
<td>1000 17.5 50</td>
<td></td>
<td>No detectable change</td>
<td>Elimination of frequent premature ventricular systoles</td>
</tr>
<tr>
<td>14</td>
<td>Aur. fib.</td>
<td>2 years</td>
<td>0</td>
<td>1800 31.9 75</td>
<td></td>
<td>Slowing of auricular rate</td>
<td>Runs of ventricular tachycardia and intraventricular block</td>
</tr>
<tr>
<td>15</td>
<td>Aur. fib.</td>
<td>1 mo.</td>
<td>+</td>
<td>2000 20.1 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Aur. fib.</td>
<td>5 years</td>
<td>+</td>
<td>2000 23.0 75</td>
<td></td>
<td>No detectable change</td>
<td>Electrical alternans</td>
</tr>
<tr>
<td>17</td>
<td>Aur. flut.</td>
<td>2 days</td>
<td>+</td>
<td>500 8.1 50</td>
<td></td>
<td>No detectable change</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Aur. flut.</td>
<td>2 days</td>
<td>+</td>
<td>1000 15.5 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td></td>
</tr>
<tr>
<td>19a</td>
<td>Aur. flut.</td>
<td>3 days</td>
<td>0</td>
<td>1000 17.0 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td></td>
</tr>
<tr>
<td>19b</td>
<td>Aur. flut.</td>
<td>4 days</td>
<td>0</td>
<td>1000 17.0 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Aur. flut.</td>
<td>2 mo.</td>
<td>+</td>
<td>1500 18.3 50</td>
<td></td>
<td>Slowing of auricular rate</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Nodal tachy.</td>
<td>1 day</td>
<td>+</td>
<td>300 3.3 50</td>
<td></td>
<td>Conversion to sinus rhythm</td>
<td>Left bundle branch block</td>
</tr>
<tr>
<td>22</td>
<td>Aur. tachy.</td>
<td>2 days</td>
<td>+</td>
<td>1000 20.0 50</td>
<td></td>
<td>Conversion to sinus tachycardia</td>
<td>Marked tachycardia</td>
</tr>
<tr>
<td>23</td>
<td>Aur. tachy.</td>
<td>2 days</td>
<td>+</td>
<td>2000 33.3 80</td>
<td></td>
<td>Conversion to sinus rhythm</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>Pre. aur. syst.</td>
<td>Unknown</td>
<td>0</td>
<td>650 9.3 50</td>
<td></td>
<td>Elimination of pre. aur. syst.</td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>Pre. aur. syst.</td>
<td>3 days</td>
<td>+</td>
<td>1000 12.2 50</td>
<td></td>
<td>Decrease in frequency of pre. aur. syst.</td>
<td></td>
</tr>
</tbody>
</table>

* More extensive tabular data concerning the electrocardiographic changes will be included with reprints of this article.
auricular fibrillation recently, with the onset of fibrillation occurring a few hours to a maximum of two months prior to treatment. The 5 patients satisfactorily converted to and maintained in normal sinus rhythm fell into this group. The remaining 2 patients were subsequently treated with quinidine and one patient converted to normal sinus rhythm. Of the 16 patients 9 could be classified as having chronic auricular fibrillation of several years duration. Further attempts at conversion with other drugs were not undertaken in this group.

in which conversion resulted, 3 (cases 4, 5, 6a) developed slowing of the auricular rate and subsequently auricular flutter prior to conversion to sinus rhythm (figs. 1 and 2). In those patients in whom arrhythmia was not abolished, 3 (cases 9, 14, 15) showed measurable slowing of the auricular rate with coarsening and widening of the f waves approaching flutter in configuration, as shown by figure 3. In these 3 patients decreases in the auricular rates from 400 to 250, 520 to 320, and 540 to 275, respectively, occurred. The auricular rates were calculated over a 12 second period and although the finer fibrillatory waves of the control electrocardiogram could not be

The dosage of procaine amide given intravenously in the 6 patients in whom auricular fibrillation was converted to sinus rhythm varied from 6.3 mg. per Kg. of body weight to 13 mg. per Kg. of body weight. Conversion occurred during administration in 4 cases, and within 10 minutes after completion of injection in the other 2. The cases which were not converted received from 7 to 31.9 mg. per Kg. of body weight.

From an electrocardiographic standpoint there could be no doubt that procaine amide had a definite effect on the auricles, whether conversion occurred or not. Of the 6 patients accurately measured, the subsequent changes in rates were easily measurable and significant.

In 10 cases the fibrillatory waves were either of such low amplitude or so indistinguishable that reliable conclusions could not be drawn.

During the administration of procaine amide hydrochloride an increase in the ventricular rate while the auricles were still fibrillating was a constant and at times striking finding in all 16 patients. This was more noticeable in those in whom digitalization was either inadequate or had not been undertaken prior to treatment. In this group, which included 5 patients (cases 1, 3, 6, 8, 14), the maximum increase in ven-
tricular rate was 20, 10, 60, 60, and 60 beats per minute, respectively, with an average increase in rate of 42 beats per minute. The maximal increase in ventricular rate of the 11 patients adequately digitalized varied from 12 to 35 beats per minute with an average increase of 19.5 beats per minute. The increase in the ventricular rate was gradual and maximal usually at the end of administration. Of the cases converted to normal sinus rhythm 3 patients had not had adequate digitalization.

![Graphs](image)

**Fig. 3.** Case 15, lead V1. A. Prior to administration of procaine amide. B. After 400 mg. of procaine amide intravenously in eight minutes. C. After 2000 mg. of procaine amide intravenously in 40 minutes.

**Auricular Flutter**

There were 4 patients with auricular flutter (cases 17, 18, 19a, b, 20) who were treated with intravenous procaine amide but in no instance was the arrhythmia abolished.

In all 4 patients, however, measurements of the auricular rate showed gradual slowing of the flutter waves during the intravenous administration of procaine amide with maximal decreases of 40, 80, 75, and 81 beats per minute. There was a slower gradual rise in auricular rate promptly after stopping administration. This was well demonstrated by case 20, in which 1500 mg. was given in 30 minutes, and a gradual slowing from the control flutter rate of 285 per minute to 204 per minute at the end of injection resulted. A slower gradual rise to 230 in 45 minutes was recorded, but in a 12 hour follow-up the auricular rate was still 260 or 25 beats slower than the control rate. The easily measurable auricular rates in flutter thus appeared to be a very sensitive indicator of speed and duration of action of this drug.

In all 4 patients the auricular-ventricular ratio decreased, although not always accompanied by an increase in ventricular rate because of the associated slowing of the auricular rate.

**Paroxysmal Supraventricular Tachycardia**

All 3 patients with paroxysmal supraventricular tachycardias (cases 21, 22, 23) were converted to sinus rhythm. There were 2 patients with auricular tachycardia and one with type II nodal tachycardia. These were all of recent origin. Only in case 23 was procaine amide, given orally, necessary to treat the paroxysms of auricular tachycardia which recurred 12 hours after therapy.

**Premature Auricular Systoles**

There were 2 patients (cases 24, 25) with frequent auricular premature systoles who were treated with intravenous procaine amide. The premature contractions were eliminated in one patient and decreased in frequency in another.

**Electrocardiographic Changes**

P-R intervals were measurable in 11 patients after conversion of the arrhythmia. In only 2 patients was the P-R interval significantly prolonged, with P-R interval measurements of 0.22 second in each instance. However, in one of these first degree A-V block was present before treatment.

In 24 of 25 cases widening of the QRS interval could be demonstrated. This was usually also maximal at the end of injection. All QRS intervals were within normal limits of 0.10 second or less in the control leads. There were 5 patients who showed widening of the QRS interval of from 0.12 to 0.14 second. However, only 2 patients could be considered to have shown a 50 per cent increase in QRS time.
QRS changes consisted chiefly of widening and slurring except in case 7 in which right bundle branch block developed and in case 21 in which left bundle branch block developed.

Q-T intervals were usually more difficult to estimate with accuracy because of the underlying arrhythmia and distortion of the baseline. In 13 patients in which measurements were feasible, some prolongation of the Q-T interval was noted in every instance. By the use of the Ashman-Hull tables for determining normal Q-T intervals, all but one patient could be considered to have abnormal Q-T intervals during or immediately following administration of the drug. Only one patient had an abnormal Q-T interval prior to therapy.

S-T segment and T wave changes were on the whole not remarkable except in the 2 patients who developed bundle branch block. There were 6 patients who showed an increase in voltage of the T wave in lead II. Others showed slight flattening of T waves associated with prolongation of the Q-T interval.

The most serious electrocardiographic changes noted were short bursts of paroxysmal ventricular tachycardia. This arrhythmia occurred in 2 patients (cases 6a, b, 14). In case 6a, 1000 mg. or 10.3 mg. per Kg. was administered intravenously at a rate of 100 mg. per minute. Immediately after the injection short bursts of paroxysmal ventricular tachycardia were noted (fig. 4). These continued for 20 minutes with decreasing frequency. Occasional premature ventricular contractions could still be detected 30 minutes later. These findings were reproduced the following day when the same amount of procaine amide was again administered intravenously but at half the previous rate (case 6b). Similar findings were noted in case 14 in which 31.9 mg. per Kg. of body weight was given. Administration was discontinued when a sudden paroxysm of ventricular tachycardia developed. The tachycardia stopped spontaneously in 10 seconds and recurred several times in the next three minutes. In the following 30 minutes only an occasional premature ventricular contraction was seen. As in the previous patient the development of an occasional ventricular premature contraction heralded the onset of ventricular tachycardia and should probably constitute an indication for prompt cessation of administration. It is worth noting that in the latter patient the toxic dose was three times as great in terms of mg. per Kg. of body weight. No subjective symptoms were observed in either patient.

**General Clinical Findings and Dosage**

Blood pressure recordings were made at two minute intervals on 16 patients. Of the 16 patients, 12 showed a slight to moderate drop in systolic pressures and to a lesser degree in diastolic pressures. Four patients (cases 1, 3, 14, 25) could be considered to have a significant fall in blood pressure with at least a 50 mm. lowering of systolic pressure. The changes in blood pressure were noted fairly early during administration of procaine amide. In many cases temporary slowing of the rate of administration was necessary to control the hypotension. No correlation could be made between symptoms and the degree of hypotension.
Subjective symptoms were minimal and consisted of a moderately severe headache in one instance, nausea in another, and a mild sedative effect in four others. Several patients noted a sense of relief at the time of conversion.

No constant correlation could be found between dosages used and electrocardiographic changes, changes in blood pressure, and symptoms. There were as many undesirable changes clinically and electrocardiographically in the 14 patients given from 3.3 to 14.5 mg. per Kg. of body weight as there were in the 11 patients in whom the dosage varied from 15 to 33.3 mg. per Kg. There appeared to be a rather marked variation in individual response or sensitivity to intravenously administered procaine amide.

DISCUSSION

Although the chief action of procaine amide is considered to be limited to the ventricles with little effect on the auricles, this study suggests that procaine amide given intravenously in doses of from 3.3 to 33.3 mg. per Kg. has a pronounced effect on the auricles. This was demonstrated by conversion of auricular fibrillation in 6 patients and of paroxysmal supraventricular tachycardia in 3 patients to normal sinus rhythm and the elimination of frequent premature auricular contractions in one patient. In addition, whenever auricular rates could be calculated, as in the patients with auricular flutter or coarse fibrillation, definite and pronounced slowing of the auricular rate with widening and coarsening of the T waves could be observed whether conversion was achieved or not.

The constant finding of an increase in ventricular rate during administration of procaine amide in patients with auricular fibrillation and a decrease in auricular-ventricular ratio in patients with flutter would suggest an atropine-like action of procaine amide, as has been described with quinidine. However, this could also be attributed to the slowing of the auricular rate.

Other electrocardiographic changes indicative of the effect of this drug on the myocardium were quite common. These consisted of widening of the QRS and Q-T interval and minor changes of the S-T segment and T wave. Mark and associates, however, reported only a 10 per cent incidence of such findings.

That this drug should be used intravenously with caution was evidenced by "toxic" or undesirable changes which occurred in 10 instances or in 8 of the 25 patients treated with intravenous procaine amide. These consisted of two instances of short paroxysms of ventricular tachycardia; three instances in which the QRS widened 50 per cent or a bundle branch block developed; one instance in which electrical alternans developed, and four instances in which the degree of hypotension was significant. In addition a pronounced increase in ventricular rate occurred in 3 patients. In many patients this would be an undesirable effect but probably could be prevented by adequate digitalization.

Although hypotensive effects have been described, the other changes have not as yet been reported and deserve serious consideration when the drug is administered intravenously. Fortunately none of the changes described above proved to be of serious clinical significance. Slower rates of administration and smaller doses might have prevented some of these changes. However, it would appear that electrocardiographic control and frequent determinations of the blood pressure would be of utmost importance during the intravenous administration of procaine amide.

SUMMARY

1. The effect of the intravenous administration of procaine amide in 25 patients with supraventricular arrhythmias was studied.

2. A pronounced effect on the auricles was demonstrated by the following findings: (a) conversion to normal sinus rhythm of 6 cases of auricular fibrillation, and 3 cases of supraventricular tachycardia; (b) elimination of premature auricular contractions in one patient; (c) marked slowing and changes in the configuration of the auricular waves in 7 other patients.

3. In 4 patients with auricular flutter conversion to normal sinus rhythm was not achieved.

4. Other electrocardiographic evidence of
the effect of this drug on the heart was demonstrated in nearly all patients by mild to marked degrees of QRS and Q-T interval prolongation.

5. An increase in ventricular rate in auricular fibrillation and a decrease in auricular-ventricular ratio in auricular flutter was a constant finding.

6. "Toxic" or undesirable changes were observed in 8 patients. Two patients with short paroxysms of ventricular tachycardia deserve special emphasis.

7. Considerable variation in individual sensitivity to procaine amide and the frequent unfavorable manifestations seen make necessary careful electrocardiographic and blood pressure control during intravenous administration of this drug.

Acknowledgment

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References


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