

# Pharmacodynamics of Intravenous Procainamide as Used During Acute Electropharmacologic Testing

FRED MORADY, MD, WILLIAM H. KOU, MD, STEPHEN SCHMALTZ, MPH,  
THOMAS ANNESLEY, PhD, MICHAEL DE BUILTEIR, MD, STEVEN D. NELSON, MD,  
and JEFFREY A. KUSHNER, MD

No previous studies have determined the pharmacodynamics of intravenous procainamide when administered in a dose of 15 mg/kg and at a rate of 50 mg/min, as is common practice during electropharmacologic testing. In this study, 30 patients received procainamide in this fashion; the right ventricular effective refractory period and the QRS duration at a ventricular pacing rate of 120/minute were then determined every minute for 20 minutes. Ten patients received no maintenance infusion of procainamide (group A), 10 received a 4 mg/min maintenance infusion (group B) and 10 received an 8 mg/min maintenance infusion (group C). Ten additional patients received no procainamide and served as control subjects (group D). The plasma procainamide concentration was measured at 1, 5, 10, 15 and 20 minutes after the loading dose was administered. A stable plasma procainamide concentration was not present in group A, B, or C until 15 minutes after infusion of the loading dose. The effective refractory period and QRS duration in-

creased compared with baseline at 1 minute, decreased between 1 and 10 minutes and then remained essentially unchanged between 10 and 20 minutes in all 3 treatment groups. Concentration-effect relation was linear in each treatment group. The plasma procainamide concentrations in group C were significantly greater than in group A; however, the effects on refractoriness and QRS duration were similar in both groups. These findings indicate that with a procainamide dosing method commonly used during electropharmacologic testing, the plasma procainamide concentration decreases significantly during the first 15 minutes after the loading dose is administered; the effects of procainamide on ventricular refractoriness and conduction parallel the changes in the plasma procainamide concentration; and an 8 mg/min maintenance infusion of procainamide results in higher plasma procainamide concentrations without an associated increase in ventricular refractoriness or slowing of conduction.

(Am J Cardiol 1988;61:93-98)

Intravenous procainamide has been used extensively to suppress the induction of ventricular tachycardia during electropharmacologic testing<sup>1-11</sup>; the most commonly used dose is 1 g or 15 mg/kg administered at a rate of 50 mg/min.<sup>1,3-11</sup> In some electrophysiology laboratories a maintenance infusion of procainamide is not used,<sup>1-4,9-11</sup> whereas in others a continuous maintenance infusion between 2 and 8 mg/min is used.<sup>5-8</sup>

From the Division of Cardiology, the Clinical Research Center and the Departments of Internal Medicine and Pathology, University of Michigan Medical Center, Ann Arbor, Michigan. This work was supported in part by grant 5M01-RR00042-25 from the National Institutes of Health, Bethesda, Maryland. Manuscript received July 21, 1987; revised manuscript received and accepted August 25, 1987.

Address for reprints: Fred Morady, MD, Division of Cardiology, University Hospital, 1500 East Medical Center Drive, UB B1 F245-0022, Ann Arbor, Michigan 48109-0022.

However, no data are available on the electrophysiologic effects of a maintenance infusion of procainamide after the administration of a large loading dose. We determined the acute pharmacodynamics of intravenous procainamide as it is commonly used during electropharmacologic testing.

## Methods

**Study design and rationale:** There were 4 groups of 10 patients each. In 3 of the groups, a 15 mg/kg dose of procainamide was administered at a rate of 50 mg/min. These 3 groups of patients then received either no maintenance infusion of procainamide (group A), a maintenance infusion of 4 mg/min (group B) or a maintenance infusion of 8 mg/min (group C, Table I). The effects of procainamide on right ventricular effective refractory period and QRS duration were determined before and every minute for 20 minutes after the administration of the loading dose of procain-

TABLE I Study Groups

Group	No. of Patients	Procainamide Dose	
		Loading Dose (mg/kg)	Maintenance Infusion (mg/min)
A	10	15	0
B	10	15	4
C	10	15	8
D (control)	10	0	0

amide. Plasma drug concentrations were determined at regular intervals during the 20-minute testing interval. The fourth group of patients (group D) served as a control and received no drug.

QRS duration during ventricular pacing was used as an index of global intraventricular conduction. A pacing rate of 120/min was used to detect procainamide's rate-dependent effects on intraventricular conduction.<sup>12</sup> The testing interval was limited to 20 minutes to minimize patient discomfort, and also because in clinical practice, drug testing with programmed ventricular stimulation is usually accomplished within 20 minutes.<sup>13,14</sup> A loading dose of 15 mg/kg at a rate of 50 mg/min was used in this study because procainamide commonly has been administered in this fashion in clinical practice during electrophysiologic testing.<sup>1,3-11</sup> Ideal body weight was used to calculate the actual procainamide dose because procainamide does not distribute acutely to adipose tissue.<sup>13</sup> The infusion rates of 0, 4 and 8 mg/min were chosen to represent the usual range of infusion rates used in clinical practice. A control group was included in the study design to ascertain whether ventricular refractoriness and QRS duration change over time in the absence of drug.

**Characteristics of subjects:** The subjects were recruited from a pool of patients who underwent an electrophysiologic study that was clinically indicated. Exclusion criteria included an elevated serum creatinine concentration (>1.1 mg/dl), a systolic blood pressure <100 mm Hg or the previous administration of any antiarrhythmic drug during the electrophysiologic study. In addition, patients were excluded if the onset or termination of the QRS complexes during ventricular pacing was not well demarcated in any of the frontal plane leads.

There were 21 men and 19 women, and their mean age was  $54 \pm 16$  years (mean  $\pm$  standard deviation). Twenty patients had coronary artery disease, 5 had a dilated cardiomyopathy, 2 had mitral valve prolapse, 2 had a hypertrophic cardiomyopathy and 11 had no structural heart disease. The mean serum creatinine concentration was  $1.0 \pm 0.1$  mg/dl. There were no significant differences between the 4 groups of patients with regard to age, type of underlying heart disease, left ventricular ejection fraction, ideal body weight or serum creatine concentration.

**Electrophysiologic testing protocol:** Studies were performed in the fasting, unседated state after informed consent was obtained. All electrophysiologic studies were performed at least 5 half-lives after dis-

continuation of antiarrhythmic drug therapy. A quadripolar electrode catheter inserted through a femoral vein was positioned against the right ventricular apex. A stable catheter position with a pacing threshold of <0.6 mA was obtained under fluoroscopic guidance. A 5Fr cannula in a femoral artery was used to continuously monitor the arterial pressure and for drawing blood samples. Leads V<sub>1</sub>, I and III and the intracardiac electrogram recorded at the right ventricular apex were displayed on an oscilloscope and recorded at a paper speed of 25 mm/s on a Siemens Elema Minograf 7 recorder. When ventricular pacing at a rate of 120/min was performed to assess QRS duration, leads I, II, III, aVR, aVL and aVF were recorded at a paper speed of 200 mm/s. A programmable stimulator (Bloom Associates, Ltd.) was used for pacing. The pacing stimuli were twice the diastolic threshold and 2 ms in duration.

**Determination of right ventricular effective refractory period and QRS duration:** The effective refractory period was determined using an 8-beat drive train at a rate of 120/min and a single extrastimulus (S<sub>2</sub>). The intertrain interval was 3 seconds. The extrastimulus was moved closer to the last beat of the drive train (S<sub>1</sub>) in 10-ms steps and the effective refractory period was defined as the longest S<sub>1</sub>S<sub>2</sub> interval that failed to evoke a response. For the first determination of the effective refractory period, the initial S<sub>1</sub>S<sub>2</sub> interval was 350 ms. In subsequent determinations of the effective refractory period, the initial S<sub>1</sub>S<sub>2</sub> interval was always 30 ms beyond the previous effective refractory period. In all patients the effective refractory period was determined in a uniform fashion, with the first S<sub>1</sub>S<sub>2</sub> interval that did not evoke a response being considered the effective refractory period.

QRS duration was measured during ventricular pacing at a rate of 120/min. Measurements were taken from the frontal plane lead with the QRS complexes that had the most well-defined onset and termination. In each patient, all measurements of QRS duration were taken from the same lead. The intra- and interobserver reproducibility in the measurement of QRS duration was >95%.

**Drug testing protocol:** In the baseline state, the right ventricular effective refractory period and QRS duration at a ventricular pacing rate of 120/min were determined 5 times. The means of these 5 determinations were used as the baseline effective refractory period and QRS duration in each patient. Procainamide was then administered intravenously at a dose of 15 mg/kg ideal body weight. Ideal body weight was estimated using the 1983 Metropolitan Life Insurance height and weight table. The infusion rate was 50 mg/min. If the systolic blood pressure decreased to <95 mm Hg during the infusion of the loading dose, the infusion was discontinued and the patient was excluded from the study. Upon completion of administration of the loading dose, group A patients did not receive a maintenance infusion, group B patients received a maintenance infusion of 4 mg/min of procainamide and group C patients received an 8 mg/min infusion. After administration of the loading dose was complet-

**TABLE II Plasma Procainamide Concentrations**

Minute*	Plasma Procainamide Concentration (mg/liter)		
	Group A	Group B	Group C
1	15.6 ± 3.2†	16.1 ± 3.7	17.2 ± 3.9
5	10.1 ± 2.5	10.7 ± 2.3	12.2 ± 2.0
10	8.6 ± 2.2	9.1 ± 1.8	11.2 ± 1.9
15	7.5 ± 1.7	8.4 ± 1.8	10.6 ± 1.6
20	7.0 ± 1.7	8.0 ± 1.8	10.2 ± 1.6

\* Number of minutes after infusion of the loading dose of procainamide.

† Mean ± 1 standard deviation.

ed, the right ventricular effective refractory period and QRS duration were determined every minute for 20 minutes.

In the control group, no drug was infused. After the baseline determinations of effective refractory period and QRS duration, there was a 15-minute rest period, to simulate the period of drug administration in the treatment groups. The effective refractory period and QRS duration were then determined every minute for 20 minutes.

**Determination of plasma drug concentrations:** Arterial blood samples for determination of the plasma procainamide and N-acetyl procainamide concentrations were obtained at 1, 5, 10, 15 and 20 minutes after administration of the loading dose of procainamide was completed. The plasma concentrations of procainamide and N-acetyl procainamide were determined by reverse phase high performance liquid chromatography.<sup>15</sup> Because the plasma N-acetyl procainamide concentrations were negligible in all treatment groups, these data are not presented in the results.

**Statistical analysis:** The plasma procainamide concentrations, the effective refractory periods and the QRS duration were compared statistically using a repeated measures analysis of variance to determine treatment effects and time effects. Multiple comparisons were performed using Fisher's least significant difference procedure. Concentration-effect relations were determined by analysis of covariance. A p value <0.05 was considered significant.

**Results**

**Plasma procainamide concentrations:** The mean procainamide loading dose was 965 ± 98 mg. The mean plasma procainamide concentrations in the 3 treatment groups are listed in Table II and shown in Figure 1. Comparing the overall mean plasma procainamide concentrations averaged over time in the 3 treatment groups, there was a significant difference only between groups A and C (p <0.02). The difference in the plasma procainamide concentration between groups A and C was not significant at 1 or 5 minutes but was significant at 10, 15 and 20 minutes after infusion of the loading dose.

There was a significant time effect on the plasma procainamide concentration in each of the 3 treatment groups (p <0.001). The largest decrease in the plasma procainamide concentration occurred between 1 and 5 minutes after infusion of the loading dose. The magni-

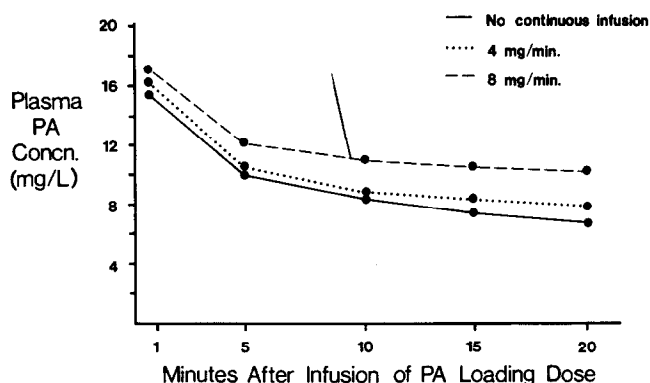
**TABLE III Right Ventricular Effective Refractory Periods**

Minute*	Effective Refractory Period (ms)			
	Group A	Group B	Group C	Group D
Baseline	223 ± 18	218 ± 20	237 ± 16	228 ± 16
1	261 ± 24	256 ± 28	272 ± 24	238 ± 17
2	254 ± 25	257 ± 28	267 ± 21	235 ± 18
3	250 ± 24	252 ± 31	264 ± 18	231 ± 18
4	245 ± 21	252 ± 28	264 ± 19	231 ± 22
5	247 ± 22	251 ± 31	266 ± 20	231 ± 21
6	249 ± 18	250 ± 31	265 ± 21	231 ± 20
7	247 ± 18	248 ± 28	263 ± 20	232 ± 21
8	249 ± 20	246 ± 25	262 ± 20	234 ± 22
9	248 ± 21	245 ± 29	263 ± 16	234 ± 20
10	246 ± 21	244 ± 26	260 ± 18	233 ± 19
11	245 ± 17	245 ± 29	259 ± 16	233 ± 18
12	243 ± 19	244 ± 27	260 ± 20	230 ± 18
13	246 ± 21	245 ± 28	262 ± 17	231 ± 18
14	244 ± 18	240 ± 27	262 ± 19	231 ± 18
15	244 ± 23	245 ± 28	262 ± 18	232 ± 15
16	243 ± 21	244 ± 26	261 ± 18	233 ± 15
17	244 ± 18	242 ± 25	262 ± 18	231 ± 15
18	243 ± 18	245 ± 25	262 ± 18	230 ± 19
19	244 ± 18	242 ± 25	260 ± 13	228 ± 15
20	241 ± 20	243 ± 27	258 ± 17	230 ± 18

\* Number of minutes after infusion of the loading dose of procainamide. Data are mean ± standard deviation.

tude of the decline in plasma procainamide concentration between 5 and 20 minutes ranged from a mean of 2.0 to 3.1 mg/l. Within each treatment group, multiple comparisons of the mean plasma procainamide concentration at various times demonstrated that only the means at 15 and 20 minutes did not differ significantly from each other. A post hoc comparison demonstrated that the decrease in the plasma procainamide concentration between minutes 1 and 20 was greater in magnitude in groups A and B than in group C (p <0.05).

**Right ventricular effective refractory periods:** The right ventricular effective refractory periods are listed in Table III. The mean effective refractory periods at selected points in time are shown in Figure 2.



**FIGURE 1. Mean plasma procainamide (PA) concentrations in the 3 treatment groups, each of which received a loading dose of 15 mg/kg. Each group consisted of 10 patients. The mean plasma procainamide concentrations in the group that received a maintenance infusion of 8 mg/min were significantly greater than in the group that received no maintenance infusion (p <0.02).**

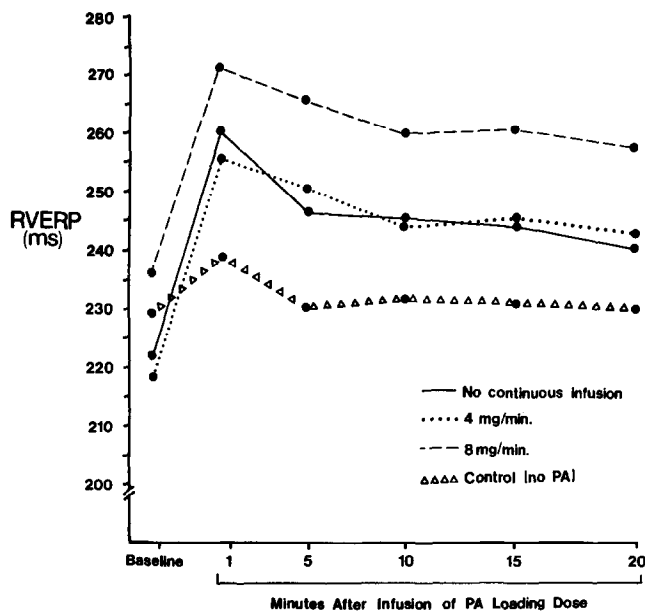
The overall mean effective refractory periods averaged over time in each of the 3 treatment groups were each significantly greater than the mean effective refractory period in the control group ( $p < 0.02$ ). Comparing the 3 treatment groups, there were no significant differences in the overall mean effective refractory periods averaged over time.

The control group did not show a significant change in effective refractory period over time ( $p = 0.2$ ). There was a significant time effect in each of the 3 treatment groups ( $p < 0.001$ ). There was a significant increase over baseline in the effective refractory period in each of the treatment groups at 1 minute after infusion of the procainamide loading dose; the effective refractory periods decreased between 1 and 10 minutes, then remained essentially unchanged between 10 and 20 minutes after infusion of the procainamide loading dose.

There was a linear concentration-effect relation in each of the 3 treatment groups and no significant differences between the 3 groups in the slopes of the regression equations. There was not a significant interaction between the 3 treatment groups and time ( $p = 0.3$ ), indicating that the time trends in groups A, B and C were parallel.

**QRS duration:** The mean QRS durations are listed in Table IV. The mean QRS durations at selected points in time are shown in Figure 3.

The mean baseline QRS durations in groups C and D were significantly greater than in groups A and B ( $p = 0.01$ ). When corrected for the difference in the baseline QRS duration, there was not a significant difference in the overall mean QRS durations averaged over time between groups A, B and C ( $p > 0.05$ ).



**FIGURE 2.** Mean right ventricular effective refractory periods (RVERP) in the 3 treatment groups and the control group. The mean effective refractory periods in the 3 treatment groups were significantly greater than in the control group ( $p < 0.02$ ), but were not significantly different from each other. PA = procainamide.

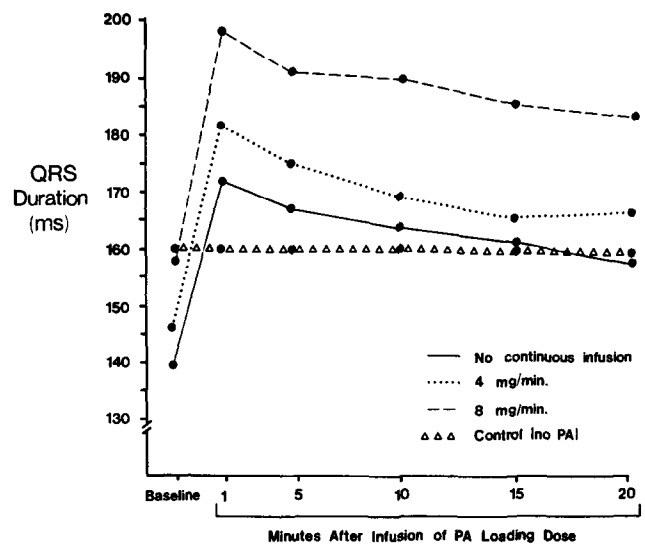
The control group did not show a significant change in QRS duration over time ( $p = 0.7$ ). A significant time effect was present in each of the treatment groups ( $p < 0.001$ ).

There was not a significant interaction between the treatment groups and time ( $p = 0.3$ ), indicating that the time trends were parallel. The overall time trend consisted of a sharp increase over baseline in QRS duration during the first minute after infusion of the procainamide loading dose, followed by a gradual decrease up until 15 minutes, then a leveling off between 15 and 20 minutes. There was a linear concentration-effect relation in each of the 3 treatment groups and no significant differences between the 3 groups in the slopes of the regression equations.

## Discussion

**Plasma procainamide concentrations:** The findings of this study indicate that a common method used for administering intravenous procainamide during acute electropharmacologic testing (15 mg/kg at 50 mg/min) results in a continuous decrease in the plasma procainamide concentration during the first 15 minutes after the loading dose is administered. The decrease in the plasma procainamide concentration, however, is attenuated by the use of an 8 mg/min maintenance infusion of procainamide. The absence of a steady-state plasma procainamide concentration during the first 15 minutes after the relatively rapid administration of a large dose of procainamide is in keeping with the distribution half-life of intravenous procainamide, which has been estimated to be 5 minutes.<sup>16</sup>

**Effects on ventricular refractoriness:** The changes in the right ventricular effective refractory period that occurred after the administration of procainamide paralleled the changes in the plasma procainamide



**FIGURE 3.** The mean QRS duration at a ventricular pacing rate of 120/min in the 3 treatment groups and the control group. When corrected for baseline differences, the QRS durations after infusion of the procainamide (PA) loading dose did not differ among the 3 treatment groups and the control group.

concentration, with a linear concentration-effect relation in each of the 3 treatment groups.

Whereas an 8 mg/min maintenance infusion of procainamide resulted in higher plasma procainamide concentrations than when the loading dose was not followed by a maintenance infusion, the higher plasma procainamide concentrations were not associated with a greater degree of lengthening of the ventricular effective refractory period. Therefore, when a procainamide loading dose is administered at a rate of 50 mg/min, the tissue effect of procainamide on the ventricular effective refractory period may not be affected by the higher plasma concentrations that result from the use of an 8 mg/min infusion of procainamide.

**Effects on intraventricular conduction:** Changes over time in the QRS duration at a ventricular pacing rate of 120/min, used as an index of global intraventricular conduction, paralleled the changes that occurred in ventricular refractoriness. When corrected for the baseline difference in QRS duration, the QRS durations during the 8 mg/min infusion of procainamide did not differ from the QRS durations in the other 2 treatment groups. Therefore, as is the case with ventricular refractoriness, the effect of procainamide on intraventricular conduction between 5 and 20 minutes after the loading dose has been administered does not appear to be affected by the use of a maintenance infusion of procainamide.

**Disposition of intravenous procainamide:** The disposition of procainamide after an intravenous infusion has been described as being consistent with a 2-compartment model, with complete distribution from the plasma compartment into the central tissue compartment generally occurring within 30 minutes.<sup>17</sup> In this type of model, it would be expected that the principal determinant of the tissue procainamide concentration during the first 20 minutes after the administration of a procainamide loading dose would be the distribution that occurs from the plasma into the central compartment as procainamide is being infused at a rate of 50 mg/min. This may explain why the use of an 8 mg/min maintenance infusion of procainamide did not significantly augment the electrophysiologic effects of procainamide despite resulting in higher plasma procainamide concentrations than in the absence of a maintenance infusion.

**Clinical implications:** Based on a pharmacokinetic approach, it has been determined that a therapeutic plasma procainamide concentration can be achieved in less than 15 minutes in a patient with normal renal function if procainamide is administered in a loading dose of 0.22 mg/kg/min for 1 hour, followed by a maintenance infusion of 2.8 mg/kg/hr.<sup>18</sup> However, approximately 2 hours are required for steady-state conditions to be reached with this dosing method. A 2-hour waiting period is not feasible in patients undergoing electropharmacologic testing. Therefore, standard practice has been to begin programmed stimulation either immediately or 5 minutes after the loading dose has been administered at a rate of 50 mg/min, and to measure the plasma procainamide concentration upon completion of the stimulation protocol.<sup>1-11</sup> When reported, the

**TABLE IV QRS Durations at a Ventricular Paced Rate of 120/min**

Minute*	QRS Duration (ms)			
	Group A	Group B	Group C	Group D
Baseline	139 ± 13	146 ± 21	158 ± 12	160 ± 21
1	173 ± 18	182 ± 29	198 ± 19	160 ± 21
2	170 ± 16	180 ± 27	196 ± 17	160 ± 21
3	170 ± 15	178 ± 26	197 ± 14	161 ± 20
4	168 ± 15	174 ± 22	194 ± 15	160 ± 20
5	167 ± 13	175 ± 22	192 ± 13	160 ± 22
6	166 ± 14	172 ± 21	192 ± 14	160 ± 22
7	168 ± 18	172 ± 21	189 ± 13	161 ± 20
8	168 ± 18	170 ± 20	190 ± 12	160 ± 22
9	164 ± 15	170 ± 20	190 ± 14	161 ± 21
10	164 ± 18	169 ± 22	190 ± 14	160 ± 21
11	165 ± 18	169 ± 21	189 ± 13	160 ± 21
12	161 ± 17	168 ± 22	189 ± 14	159 ± 22
13	161 ± 18	168 ± 22	188 ± 15	160 ± 21
14	161 ± 17	168 ± 22	188 ± 15	159 ± 20
15	161 ± 17	166 ± 21	186 ± 14	160 ± 22
16	160 ± 17	167 ± 22	185 ± 14	160 ± 21
17	160 ± 16	166 ± 22	186 ± 14	160 ± 21
18	159 ± 16	168 ± 22	186 ± 13	159 ± 20
19	158 ± 15	168 ± 22	184 ± 14	159 ± 20
20	158 ± 16	167 ± 22	184 ± 14	160 ± 22

\* Number of minutes after infusion of the loading dose of procainamide.

interval required to complete the stimulation protocol has been described as usually being 5 to 15 minutes.<sup>13</sup> During this time period, there is a continual decrease in the plasma procainamide concentration and in its effects on ventricular refractoriness and conduction. This may create a limitation in determining the effective plasma procainamide concentration relevant for long-term therapy.

The decrease in plasma procainamide concentrations that occurs in the first 15 minutes is attenuated by the use of an 8 mg/min maintenance infusion of procainamide. However, the use of a maintenance infusion may introduce an additional limitation. The maintenance infusion may result in an increase in the plasma procainamide concentration without an associated increase in the effects of procainamide on ventricular conduction and refractoriness. This suggests that the effective plasma procainamide concentration may be overestimated.

These limitations of acute drug testing may argue in favor of testing patients with oral procainamide instead of relying on the results of intravenous procainamide testing to guide long-term therapy.

**Acknowledgment:** The authors gratefully acknowledge the secretarial assistance of Lisa Hackbarth and the technical assistance of Beverly Burgie, Joan Bergeron and Linda Abbott.

## References

1. Fisher JD, Cohen HL, Mehra R, Altschuler H, Escher DJW, Furman S. Cardiac pacing and pacemakers II. Serial electrophysiologic-pharmacologic testing for control of recurrent tachyarrhythmias. *Am Heart J* 1977;93:658-667.
2. Mason JW, Winkle RA. Accuracy of the ventricular tachycardia-induction study for predicting long-term efficacy and inefficacy of antiarrhythmic drugs. *N Engl J Med* 1980;303:1073-1077.
3. Engel TR, Meister SG, Luck JC. Modification of ventricular tachycardia by procainamide in patients with coronary artery disease. *Am J Cardiol* 1980;

46:1033-1038.

4. Swiryn S, Bauernfeind RA, Strasberg B, Palileo E, Iverson N, Levy PS, Rosen KM. Prediction of response to class I antiarrhythmic drugs during electrophysiologic study of ventricular tachycardia. *Am Heart J* 1982;104:43-50.
5. Morady F, Hess D, Scheinman MM. Electrophysiologic drug testing in patients with malignant ventricular arrhythmias: importance of stimulation at more than one ventricular site. *Am J Cardiol* 1982;50:1055-1060.
6. Waxman HL, Buxton AE, Sadowski LM, Josephson ME. The response to procainamide during electrophysiologic study for sustained ventricular tachyarrhythmias predicts the response to other medications. *Circulation* 1983;67:30-37.
7. Marchlinski FE, Buxton AE, Vassallo JA, Waxman HL, Cassidy DM, Doherty JU, Josephson ME. Comparative electrophysiologic effects of intravenous and oral procainamide in patients with sustained ventricular arrhythmias. *JACC* 1984;4:1247-1254.
8. Rae AP, Greenspan AM, Spielman SR, Sokoloff NM, Webb CR, Kay HR, Horowitz LN. Antiarrhythmic drug efficacy for ventricular tachyarrhythmias associated with coronary artery disease as assessed by electrophysiologic studies. *Am J Cardiol* 1985;55:1494-1499.
9. Benson DW Jr, Dunnigan A, Green TP, Benditt DG, Schneider SP. Periodic procainamide for paroxysmal tachycardia. *Circulation* 1985;72:147-152.
10. Oseran DS, Gang ES, Roesenthal ME, Mandel WJ, Peter T. Electrophysiologic testing in sustained ventricular tachycardia associated with coronary heart disease: value of the response to intravenous procainamide in predicting the response to oral procainamide and oral quinidine treatment. *Am J Cardiol* 1985;56:883-886.
11. Gold RL, Haffajee CI, Alpert JS. Electrophysiologic and clinical factors influencing response to class IA antiarrhythmic agents in patients with inducible sustained monomorphic ventricular tachycardia. *Am Heart J* 1986;112:9-13.
12. Morady F, DiCarlo LA Jr, Baerman JM, Krol RB. Rate-dependent effects of intravenous lidocaine, procainamide and amiodarone on intraventricular conduction. *JACC* 1985;6:179-185.
13. Greenspan AM, Horowitz LN, Spielman SR, Josephson ME. Large dose procainamide therapy for ventricular tachyarrhythmia. *Am J Cardiol* 1980;46:453-462.
14. Morady F, DiCarlo LA Jr, de Buitelir M, Krol RB, Baerman JM, Kou WH. Effects of incremental doses of procainamide on ventricular refractoriness, intraventricular conduction, and ventricular tachycardia induction. *Circulation* 1986;74:1355-1364.
15. Annesley T, Matz K, Davenport R, Giachero D. A high performance liquid chromatographic assay for tocainide with alternate application for the determination of lidocaine, procainamide, and N-acetylprocainamide. *Res Comm Chem Pathol Pharmacol* 1986;51:173-181.
16. Lima JJ, Conti DR, Goldfarb AL, Tilstone WJ, Golden LH, Jusko WJ. Clinical pharmacokinetics of procainamide infusions in relation to acetylator phenotype. *J Pharmacokinet Biopharm* 1977;7:69-85.
17. Coyle JD, Lima JJ. Procainamide. In: Evans WE, Schentag JJ, Juski WJ, ed. *Applied Pharmacokinetics*. 2nd ed. Spokane, Washington: Applied Therapeutics, Inc. 1986:682-711.
18. Lima JJ, Conti DR, Goldfarb AL, Golden LH, Jusko WJ. Pharmacokinetic approach to intravenous procainamide therapy. *Eur J Clin Pharmacol* 1978;13:303-308.