Paradoxical Effects of Procainamide
— Facilitation of the Induction of Sustained Reciprocating Tachycardia after Procainamide Administration in Wolff-Parkinson-White Syndrome —

MASAHIKO FUKATANI, M.D., FUMIHIRO KIYA, M.D.
KATSUSUKE YANO, M.D., AND KUNITAKE HASHIBA, M.D.

The effects of procainamide on the refractory periods of the accessory and normal pathways in the antegrade and retrograde directions with reference to the reciprocating tachycardia were studied in 31 patients with Wolff-Parkinson-White (WPW) syndrome. Right atrial, left atrial and right ventricular pacing (incremental pacing and extrastimulus technique) were performed to induce reciprocating tachycardia and to measure antegrade and retrograde effective refractory periods (A-ERP and R-ERP) of the accessory pathway (AP) and the A-V node (AVN). Atrial extrastimulus technique was performed at 2 or more basic cycle lengths and repeated after an intravenous administration of procainamide (600 mg). Prior to the procainamide administration reciprocating tachycardias were induced in 10 of the 31 patients. After procainamide, induction of the tachycardia became impossible in 2 of these 10 patients. In 3 patients, procainamide decreased the tachycardia zone, while procainamide widened the tachycardia zone in the other 4 patients. In the remaining one, procainamide had no significant effect on the tachycardia zone. During the control study period no sustained reciprocating tachycardia was induced in 21 of the 31 patients. In 15 of these 21, no tachycardia was induced after procainamide. However, in 6 of the 21 patients, sustained reciprocating tachycardias were induced after procainamide. All reciprocating tachycardias that occurred in these patients were characterized by narrow QRS complexes, and demonstrated circus movement with antegrade conduction via the normal pathway and retrograde conduction via the accessory pathway. In 10 of the 31 patients (32%), induction of the tachycardia by an atrial premature beat after procainamide was shown while prior to its administration no tachycardia could be initiated, or the tachycardia zone was widened on procainamide administration. In these patients, procainamide could not block retrograde conduction over the AP and altered the relationship between the A-ERP\textsubscript{AP} and the A-ERP\textsubscript{AVN} by lengthening the A-ERP\textsubscript{AP} with shortening the A-ERP\textsubscript{AVN}, i.e., after procainamide the A-ERP\textsubscript{AP} became longer than the A-ERP\textsubscript{AVN}, and, by shortening the A-ERP\textsubscript{AVN}, procainamide did augment the differences in length of the ERP of the 2 A-V pathways, so that sustained reciprocating tachycardia could

---

**Key Words:**
- Wolff-Parkinson-White syndrome
- A-V reciprocating tachycardia
- Procainamide
- Refractory periods
- Accessory pathway

*The Third Department of Internal Medicine, Nagasaki University, School of Medicine, Nagasaki, Japan*

Mailing address: Masahiko Fukatani, M.D., The Third Department of Internal Medicine, Nagasaki University, School of Medicine, 7-1 Sakamoto-machi, Nagasaki 852, Japan

124 *Japanese Circulation Journal Vol. 47, January 1983*
be induced by atrial stimulation.

In conclusion, we consider that in some patients with WPW syndrome procainamide may facilitate the induction of sustained reciprocating tachycardia by prolonging the A-ERP\textsubscript{AP} and, at the same time, by shortening the A-ERP\textsubscript{AVN} but by only minimally increasing the R-ERP\textsubscript{AP}.

**Reciprocati**ng tachycardia which occurs in patients with Wolff-Parkinson-White (WPW) syndrome is usually characterized by narrow QRS complexes, and reflects a circus movement with antegrade conduction *via* normal A-V pathway and retrograde conduction *via* an accessory pathway.\textsuperscript{1–8} In patients with WPW syndrome, the effects of intravenous procainamide on the electrophysiological properties of the accessory and normal pathways and on the mechanism of reciprocating tachycardia can be studied utilizing intracardiac stimulation and recording.\textsuperscript{9–15} In this report we describe the effects of procainamide on the refractory periods of the accessory and normal pathways in the antegrade and retrograde directions with reference to the reciprocating tachycardia in WPW syndrome.

**Materials and Methods**

Thirty-one patients, 22 males and 9 females, with WPW syndrome were studied. According to Rosenbaum's classification 17 patients be-

![Fig. 1. Effects of procainamide on the effective refractory periods (ERPs) of the accessory pathway (AP) in the antegrade and retrograde directions. Broken line indicates the antegrade block of the AP after procainamide. Abbreviations: A-ERP\textsubscript{AP} = antegrade effective refractory period of the accessory pathway; R-ERP\textsubscript{AP} = retrograde effective refractory period of the accessory pathway; BCL = basic cycle length; C = control study; P = after administration of procainamide]
longed to type A and 14 to type B. In 4 of these 31 patients WPW syndrome was intermittent. Ages of these patients ranged from 14 to 62 years (mean ± SD: 28.7 ± 14.3).

Electrophysiological studies were performed in the postabsorptive nonsedated state. Antiarrhythmic therapy was discontinued at least 5 days prior to the study. Under local anesthesia, 2 quadripolar electrode catheters for recording and stimulating were introduced through the right great saphenous vein and advanced to the apex of the right ventricle and the high right atrium under fluoroscopic control. A third quadripolar electrode catheter was introduced via an antecubital vein and advanced to the coronary sinus. A tripolar or quadripolar electrode catheter was introduced percutaneously via the right femoral vein and positioned across the tricuspid valve to record a His bundle electrogram. Leads I, aVF, and V1 of a standard ECG, and electrograms from the high right atrium, the proximal and distal coronary sinus, the His bundle and the right ventricle were recorded simultaneously. Electrograms were recorded on an 8 channel inkjet recorder at a paper speed of 100 mm/sec (Siemens Mingograph 800). Intracardiac electrograms were recorded at filter frequencies of 40 to 500 Hz (Fukuda Electronics Recorder, MCM-8000). Stimulation studies were performed using a programmable stimulator (Nihon Kohden Cardiac Stimulator, SEC-2102) which delivered impulses of 1 msec duration at twice the diastolic threshold. All electrical equipment was carefully grounded.

Electrophysiological studies consisted of incremental high right atrial pacing, incremental left atrial pacing from the coronary sinus, incremental right ventricular apical pacing, atrial (right and left) extrastimulus technique and right ventricular extrastimulus technique. Incremental pacing was performed at increasing rates to assess antegrade AV refractoriness. The antegrade and retrograde refractory periods of the normal and accessory pathways were determined using the extrastimulus technique. The atrial extrastimulus technique was first performed at the longest basic cycle length assuring atrial capture, then, in most patients, was repeated at one or more basic cycle lengths which were shortened in 100–200 steps.

Following the completion of the control studies, the above-mentioned procedures were repeated, with the catheters in the same positions, 10 min after the termination of an intravenous administration of procainamide, 600 mg, at a rate of 50 mg/min. The electrophysiological studies were repeated within 20 min.

The effective refractory period (ERP) of the accessory pathway (AP) in antegrade direction (A-ERP<sub>AP</sub>) was defined as the longest atrial premature stimulus interval that did not conduct to the ventricle over the AP. The ERP of the AP in retrograde direction (R-ERP<sub>AP</sub>) was defined as the longest right ventricular premature stimulus
Fig. 2. A representative example in which sustained reciprocating tachycardia is induced by right atrial extrastimulus technique after an administration of procainamide (right panels) while prior to its administration no tachycardia can be induced (left panels). Abbreviations: $S_{7}$, $S_{8}$, and $S_{E}$ = 7th and 8th basic driven and the extra pacing stimuli, respectively; HRA = high right atrial electrogram; HBE = His bundle electrogram; $A_{1}$ and $A_{2}$ = the atrial electrograms of the basic driven and the premature atrial beat, respectively; PSVT = paroxysmal supraventricular tachycardia, that is reciprocating tachycardia incorporating the AP; ERP$_{AVN}$ = antegrade effective refractory period of the A-V node. The $A_{1}$, $A_{2}$, interval and BCL are listed in msec.

interval that was not followed by an atrial activation.

The antegrade "tachycardia zone" was defined as the interval during which a premature atrial impulse delivered during a basic cycle length resulted in sustained reciprocating tachycardia utilizing the AP. A "sustained" reciprocating tachycardia was defined as the tachycardia which continued one min or more in duration. A similar retrograde tachycardia zone was defined by corresponding ventricular stimulation data.

RESULTS

The atrial extrastimulus technique was performed on all 31 patients both before and after an administration of procainamide. Following procainamide the antegrade block of the AP developed in 11 patients and the A-ERP$_{AP}$ increased in 16 (Fig. 1, upper 3 panels). In 4 out of the total series of 31 patients, WPW syndrome was intermittent and the antegrade block of the AP was observed in control studies. In patients with increased A-ERP$_{AP}$ after procainamide, the A-ERP$_{AP}$ ranged from 250 to 320 msec (mean ± SD, 288 ± 25) during control study and ranged from 290 to 350 (322 ± 19) msec after procainamide at a basic cycle length of 700 msec. At a basic cycle length of 600 msec, the A-ERP$_{AP}$ increased from 285 ± 14 (260 – 310) to 313 ± 22 (290 – 360) msec after procainamide. At a basic cycle length of 500 msec, the A-ERP$_{AP}$ increased from 271 ± 17 (240 – 310) to 301 ± 24 (270 – 360) msec after procainamide.

The ventricular extrastimulus technique was performed on 25 patients. Following procainamide the retrograde block of the AP developed in 3 patients and the R-ERP$_{AP}$ increased in 18 patients (Fig. 1, lower 3 panels). In 2 of the 25
Patients, the retrograde block of the AP was observed in control studies. These patients had AP that conducted only in the antegrade direction. In the remaining 2 patients, determination of the refractory period was impossible because the ventricle became refractory before a block in the AP developed. In patients with increased R-ERP\textsubscript{AP} after procainamide, the R-ERP\textsubscript{AP} increased from 285 ± 39 (250 - 350) to 398 ± 19 (370 - 420) msec after procainamide at a basic cycle length of 700 msec. At a basic cycle length of 600 msec, the R-ERP\textsubscript{AP} increased from 277 ± 22 (230 ± 350) to 338 ± 50 (250 - 420) msec after procainamide. At a basic cycle length of 500 msec, the R-ERP\textsubscript{AP} increased from 267 ± 22 (230 - 300) to 318 ± 48 (260 - 450) msec after procainamide. Procainamide increased both the antegrade and retrograde ERP of the AP at any basic cycle length.

As shown in Table I, prior to procainamide administration reciprocating tachycardias were induced in 10 patients. After procainamide, induction of sustained tachycardia became impossible in 2 patients, who showed retrograde block of the AP or prolonged R-ERP\textsubscript{AP}. Although the A-ERP\textsubscript{AP} had lengthened, induction of tachycardia by a single atrial premature beat was still possible in 8 patients after procainamide. These 8 patients showed V-A conduction through the AP with only a slight increase in the R-ERP\textsubscript{AP}. In 3 of these 8, procainamide decreased the tachycardia zone, while in 4 of the 8 patients, procainamide widened the tachycardia zone. In the remaining one, procainamide had no significant effect on the tachycardia zone. During control studies no sustained reciprocating tachycardia was induced in the other 21 patients. In 15 of these 21, no tachycardia was induced after procainamide. However, in 6 of the 21 patients, sustained reciprocating tachycardias were induced after the administration of procainamide.

A representative example of one of the above-mentioned phenomena is shown in Fig. 2. In panel A, the right atrium was paced at a basic cycle length of 600 msec. Following 8 basic drive beats, a premature atrial depolarization (A\textsubscript{2}) was introduced at a coupling interval (A\textsubscript{1} A\textsubscript{2}) of 280 msec and it was conducted with ventricular pre-excitation. In panel B, the A\textsubscript{1} A\textsubscript{2} coupling interval was decreased to 270 msec and A\textsubscript{2} was blocked in both normal and accessory pathways. Before procainamide, the A-ERP\textsubscript{AP} was 270 msec and the antegrade ERP of the A-V node (A-ERP\textsubscript{AVN}) was equal or longer than that of the AP. In panels C and D, this same sequence was performed after the administration of procainamide (600 mg). In panel C, at a basic cycle length of 600 msec, and atrial extrastimulus was introduced at an A\textsubscript{1} A\textsubscript{2} coupling interval of 300 msec. Both A\textsubscript{1} and A\textsubscript{2} were conducted via the accessory pathway. In panel D, the A\textsubscript{1} A\textsubscript{2} interval was decreased to 290 msec and A\textsubscript{2} was blocked in the accessory pathway and conducted in antegrade direction through the normal pathway with an induction of sustained reciprocating tachycardia. When the A\textsubscript{1} A\textsubscript{2} interval was decreased to 265 msec A\textsubscript{2} was blocked in both normal and accessory pathways. Following procainamide, the A-ERP\textsubscript{AP} increased from 270 to 290 msec, with shortening of the A-ERP\textsubscript{AVN} to 265 msec. In this case, after procainamide, with increasing prematurity of atrial extrastimuli, accessory pathway conduction failed before A-V node conduction, so that sustained reciprocating tachycardia was induced with programmed atrial
The antegrade block of the AP was observed in 3 patients both before and after procainamide. After administration of procainamide, the A-ERPAP increased in the 12 patients, with complete block of the AP in 3 patients. Five patients depicted in white arrows demonstrated simultaneous shortening of the A-ERP_{AVN} following procainamide. In these patients, procainamide decreased the tachycardia zone and, thus, decreased the ability to induce reciprocating tachycardia, prevented pacing-induced initiation of tachycardia, or eliminated the tachycardia zone. In 2 of these 5 patients, induction of sustained tachycardia became impossible and retrograde block of the AP or prolonged R-ERP_{AP} was also demonstrated after procainamide. On the other hand, 7 patients depicted in black arrows demonstrated simultaneous shortening of the A-ERP_{AVN} following procainamide. In these patients, procainamide widened the tachycardia zone, i.e., reciprocating tachycardia was easily induced by premature atrial beats, or sustained reciprocating tachycardia could be produced during pacing following procainamide where no tachycardia could be produced under control conditions.

**DISCUSSION**

There have been some reports on the effect of procainamide on refractory periods of the accessory and normal pathways and reciprocating tachycardia in WPW syndrome. In our study, procainamide decreased the tachycardia zone and, thus, decreased the ability to induce reciprocating tachycardia, or prevented pacing-induced initiation of tachycardia in 5 patients. On the other hand, procainamide widened the tachycardia zone in 4 patients, or sustained reciprocating tachycardias were produced during pacing after procainamide where no tachycardia was induced under control studies in 6 patients. Sellers et al. described 2 patients in whom the echo interval was widened on procainamide therapy. However, little attention was focused on the paradoxical effect of procainamide that facilitated the induction of reciprocating tachycardia in WPW syndrome. In the following discussion, we shed a light on the paradoxical effect of procainamide, one of the commonly used antiarrhythmic agent, in patients with WPW syndrome.

The most frequent reciprocating tachycardia in WPW syndrome is characterized by narrow
QRS complexes, and reflects a circus movement with antegrade conduction via the A-V node and retrograde conduction via the AP. We have reported\textsuperscript{16} that a failure to induce tachycardias due to this form of circus movement was observed in patients with one of the following phenomena: 1) absent or poor retrograde conduction of the AP; 2) the A-ERP\textsubscript{AP} was equal or shorter than the A-ERP\textsubscript{AVN}; 3) even though the A-ERP\textsubscript{AP} was longer than the A-ERP\textsubscript{AVN}, the difference between the A-ERP\textsubscript{AP} and the A-ERP\textsubscript{AVN} was smaller than 30 msec; 4) prolonged A-ERP\textsubscript{AVN}. Complete block of retrograde conduction through the AP or significant prolongation of the R-ERP\textsubscript{AP} is the most important for the elimination of the reciprocating tachycardia\textsuperscript{16-18}.

Wellens et al\textsuperscript{15} have reported that the effect of procainamide on the ERP of the AP in the antegrade and retrograde directions was different. Our study also demonstrated a difference between the effect of procainamide on the A-ERP\textsubscript{AP} and that on the R-ERP\textsubscript{AP}. In our study, procainamide increased the antegrade and retrograde refractory periods of the AP in all patients. However, the degree of lengthening of refractory periods in the antegrade and retrograde directions was different in each patient. Complete antegrade block over the AP was obtained in 11 patients after procainamide, while complete retrograde block was observed in only 3 instances. These findings explain why in some patients the reciprocating tachycardias are induced after procainamide that completely blocks antegrade conduction through the AP. Procainamide does not block retrograde conduction over the AP in these patients.

In all of our patients with inducible reciprocating tachycardia before and/or after procainamide, retrograde accessory pathway conduction was observed. However, in patients with retrograde conduction through the AP, there were patients without inducible reciprocating tachycardia. These patients had inadequate antegrade A-V nodal conduction for sustaining reciprocating tachycardia. Inadequate A-V nodal properties for induction of reciprocating tachycardia\textsuperscript{16,17} are shown in upper two schemata of Fig. 4; 1) the A-ERP\textsubscript{AVN} greater than the A-ERP\textsubscript{AP} at all tested coupling intervals with atrial extrastimulus technique and at all atrial paced cycle lengths (Fig. 4, upper left schema). In patients with this property, there was no demonstrable antegrade A-V nodal conduction when accessory pathway block was achieved; 2) the inability for antegrade A-V nodal conduction of more than one single echo (Fig. 4, upper right schema). In patients with this property, exclusive antegrade A-V nodal conduction was achieved, with retrograde conduction through the AP back to the atria for a single atrial echo. The single atrial echo unable to conduct antegradely to the bundle of His, suggesting inability for sequential antegrade A-V nodal conduction. Effective prophylactic drug therapy should affect the properties of either antegrade normal pathway, or retrograde accessory pathway, making them similar to those seen in patients without inducible reciprocating tachycardia.

However, in 10 of 31 patients (32%) in our study group, induction of the tachycardia by an atrial premature beat after procainamide administration was shown while prior to its administration no tachycardia could be initiated, or the tachycardia zone was widened on procainamide administration (Table I). Procainamide, as shown in patients depicted by black arrows in Fig. 3, altered the relationship between the A-ERP\textsubscript{AP} and the A-ERP\textsubscript{AVN} by lengthening the A-ERP\textsubscript{AP} with shortening the A-ERP\textsubscript{AVN} by its anti-cholinergic effect\textsuperscript{19} As shown in lower two schemata of Fig. 4, after procainamide the A-ERP\textsubscript{AP} became longer than the A-ERP\textsubscript{AVN} and, by shortening the A-ERP\textsubscript{AVN}, procainamide did augment the differences in length of the ERP of the two A-V pathways. In patients with antegrade A-V nodal properties depicted in lower two schemata of Fig. 4, sustained reciprocating tachycardia could be induced by atrial ativation. We considered that procainamide facilitated the induction of sustained reciprocating tachycardia by prolonging the A-ERP\textsubscript{AP} and, at the same time, by shortening the A-ERP\textsubscript{AVN} but by only minimally increasing the R-ERP\textsubscript{AP}.

Acknowledgement

We are indebted to our colleagues, Drs. T. Mitsuoka, Y. Matsumoto and C. Ueyama for assistance during electrophysiologic studies, and Miss A. Yamaguchi for typing this manuscript.

REFERENCES

3. WELLENS HJ, DURRER D: The role of an ac-


5. WELLENS HJJ: Modes of initiation of circus movement tachycardia in 139 patients with the Wolff-Parkinson-White syndrome studied by programmed electrical stimulation. In Re-entrant arrhythmias: Mechanisms and Treatment, ed by KULBERTUS E, MTP, Lancaster, 1977, p 153


12. SELLERS TD Jr, CAMPBELL RWF, BASHORE TM, GALLAGHER JJ: Effects of procainamide

and quinidine sulfate in the Wolff-Parkinson-White syndrome. Circulation 55: 15, 1977


