Effects of Quinidine on Atrioventricular Nodal
Reentrant Paroxysmal Tachycardia

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SUMMARY Electrophysiologic studies were performed in 14 patients with atrioventricular nodal reentrant paroxysmal tachycardia (PSVT) before and after oral administration of 1.2-1.6 g quinidine sulfate over a 24-hour period (0.3-0.4 g every 6 hours). Studies were performed after 0.5-1 mg i.v. atropine before and after quinidine. All 14 patients had induction of sustained PSVT before quinidine, with or without atropine. After quinidine, 11 patients lost the ability to induce echoes or sustain PSVT, reflecting depression of the retrograde pathway with either absence of atrial echoes (six patients) or induction of nonsustained PSVT, with termination of echoes or PSVT occurring after QRS (block in retrograde pathway) (five patients). In only one of these 11 patients was sustained PSVT inducible after addition of atropine. All 11 were discharged on the same dose of quinidine. In three patients, quinidine was discontinued because of side effects. Follow-up in the remaining eight patients for 8 ± 2 months showed no recurrence of sustained PSVT. Three of the 14 patients had induction of sustained PSVT after quinidine. Ventricular paced cycle length producing ventriculoatrial block was 314 ± 7 msec (mean ± SEM) before and 392 ± 13 msec after quinidine (p < 0.01) in the 14 patients, suggesting depression of the retrograde pathway with quinidine.

In summary, quinidine inhibited induction of sustained atrioventricular nodal reentrant tachycardia with depression of the retrograde pathway. It is very effective in preventing recurrence of PSVT in most patients.

DUAL PATHWAY atrioventricular (AV) nodal reentrant tachycardia, using a slow pathway for antegrade and a fast pathway for retrograde conduction, is a common arrhythmia. Propranolol, digitalis and verapamil inhibit arrhythmia attacks by depression of antegrade slow pathway conduction. Procainamide inhibits arrhythmia attacks by depression of retrograde fast pathway conduction. Quinidine has also been recommended for treatment of paroxysmal supraventricular tachycardia (PSVT). Although data regarding the effects of quinidine on AV reentrant tachycardia are available, little information is available concerning the effects of quinidine on induction of AV nodal reentrant tachycardia. We systematically examined the effects of oral quinidine sulfate and atropine on induction and maintenance of AV nodal reentrant tachycardia.

Methods

Criteria for inclusion in this study were (1) a history of electrocardiographically documented recurrent PSVT that required termination with i.v. medication; (2) electrophysiologic demonstration of AV nodal reentrant tachycardia using atrial and ventricular stimulatory techniques and mapping of atrial activation sequence during induced tachycardia; (3) electrical induction of sustained PSVT with all induced episodes of PSVT requiring electrical termination on the day of control study; and (4) electrophysiologic exclusion of AV reentrant tachycardia incorporating a retrogradely conducting anomalous pathway.

Fourteen patients, two males and 12 females, ages 23-66 years (mean 44 ± 13 years [± sd]), were studied. All had a PSVT characterized by antegrade...
slow pathway and retrograde fast pathway conduction, with atrial activation simultaneous with or slightly before QRS response in 11 patients and immediately after QRS response in three patients. Patients with unusual types of AV nodal reentry were excluded from the study.\textsuperscript{21, 22}

**Electrophysiologic Studies**

Electrophysiologic studies were performed in the supine and nonsedated state after having obtained a written, informed consent. All cardiac medicines were stopped at least 3 days before the study. A #6\textsuperscript{F} quadripolar electrode catheter was positioned across the tricuspid valve percutaneously through the right femoral vein. The proximal two electrodes were used for His bundle recording while the distal two electrodes were used for ventricular pacing. A second #7 hexapolar electrode catheter was positioned in the midcoronary sinus through an antecubital vein. In this position, the proximal four electrodes were contiguous to the lateral wall of the right atrium close to the junction of superior vena cava and the right atrium. The distal two electrodes were used to record the left atrial electrogram from the coronary sinus, the middle two electrodes to record the right atrial electrogram, and the proximal two electrodes for atrial pacing. Multiple electrocardiographic leads and intracardiac electrograms were simultaneously recorded on a multichannel oscilloscopic photographic recorder (Electronic for Medicine, VR-16) at a paper speed of 100 or 150 msec/sec. Stimuli were provided by a programmable digital stimulator (Bloom and Associates) with a strength of approximately twice diastolic threshold and 2 msec long.

Conduction properties and mechanisms of PSVT were evaluated using (1) incremental atrial pacing to a paced cycle length producing AV block; (2) atrial extrastimulus testing (A\textsubscript{1}A\textsubscript{2} testing or A\textsubscript{1}A\textsubscript{2}A\textsubscript{2} testing if A\textsubscript{1}A\textsubscript{2} testing failed to induce echoes or PSVT) at a driven cycle length of 500 msec; (3) incremental ventricular pacing up to a paced cycle length producing ventriculatoatrial (VA) block; (4) ventricular extrastimulus testing at a driven cycle length of 500 msec; (5) mapping of atrial activation sequence during induced PSVT; and (6) ventricular extrastimulus testing during induced PSVT. After the control study, the hexapolar catheter was withdrawn from the coronary sinus, advanced to the right ventricular apex, and left there for subsequent electrophysiologic studies. Electrophysiologic studies were repeated after oral administration of 1.2 g (nine patients) or 1.6 g (five patients) of quinidine sulfate in four divided doses (300 mg or 400 mg every 6 hours) over 24 hours. The studies were performed 1–2 hours after the last dose. PSVT induction was also performed after 0.5–1 mg of i.v. atropine after control and quinidine studies.

**Electrophysiologic Definitions**

RA\textsubscript{1}, CS\textsubscript{1}, A\textsubscript{1}, H\textsubscript{1}, and V\textsubscript{1} are right atrial, left atrial (recorded from coronary sinus), low septal right atrial, His bundle and ventricular responses to the driven stimuli (S\textsubscript{1}). RA\textsubscript{2}, CS\textsubscript{2}, A\textsubscript{2}, H\textsubscript{2}, and V\textsubscript{2} are right atrial, left atrial, low septal right atrial, His bundle, and ventricular responses to the extrastimulus (S\textsubscript{2}). Conduction intervals, refractory periods, and echo zone were measured and defined as previously described.\textsuperscript{23} Critical AH or AV intervals are the shortest AH or AV intervals initiating PSVT.\textsuperscript{24} Diagnosis of AV nodal reentrant tachycardia was made using the previously described criteria.\textsuperscript{1, 6, 14, 15, 24–29}

Sustained tachycardia was defined when induced PSVT lasted longer than 2 minutes, requiring termination with electrical stimulation. Nonsustained tachycardia was defined when induced PSVT terminated spontaneously. The weak link of the reentrant circuit was defined as the site of increased refractoriness that prevented induction or maintenance of PSVT. The antegrade weak link was defined when echoes or PSVT were terminated with an atrial response not being followed by a QRS response. The retrograde weak link was defined when echoes or PSVT were terminated with a QRS response not being followed by an atrial response, or when an AV interval longer than the critical AV interval was achieved without inducing AV nodal reentrant atrial echoes or PSVT.

**Results**

**Induction of PSVT (table 1)**

Sustained AV nodal reentrant tachycardia was inducible in all 14 patients during the control study (figs. 1–4). PSVT was inducible with incremental atrial pacing in every patient, in 12 patients with atrial extrastimulus testing (A\textsubscript{1}A\textsubscript{2}) with definition of an echo zone (cases 2–11, 13 and 14); in two with incremental ventricular pacing (cases 10 and 13); and in one with ventricular extrastimulus testing with definition of an echo zone (case 10). Induction of PSVT with incremental atrial pacing or atrial extrastimulus testing was related to achievement of a critical AH (or AV) interval, reflecting antegrade block of a fast AV nodal pathway with resultant antegrade slow pathway conduction. Induction of PSVT with incremental ventricular pacing or ventricular extrastimulus testing reflected retrograde block of a slow AV nodal pathway as manifested by lack of VA delay. In all 14 patients, PSVT induction was also performed after administration of atropine, and all had induction of sustained PSVT after atropine.

After quinidine, sustained PSVT was inducible in only three patients, cases 1–3 (fig. 1C). In cases 4–6, PSVT was no longer sustained after quinidine (fig. 2C). Termination of PSVT in these three patients occurred when the QRS complex was not followed by an atrial response, suggesting a retrograde weak link. In cases 7 and 8, only a single AV nodal reentrant echo was induced (fig. 3C). In both patients, the echo was terminated with QRS response not followed by an atrial response, suggesting a retrograde weak link. In cases 9–14, echoes or PSVT could not be induced after quinidine (fig. 4C). In these patients, AV intervals...
longer than the critical AV interval observed during control study were achieved with either incremental atrial pacing or double atrial extrastimulus testing (A1A2A3 testing), suggesting a retrograde weak link (fig. 4C).

In the 11 patients (cases 4–14) without induction of sustained PSVT after quinidine, electrophysiologic induction of PSVT was repeated after atropine (figs. 3E and 4E); only in case 4, who had nonsustained PSVT after quinidine, was sustained PSVT inducible after atropine.

Cycle Lengths of PSVT (table 1)

The cycle lengths of PSVT ranged from 312–426 msec (mean 366 ± 34 msec [± sp]) during the control study. The cycle lengths of PSVT before and after quinidine could be compared in six patients with either sustained or nonsustained PSVT, and was 376 ± 18 msec before and 389 ± 21 msec after quinidine (NS) (fig. 1A). These findings suggest that quinidine does not affect the antegrade slow pathway conduction time.

Antegrade Properties (table 1)

In cases 2–10, 13 and 14, the antegrade echo zone could be defined during the control study (figs. 1A, 2A, 3A and 4A). In cases 1 and 12, without definition of an echo zone, PSVT could be induced with a second atrial extrastimulus (A1A2A3 testing). Only in cases 2 and 3 was the antegrade echo zone defined after quinidine (fig. 1C); the echo zone was narrowed in both patients. The echo zone could not be defined after quinidine in the other 12 patients. Abolition of the echo zone could reflect either an increase in the atrial functional refractory period or an increase in the effective refractory period of the retrograde fast path after quinidine; therefore, double atrial extrastimulus testing (A1A2A3) was performed in all 12 patients. Cases 4–8 had induction of echoes or PSVT with double atrial extrastimulus testing (figs. 2C and 3C). In cases 9–14, echoes or PSVT was not inducible with double atrial extrastimulus testing. Despite achieving AV intervals longer than the critical AV interval observed before quinidine (fig. 4C). These findings suggest that an increase in the retrograde fast pathway
refractory period rather than an increase in the atrial functional refractory period caused the abolition of the echo zone after quinidine administration.

Atrial paced cycle lengths producing AV block ranged from 240–360 msec (mean 301 ± 9 msec) before quinidine; the site of block was located at the AV node in all 14 patients. The cycle length producing AV block increased to 339 ± 11 msec (range 275–400 msec) after quinidine (p < 0.01). His bundle recordings were not performed after quinidine, so the site of block could not be ascertained.

The cycle length of PSVT (366 ± 9 msec) was

**FIGURE 1.** Recordings from case 3 showing induction of sustained paroxysmal supraventricular tachycardia (PSVT) before and after quinidine (panels A and C) and effects of quinidine on retrograde conduction (panels B and D). Shown are electrocardiographic leads I, aVF, V1, right atrial electrogram (RA), left atrial electrogram recorded from coronary sinus (CS) and His bundle electrogram (HBE). A1, H1, and V1 = atrial, His bundle, and ventricular response to basic driven beat (S1); A2, H2, and V2 = atrial, His bundle and ventricular response to the extrastimulus (S2); A* = atrial response of the echo beat or during PSVT; S = the stimulus artifact during rapid pacing; CL = cycle length. Paper speed is 100 mm/sec. Asterisk indicates ventricular beat without ventriculoatrial conduction (VA). (A) Induction of sustained PSVT at an A1A2 of 350 msec before quinidine. The CL of PSVT was 426 msec. (B) Development of VA block at a ventricular paced CL of 330 msec before quinidine. (C) Induction of sustained PSVT at an A1A2 of 300 msec after quinidine. The CL of PSVT was 470 msec. (D) Development of VA block at a ventricular paced CL of 430 msec after quinidine.
longer than the cycle length that produced AV nodal block (301 ± 9 msec) during the control study. In cases 1-6, who had induction of sustained or nonsustained PSVT after quinidine, the cycle length of PSVT (389 ± 21 msec) was longer than the cycle length that produced AV block (329 ± 20 msec). Of the eight patients with induction of only a single AV nodal reentrant echo or without induction of echoes after quinidine, four (cases 7, 8, 10, and 14) had a cycle length of PSVT (before quinidine) longer than the cycle length that produced AV block after quinidine. These findings were consistent with the observation that the antegrade limb was not the limiting factor in the induction or sustaining of PSVT after quinidine.

**Retrograde Properties (table 1, fig. 5)**

Retrograde properties of the fast pathway were evaluated by noting the longest ventricular paced cycle length that produced VA block. During the control study, the ventricular paced cycle lengths that produced VA block ranged from 280-360 msec (mean 314 ± 7 msec). After quinidine, the ventricular paced cycle length that produced VA block increased to 392 ± 13 msec (p < 0.01) (range 300-460 msec) (figs. 1B and D, 2B and D, 3B and D, and 4B and D). In all 14 patients, the cycle length of PSVT (366 ± 9 msec) was longer than the cycle length that produced VA block (314 ± 7 msec) before quinidine (figs. 1A and B, 2A and B, 3A and B, and 4A and B). In cases 7-14, in whom the ability to induce PSVT was lost after quinidine, the cycle length that produced VA block after quinidine was longer, 413 ± 14 msec, than the cycle length of PSVT observed during the control study, 358 ± 8 msec (figs. 3A and D and 4A and D). In cases 4-6, with induction of nonsustained PSVT after quinidine, the cycle length that produced VA block was longer than the cycle of PSVT (fig. 2A). In cases 1-3, with induction of sustained PSVT after quinidine, the cycle length that produced VA block was shorter than the cycle length of PSVT (fig. 1).

The retrograde effective refractory period of the VA

**Figure 2.** Recordings from case 6 show induction of sustained paroxysmal supraventricular tachycardia (PSVT) before quinidine (panel A), induction of nonsustained PSVT after quinidine (panel C), and effects of quinidine on retrograde conduction (panels B and D). A1 and V1 = atrial and ventricular response to the second extrasimulus (S2); V2 = ventricular response of the echo or PSVT beat. (A) Induction of sustained PSVT at an A1A2 of 290 msec before quinidine. The CL of PSVT was 360 msec. (B) One-to-one ventriculoatrial (VA) conduction at a ventricular paced CL of 360 msec before quinidine. (C) Induction of nonsustained PSVT with A1A2A3 testing after quinidine. Termination of PSVT occurred when the QRS complex was not followed by an atrial response (tracing was interrupted). (D) Development of VA block at a ventricular paced CL of 400 msec. The paper speed is 100 mm/sec.
conduction system could be compared in cases 3, 4, 6, 8-11 and 13 before and after quinidine. The retrograde effective refractory period increased from \( \leq 253 \pm 15 \) before to \( 348 \pm 23 \) msec after quinidine (\( p < 0.01 \)). Although the site of conduction failure could not be determined, it could have reflected a failure in the fast pathway in some patients.

**Follow-up Study**

All 11 patients with loss of the ability to induce or sustain PSVT after quinidine were discharged on quinidine sulfate at a dose similar to that during electrophysiologic studies. In three patients (cases 4, 8 and 9), the drug was discontinued due to gastrointestinal side effects. The remaining eight patients have been followed for 8 ± 2 months, and have been free of symptomatic arrhythmia.

**Discussion**

In paroxysmal AV nodal reentrant tachycardia, the reentrant circuit consists of a slow AV nodal pathway, a fast pathway (most likely intranodal), a proximal connection (probably intranodal), and a distal connection. The usual form of AV nodal reentry occurs

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**Figure 3.** Recordings from case 7 showing induction of sustained paroxysmal supraventricular tachycardia (PSVT) before quinidine (panel A), induction of a single atrioventricular (AV) nodal reentrant echo after quinidine with or without addition of atropine (panels C and E), and effects of quinidine on retrograde conduction (panels B and D). (A) Induction of sustained PSVT at an \( A_1A_2 \) of 300 msec before quinidine. The cycle length (CL) of PSVT was 360 msec. (B) One-to-one ventriculoatrial (VA) conduction at a ventricular paced cycle length of 360 msec. (C) Induction of a single echo with \( A_1A_2A_3 \) after quinidine. The echo beat was terminated with a QRS complex \( V_e \) not followed by an atrial response. (D) Development of VA block at a ventricular paced CL of 400 msec after quinidine. (E) Induction of only a single echo even after atropine. \( V_e \) was not followed by an atrial response.
with a circuit using the slow pathway for antegrade and the fast pathway for retrograde conduction.\textsuperscript{1,13} The cycle length of tachycardia reflects the sum of conduction times in all components of the reentrant circuit. A sustained tachycardia requires a cycle length of tachycardia being longer than the refractory period of any of the components of the circuit.\textsuperscript{8,38} Drugs which increase the antegrade slow pathway or the retrograde fast pathway refractory periods without lengthening of the conduction time of the circuit (especially the antegrade slow pathway conduction time) can prevent induction or sustenance of PSVT.\textsuperscript{8,12,36}

Propranolol, digitalis and verapamil increase antegrade slow pathway or the retrograde fast pathway refractory periods without lengthening of the conduction time of the circuit (especially the antegrade slow pathway conduction time) can prevent induction or sustenance of PSVT.\textsuperscript{8,12,36}

A CL-50C
\[ A, A_2 = 290 \]
RA
CS
HBE

**Figure 4.** Recordings from case 14 showing induction of sustained paroxysmal supraventricular tachycardia (PSVT) before quinidine (panel A), failure to induce echo after quinidine with or without addition of atropine (panels C and E), and effects of quinidine on retrograde conduction (panels B and D). (A) Induction of sustained PSVT at an $A_1A_2$ of 290 msec before quinidine. The cycle length (CL) of PSVT was 380 msec. (B) One-to-one ventriculoatrial (VA) conduction at a ventricular paced CL of 400 msec before quinidine. (C) Failure to induce echo with $A_1A_2A_3$ after quinidine. (D) Development of VA block at a ventricular paced CL of 400 msec. (E) Induction of a single echo after atropine. The echo beat was terminated with a QRS complex ($V_o$) followed by an atrial response.
mide potentiate induction of sustained PSVT because of an enhanced antegrade slow pathway conduction. Atropine enhances both antegrade slow and retrograde fast conduction and potentiates the ability to induce and sustain PSVT.\(^\text{36, 37}\)

The present study suggests that quinidine depresses retrograde fast pathway conduction and thus inhibits the ability to induce or sustain PSVT. These effects were substantiated by failure to induce AV nodal reentrant atrial echo with achievement of an AV interval longer than the critical AV interval during control study, loss of the ability to sustain PSVT with termination of PSVT occurring with a QRS not followed by an atrial response, and lengthening of the longest ventricular paced cycle length producing VA block. Quinidine also had no effect on the cycle length of PSVT. These findings are similar to previous observations with procainamide.\(^\text{9}\) In contrast to procainamide, quinidine did not enhance antegrade slow pathway conduction. Quinidine might have depressed antegrade slow pathway conduction in some patients, but antegrade slow pathway conduction did not appear to be a limiting factor in inducing or sustaining PSVT after quinidine. Nevertheless, the previous procainamide study was performed with i.v. drug administration and the present study of quinidine was performed with oral drug administration. A more prominent effect of hypotension or vagolysis after i.v. medication may have accounted for the difference in antegrade slow pathway properties between these two drugs.

The conduction properties of both antegrade slow and retrograde fast pathway are autonemically mediated, which may vary from day to day.\(^\text{36, 37}\) Variation in the conduction properties of either the antegrade slow or the retrograde fast pathway may render oral pharmacologic study less valid. Therefore, we administered atropine to overcome this possibility. In the 11 patients with loss of the ability to induce or sustain PSVT after quinidine, sustained PSVT occurred in only one patient after administration of atropine, which enhanced retrograde fast pathway conduction. Thus, the depressed effect of quinidine on retrograde fast pathway conduction was maintained even after elimination of vagal influence, suggesting that this effect was not subject to diurnal variation of retrograde fast pathway conduction properties. The short-term follow-up in this study further supported this observation.

In conclusion, quinidine depresses retrograde fast pathway conduction and thus inhibits induction or sustenance of PSVT in patients with AV nodal reentrant tachycardia. Oral quinidine does not enhance antegrade slow pathway conduction and, therefore, does not potentiate PSVT. It is a useful drug in preventing recurrence of PSVT.

**References**

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