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Electrophysiologic and Hemodynamic Effects of Intravenous Propafenone in Patients With Recurrent Ventricular Tachycardia

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Electrophysiologic and hemodynamic studies were performed before and after intravenous infusion of a new antiarrhythmic agent, propafenone, in 28 patients with recurrent ventricular tachycardia. Propafenone was given at a loading dose of 2 mg/kg in all patients. Subsequently, group A, the first 14 patients, received 1 mg/min and group B, the second 14 patients, received 2 mg/min continuous infusion. Propafenone exerted no effect on sinus nodal recovery time and sinoatrial conduction time, but significantly prolonged atrioventricular (AV) nodal and His-Purkinje conduction time and the QRS duration (respectively, 95 ± 19, 48 ± 10 and 120 ± 23 ms before, and 110 ± 28, 53 ± 10 and 135 ± 27 ms after; $p < 0.001$). Propafenone did not change the mean arterial blood pressure but slightly increased right atrial, pulmonary artery and capillary wedge pressures resulting in mild depression of the cardiac index (2.6 ± 0.8 liters/min per m^2 before and 2.3 ± 0.7 liters/min per m^2 after; $p < 0.001$). None of the patients were symptomatic from these changes.

In group A, propafenone did not affect the inducibility of ventricular tachycardia except for one patient whose arrhythmia was sustained before and became nonsustained after propafenone. In group B, sustained ventricular tachycardia became noninducible in three patients and nonsustained in two patients, and nonsustained ventricular tachycardia became noninducible in one patient after propafenone. Therefore, an appropriate loading dose of intravenous propafenone such as 2 mg/kg followed by 2 mg/min infusion may be given safely and may suppress ventricular tachycardia. Propafenone may be a useful addition to currently available antiarrhythmic agents.

The medical management of patients with recurrent ventricular tachycardia, a harbinger of sudden death, has been less than satisfactory. Conventional agents are frequently ineffective. Experimental agents are sometimes more efficacious, but are associated with increased side effects (1). Propafenone* is a new antiarrhythmic agent with quinidine-like and mild sympatholytic and calcium entry blocking effects (2). In the oral or intravenous form, it has been reported (3,4) to be well tolerated and very effective in suppressing frequent ventricular premature beats, with complete or greater than 90% reduction in 50 to 80% of patients.

To define the electrophysiologic and hemodynamic effects of intravenous propafenone, we studied 28 patients with recurrent ventricular tachycardia. The findings suggest that propafenone may have mild cardiac depressant effects. However, an appropriate dose of intravenous propafenone may be effective in suppressing ventricular tachycardia in certain patients.

*(2′-(-2-hydroxy-3-propylamino-propoxy)-3-phenylpropiophenone) marketed since 1977 in Germany as Rytmonorm by Knoll AB.

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Methods

Patients (Table 1). Twenty-eight patients with recurrent episodes of ventricular tachycardia were enrolled in the study. There were 25 men and 3 women, ranging in age from 18 to 71 years (mean 58). Twenty-one patients had atherosclerotic heart disease (19 with prior myocardial infarction and 2 with ventricular aneurysm), 2 patients had congestive

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cardiomyopathy, 2 patients had hypertensive cardiovascular disease, 1 patient had rheumatic valvular disease and 2 patients had no clinical evidence of structural heart disease except for the rhythm disturbance. All these patients had recurrent episodes of either sustained or nonsustained ventricular tachycardia documented by electrocardiogram. During ventricular tachycardia, all patients were symptomatic with palpitation, dizziness, syncope or angina pectoris. Four patients had aborted sudden death. Conventional antiarrhythmic agents had proven ineffective clinically in all 28 patients, who had tried an average of 2.7 ± 1.0 agents. Testing by programmed ventricular stimulation of at least one conventional agent (generally intravenous procainamide) had been unsuccessful in eight patients and eight patients also could not tolerate one or more conventional agents because of side effects. In five patients, a clinical trial of experimental agents had also failed.

Electrophysiologic study. All patients gave informed consent and studies were performed in a nonsedated, postabsorptive state. All antiarrhythmic agents had been withheld for more than five half-lives.

Catheter placement and recordings. A quadripolar electrode catheter was introduced into the right femoral vein and advanced across the tricuspid valve to record the His bundle potential. Another quadripolar electrode catheter was likewise advanced by way of the right femoral vein and placed in the high right atrium for programmed atrial stimulation or in the right ventricle for programmed ventricular stimulation. The intracardiac electrograms were simultaneously displayed with surface electrocardiographic leads V_1, I and III on a multichannel oscilloscope (Electronics for Medicine, VR-12). Recordings were made at a paper speed of 50 or 100 mm/s, using filter frequency settings of 30 to 500 Hz. Throughout the study, the blood pressure was monitored by way of a femoral artery line.

Pacing and extrastimulation. A programmed digital stimulator (Bloom & Associates) was used to deliver electrical impulses of 2.0 ms duration at 2 to 2.5 times diastolic threshold. The study protocol consisted of incremental pacing and extrastimulation as described previously (5). During extrastimulation, the right atrium or right ventricle was driven at one or more cycle lengths (S_1S_1) (usually 500 and 400 ms). An atrial or ventricular premature beat (S_2) was introduced from late diastole at progressively shorter coupling intervals (S_1S_2) after every eighth paced beat until atrial or ventricular refractoriness was encountered.

If a single ventricular premature stimulus (S_2) failed to elicit ventricular tachycardia, timed double or triple ventricular stimuli were delivered. The protocol was continued until it evoked ventricular tachycardia or until all extrastimuli failed to evoke a ventricular response (6). If programmed right ventricular stimulation failed to evoke ventricular tachycardia, a bipolar electrode catheter was introduced from the right femoral artery and placed in the left ventricle. The same study protocol was then used in the left ventricle for induction of ventricular tachycardia.

Hemodynamic study and intravenous administration of propafenone. After spontaneous or electrical termination of ventricular tachycardia to normal sinus rhythm, the right ventricular electrode catheter was withdrawn and replaced with a Swan-Ganz catheter for hemodynamic study, during which control right atrial, pulmonary artery and pulmonary capillary wedge pressures, cardiac index, pulmonary vascular resistance and systemic vascular resistance were measured.

Propafenone was given intravenously at a loading dose of 2 mg/kg of body weight over a 10 minute period in all 28 patients. Subsequently, group A, the first 14 patients, received a continuous infusion of propafenone at 1 mg/min, and group B, the subsequent 14 patients, received a continuous infusion of propafenone at 2 mg/min. During the continuous infusion, the effects of propafenone on hemodynamic variables were assessed. The Swan-Ganz catheter was then withdrawn and replaced with the previous catheter for repeat programmed atrial and ventricular stimulation. Blood samples were obtained before and during propafenone infusion for determination of plasma concentrations (7).

Definition of terms. Sinus node recovery time, sinoatrial conduction time and atrioventricular (AV) conduction intervals and refractory periods were defined and measured as conventionally described (8,9).

Inducibility of ventricular tachycardia was considered positive only if the induced repetitive ventricular beats were of the intraventricular reentrant type. Bundle branch reentrant beats (10) were not considered a positive response and were excluded from analysis. Sustained ventricular tachycardia was defined as ventricular tachycardia lasting for longer than 30 seconds or requiring electrical intervention before that time because of circulatory collapse. Nonsustained ventricular tachycardia was defined as ventricular tachycardia of at least six beats in duration, terminating spontaneously within 30 seconds.

A favorable response was defined as one in which baseline sustained ventricular tachycardia became nonsustained or noninducible, or in which nonsustained ventricular tachycardia became noninducible after drug administration.

Statistical analysis. Sinus node recovery time, sinoatrial conduction time, AV conduction intervals and refractory periods and hemodynamic variables were expressed as mean ± 1 standard deviation (SD). Paired data were analyzed using the two-tailed Student's *t* test. Unpaired data were analyzed using the unpaired Student's *t* test. A probability (p) value of 0.05 or less was considered significant.

Results

Plasma propafenone concentration. At the end of the loading dose of propafenone (2 mg/kg), which was given

Table 1. Clinical Profile

Case	Age (yr) & Sex	Cardiac Diagnosis	VT Symptoms	Previous Therapy
1	68M	ASHD, HMI	Aborted sudden death	Q, Pa, Pl, Am
2	63M	ASHD, HMI	Syncope	Q, Pa, D
3	63M	ASHD, HMI	Syncope	Pa, Pl, B, L
4	71M	ASHD, HMI	Dizziness	Pa, Pl, B, L
5	42M	RHD	Aborted sudden death	Q
6	60M	ASHD, HMI	Syncope	Q, E
7	64M	ASHD, HMI	Dizziness	Q, Pa, Pl
8	60M	ASHD, HMI	Syncope	Q, Pa, D
9	18M	None	Palpitation	Pa, D
10	67M	ASHD, HMI	Aborted sudden death	Q, Pa
11	64M	ASHD, HMI	Palpitation and chest pain	Q
12	49M	ASHD, HMI	Aborted sudden death	Q, Pa, D, Pn
13	67M	ASHD, HMI	Dizziness	Q, Pa, D, Pl
14	65M	ASHD, HMI	Syncope	Q, Pa, L
15	63F	Cardiomyopathy	Syncope	Q, Pa, D
16	65M	ASHD, HMI	Dizziness	Q, Pa, D, Pl, L, Me
17	62M	Hypertension	Syncope	Pa
18	63M	ASHD, HMI	Palpitation	Q, Pl
19	62M	ASHD, HMI	Syncope	Q, D, Pl, L
20	60M	ASHD, HMI	Palpitation	Q, Pa, D
21	61M	ASHD, HMI	Syncope	Pa, Am
22	65M	ASHD, HMI	Palpitation and chest pain	Pa, D, Pn
23	53M	Cardiomyopathy	Dizziness	Q, Pa
24	25F	None	Palpitation	Q, Pa, Pl
25	52M	ASHD, HMI	Chest pain	Pa, L, B
26	63F	ASHD, HMI	Palpitation	Q, Pa, D, L
27	66M	ASHD, HMI	Dizziness	Q, Pa, D
28	69M	Hypertension	Dizziness	Q, Pa

Am = amiodarone; ASHD = arteriosclerotic heart disease; B = bretylium; D = disopyramide; E = encainide; F = female; HMI = healed myocardial infarction; L = lidocaine; M = male; Me = mexiletine; Pa = procainamide; Pl = propranolol; Pn = phenytoin; Q = quinidine; RHD = rheumatic heart disease; VT = ventricular tachycardia.

over a 10 minute period, the plasma propafenone levels were similar in both groups of patients (2,624 ± 1,624 ng/ml in group A and 2,587 ± 1,186 ng/ml in group B; p = not significant [NS]). Continuous propafenone infusion was initiated at the end of the loading dose. Ten minutes later, the plasma levels were still comparable (1,220 ± 450 ng/ml in group A [propafenone infusion rate 1 mg/min] and 1,494 ± 490 ng/ml in group B [infusion rate 20 mg/min]; p = NS). At this time, repeat measurements of hemodynamics and AV conduction patterns were made. Twenty minutes after the initial loading dose, repeat programmed electrical stimulation was performed. The plasma propafenone concentration was higher in group B (1,447 ± 347 ng/ml) than in group A (934 ± 381 ng/ml; $p < 0.05$). The difference persisted up to completion of programmed electrical stimulation, which occurred about 50 minutes after the loading dose of propafenone (959 ± 442 ng/ml in group A and 1,564 ± 578 ng/ml in group B; $p < 0.05$).

Sinus node function (Table 2). There was no significant change in the spontaneous sinus cycle length (842 ± 172 ms before and 857 ± 165 ms after propafenone; p = NS) and sinoatrial conduction time (198 ± 123 ms before and 163 ± 79 ms after propafenone; p = NS).

Refractory periods (Table 2). There was a significant increase in the atrial effective refractory period (251 ± 50 ms before and 287 ± 74 ms after propafenone; $p < 0.05$) but not the atrial functional refractory period (295 ± 30 ms before and 317 ± 78 ms after propafenone; p = NS). The AV nodal effective and functional refractory periods were both significantly prolonged (324 ± 74 and 448 ± 68 ms, respectively, before and 364 ± 95 and 484 ± 77 ms after propafenone; both $p < 0.01$). The effective refractory period of the right ventricle was slightly increased (223 ± 32 ms before and 244 ± 32 ms after propafenone), but the change did not reach statistical significance.

AV conduction intervals (Table 3). Propafenone significantly prolonged the AV nodal conduction time (AH interval 95 ± 19 ms before and 110 ± 28 ms after propafenone; $p < 0.001$), His-Purkinje conduction time (HV interval 48 ± 10 ms before and 53 ± 10 ms after propafenone, $p < 0.001$) and intraventricular conduction time (QRS duration 120 ± 23 ms before and 135 ± 27 ms after propafenone; $p < 0.001$). There was also a slight prolongation of the QTc ($QT/\sqrt{R\text{-}R}$) interval (422 ± 42 ms before and 425 ± 40 ms after propafenone) but the change did not reach statistical significance.

Table 2. Sinus Node Function and Cardiac Refractoriness

	Control* (ms)	Propafenone* (ms)	Difference (ms)	Difference (%)	p Value
SCL	842 ± 172	857 ± 165	15	2	NS
CSNRT	319 ± 162	387 ± 210	68	21	NS
SACT	198 ± 123	163 ± 79	−35	−18	NS
AFRP	295 ± 30	317 ± 78	32	11	NS
AERP	251 ± 50	287 ± 74	36	15	<0.05
AVNFRP	448 ± 68	484 ± 77	36	8	<0.01
AVNERP	324 ± 74	364 ± 95	40	12	<0.01
RVERP	233 ± 32	244 ± 32	11	5	0.05 < p < 0.1

*Values expressed as mean ± standard deviation. AERP = atrial effective refractory period; AFRP = atrial functional refractory period; AV = atrioventricular; AVNERP = AV nodal effective refractory period; AVNFRP = AV nodal functional refractory period; CSNRT = corrected sinus nodal recovery time; NS = not significant; p = probability; RVERP = right ventricular effective refractory period; SACT = sinoatrial conduction time; SCL = sinus cycle length.

Hemodynamics (Table 4). Propafenone did not change the mean arterial blood pressure (97 ± 14 mm Hg before and 96 ± 14 mmHg after propafenone; p = NS), but significantly increased right atrial, pulmonary artery and pulmonary capillary wedge pressures (5 ± 3, 17 ± 6 and 9 ± 5 mm Hg, respectively, before and 6 ± 4, 22 ± 8 and 14 ± 6 mm Hg, respectively, after propafenone; $p < 0.05$, < 0.01 and < 0.001, respectively). The cardiac index was mildly decreased (from 2.6 ± 0.8 before to 2.3 ± 0.7 liters/min per m^2 after propafenone; $p < 0.001$). The systemic and pulmonary vascular resistances were both increased (1,610 ± 48 and 300 ± 110 dynes·s·cm^{-5}, respectively, before and 1,870 ± 500 and 470 ± 250 dynes·s·cm^{-5}, after propafenone; both $p < 0.001$). None of the patients were symptomatic from these changes. One patient (Case 4) with prior myocardial infarction developed a marked increase in pulmonary capillary wedge pressure (from 10 to 32 mm Hg), pulmonary artery pressure (from 31/5 to 55/30 mm Hg) and right atrial pressure (from 6 to 17 mm Hg) accompanied by a decrease in cardiac index (from 1.9 to 1.4 liters/min per m^2). The patient remained asymptomatic but consequently did not undergo repeat programmed electrical stimulation. These hemodynamic alterations induced by propafenone returned to baseline after intravenous furosemide treatment.

Inducibility of ventricular tachycardia. *Group A (13 patients).* Nine patients (Cases 1, 3, 6 to 9, 11, 12 and 14) had inducible sustained ventricular tachycardia in the baseline state. Ventricular tachycardia remained inducible and sustained in eight patients and became nonsustained in one patient (Case 1) after intravenous propafenone. The remaining four patients (Cases 2, 5, 10 and 13) had inducible nonsustained ventricular tachycardia in the baseline state. Nonsustained ventricular tachycardia remained inducible in these latter four patients. However, the cycle length of ventricular tachycardia was prolonged in 10 patients and remained unchanged in 3 patients. Overall, the cycle length of ventricular tachycardia increased from 290 ± 88 to 357 ± 117 ms ($p < 0.001$) (Table 5; Fig. 1).

Group B (14 patients). Eleven patients (Cases 16 to 18, 20 to 23 and 25 to 28) had inducible sustained ventricular tachycardia in the baseline state. After intravenous propafenone administration, sustained ventricular tachycardia became noninducible in three patients (Cases 16, 17 and 20) (Fig. 2), became nonsustained in two patients (Cases 18 and 23) and remained inducible and sustained in six patients (Cases 21, 22 and 25 to 28). The remaining three patients had inducible nonsustained ventricular tachycardia in the baseline state. After propafenone, ventricular tachycardia became noninducible in one patient (Case 24), became inducible and sustained in one patient (Case 19) and remained inducible and nonsustained in one patient (Case 15).

Follow-up. The seven patients (Cases 1, 16, 17, 18, 20, 23 and 24) who had a favorable response to intravenous propafenone continued oral propafenone (600 to 1,200 mg/day). Six (85%) of these seven had remained asymp-

Table 3. Atrioventricular Conduction Intervals

Interval	Control* (ms)	Propafenone* (ms)	Difference (ms)	Difference (%)	p Value
AH	95 ± 19	110 ± 28	15	16	<0.001
HV	48 ± 10	53 ± 10	5	10	<0.001
PR	169 ± 21	198 ± 26	29	17	<0.001
QRS	120 ± 23	135 ± 27	15	13	<0.001
QT_c	422 ± 42	425 ± 40	3	1	NS

*Values expressed as mean ± standard deviation. NS = not significant; p = probability.

Table 4. Hemodynamics

	Control*	Propafenone*	Difference	(%)	p Value
$\overline{BP}$ (mm Hg)	97 ± 14	96 ± 14	-1	-1	NS
$\overline{RA}$ (mm Hg)	5 ± 3	6 ± 4	1	20	<0.05
$\overline{PA}$ (mm Hg)	17 ± 6	22 ± 8	5	29	<0.01
$\overline{PCW}$ (mm Hg)	9 ± 5	14 ± 6	5	55	<0.001
HR (beats/min)	71 ± 17	70 ± 17	-1	-	NS
CI (liters/min per m^2)	2.6 ± 0.8	2.3 ± 0.7	-0.3	-12	<0.001
SVR (dynes·s·cm^{-5})	1,610 ± 480	1,870 ± 500	260	16	<0.001
PVR (dynes·s·cm^{-5})	300 ± 110	470 ± 250	170	56	<0.001

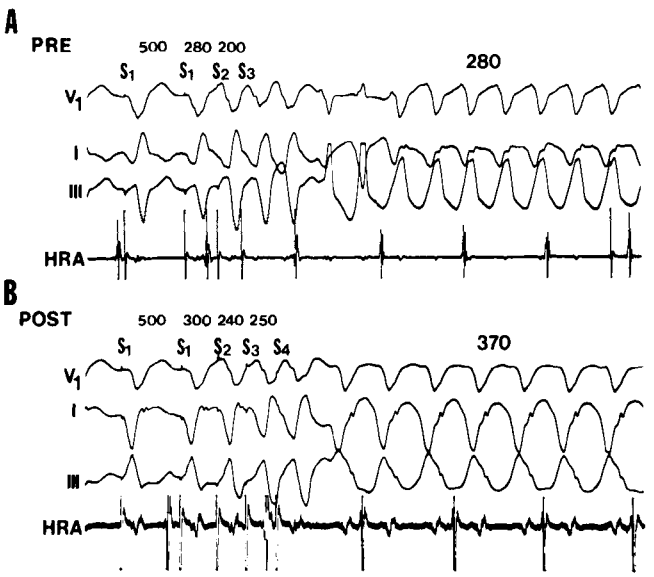
*Mean values ± standard deviation. $\overline{BP}$ = mean arterial blood pressure; CI = cardiac index; HR = heart rate; NS = not significant; p = probability; $\overline{PA}$ = mean pulmonary artery pressure; $\overline{PCW}$ = mean pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; $\overline{RA}$ = mean right atrial pressure; SVR = systemic vascular resistance.

tomatic after 11.4 ± 3.9 months. One patient (Case 1) had one episode of nonsustained ventricular tachycardia and was subsequently treated with oral amiodarone.

Of the patients who had no favorable responses to intravenous propafenone, four (Cases 3, 12, 13 and 22) were given a trial of oral propafenone as they had had no serious symptoms such as syncope or cardiac arrest associated with the occurrence of ventricular tachycardia. Two patients (Cases 12 and 13) became asymptomatic for 15.8 ± 0.3 months. One patient (Case 22) developed fast sustained ventricular tachycardia after 7 days of oral propafenone therapy and was susbsequently treated with oral amiodarone. Another patient (Case 3) had documented slow ventricular arrhythmia (100 to 120 beats/min) that was tolerated clinically.

Side effects. Of the 11 patients treated with oral propafenone, 7 developed transient metallic taste, 2 developed asymptomatic elevation of antinuclear antibody titers, 1 developed abdominal discomfort and 1 with a family history of seizure disorder developed seizures, requiring reduction of the propafenone dosage.

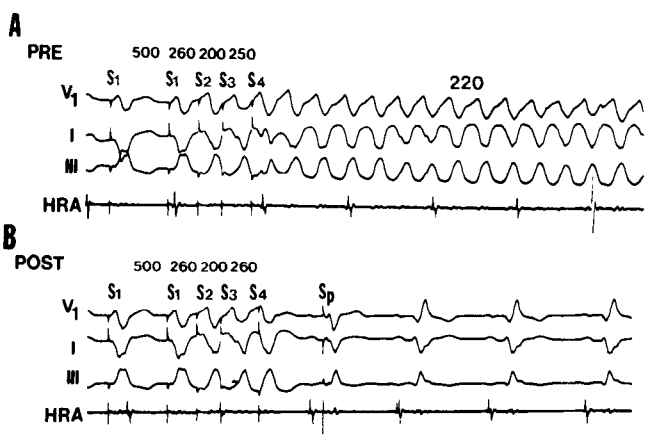
Figure 1. Case 6, group A (propafenone infusion rate 1 mg/min). **A**, Induction of sustained ventricular tachycardia in the control state before (PRE) propafenone. The tachycardia cycle length was 280 ms. The tachycardia was induced from the right ventricular apex with two extrastimuli (S_2,S_3). HRA = high right atrial intracardiac recording; V_1, I and III = standard surface electrocardiographic leads. **B**, Induction of sustained ventricular tachycardia after (POST) propafenone. The tachycardia cycle length was 370 ms. This was induced from the right ventricular outflow tract with three extrastimuli (S_2, S_3, S_4). Programmed stimulation from the right ventricular apex did not induce sustained tachycardia.



Discussion

Effects on AV conduction system. Propafenone significantly prolonged the atrial effective refractory period, increased atrioventricular (AV) node conduction time (AH

Figure 2. Case 17, group B (propafenone infusion 2 mg/min). **A**, Induction of sustained ventricular tachycardia in the control state before (PRE) propafenone. The tachycardia cycle length was 220 ms. The tachycardia was induced from the right ventricular outflow tract with three extrastimuli (S_2,S_3,S_4). **B**, Programmed ventricular stimulation in the same patient after (POST) propafenone. The tachycardia was not inducible from the same site with up to three extrastimuli or stimulation from the right or left ventricular apex. S_p = pacing stimulus from the patient's permanent ventricular demand pacemaker; other abbreviations as in Figure 1.



interval) and lengthened both the effective and the functional refractory periods of the AV node (Table 2). These findings may explain its efficacy in the suppression of certain types of supraventricular tachyarrhythmias (11). The extent to which its sympathicolytic and calcium entry blocking effects contributed is uncertain.

Propafenone has quinidine-like pharmacologic properties. These were reflected by prolongation of the His-Purkinje conduction time (HV interval) and the QRS duration (Table 3).

Effects on hemodynamics. Hemodynamically, intravenous propafenone significantly elevated pulmonary capillary wedge, pulmonary artery and right atrial pressures. The cardiac index was decreased and pulmonary and systemic vascular resistances were increased (Table 4). These findings could be seen in patients in both group A (propafenone infusion rate 1 mg/min) and group B (infusion rate 2 mg/min) and were in accordance with reports by other investigators (12,13). Although these effects are mild and generally well tolerated, we recommend that propafenone be given cautiously in patients with compromised left ventricular function.

Effects on ventricular tachycardia. The antiarrhythmic effects of intravenous propafenone were reflected by slowing of the rate of ventricular tachycardia and by suppressing the inducibility of ventricular tachycardia (Table 5, Fig. 1 and 2). Intravenous propafenone appeared to be more efficacious in suppressing the inducibility of ven-

Table 5. Ventricular Tachycardia Induction Before and After Propafenone

	Pre			Post		
Case	VT	Cycle Length (ms)	Mode of Induction	VT	Cycle Length (ms)	Mode of Induction
			Group A			
1	S	265	RV S_4	NS	400	RV S_2, spontaneous
2	NS	185	RV S_4	NS	195	RV S_4
3	S	500	RV S_3	S	590	RV S_2
4*						
5	NS	240	RV S_4	NS	250	RV S_4
6	S	295	RV S_3	S	395	RV S_4
7	S	420	RV S_3	S	520	RV S_2
8	S	260	RV S_3	S	265	RV S_3
9	S	315	RV S_2	S	410	Mechanical
10	NS	230	RV S_4	NS	245	RV S_4
11	S	310	RV OP	S	440	RV S_4
12	S	200	RV S_4	S	265	RV S_4
13	NS	280	RV S_2	NS	310	RV S_4
14	S	250	RV S_4	S	350	RV S_4
Mean ± standard deviation		290 ± 88			357 ± 117	
			Group B			
15	NS	240	LV S_2	NS	280	LV S_4
16	S	400	RV S_3	NI	—	RV, LV
17	S	195	RV S_4	NI	—	RV, LV
18	S	220	LV S_4	NS	380	LV, S_2
19	NS	365	RV S_4	S	330	RV, S_4
20	S	175	RV S_4	NI	—	RV, LV
21	S	220	RV S_4	S	300	RV S_4
22	S	300	RV S_3	S	520	RV S_2
23	S	200	RV S_3	NS	250	LV S_4
24	NS	167	RV S_3	NI	—	RV, LV
25	S	300	RV OP	S	370	RV S_3
26	S	280	RV S_4	S	375	RV OP
27	S	330	RV S_3	S	450	RV S_3
28	S	290	RV S_3	S	200	RV S_3
Mean ± standard deviation		275 ± 53			346 ± 95	

*Excluded because of hemodynamic reasons (see text). LV = left ventricle; NI = noninducible; NS = nonsustained; OP = overdrive pacing; RV = right ventricle; S = sustained; S_2 = with one extrastimuli; S_3 = with two extrastimuli; S_4 = with three extrastimuli; VT = ventricular tachycardia.

tricular tachycardia in patients in group B than in patients in group A. Only 1 of the 13 patients in group A responded compared with 6 (43%) of the 14 patients in group B. Of these six patients, four patients had no inducible ventricular tachycardia after intravenous propafenone. Group A and B patients were comparable in age (59 ± 14 versus 59 ± 11 years; p = NS), cardiac disease and baseline cycle length of ventricular tachycardia (290 ± 88 versus 275 ± 53 ms; p = NS). Therefore, we attributed the higher success rate of suppression of ventricular tachycardia inducibility to the use of a higher infusion rate (2 mg/min) in group B patients. This was supported by the finding of a significantly higher plasma propafenone level in group B than in group A patients.

When evaluating antiarrhythmic effects of intravenous propafenone, several factors should be considered. First, we studied patients (both groups A and B) who had already failed to respond to conventional antiarrhythmic agents clinically. The success rate of intravenous propafenone in suppressing the inducibility of ventricular tachycardia may conceivably be higher in patients who are not already a "refractory" group. Second, we used a rather aggressive protocol of programmed electrical stimulation; this involved three ventricular sites (two right ventricular and one left ventricular), two cycle lengths and up to three ventricular extrastimuli.

Third, the dosage employed may be another important factor. In a recent study by Karagueuzian et al. (14), propafenone was noted to be successful in abolishing spontaneous ventricular tachycardia in an acutely infarcted canine model. The loading dose was 4 mg/kg and the infusion rate was 2.2 mg/kg per min, achieving an average plasma concentration of 3 μg/ml. Understandably, the anatomic substrate and the mode of arrhythmia induction were different from ours. Nonetheless, it is quite probable that a high success rate may be attained with a higher dosage. Further studies are necessary to define the optimal clinical dosage of propafenone.

Clinical implications. Propafenone is a new antiarrhythmic agent. Intravenous infusion of propafenone at 2 mg/kg as a loading dose followed by an infusion rate of 2 mg/min is safe, and may prevent induction of sustained or nonsustained ventricular tachycardia in patients in whom conventional antiarrhythmic drugs failed clinically. However, propafenone, like most other antiarrhythmic agents, may have cardiac depressant effects. It should be given cautiously in patients with compromised left ventricular function. Assessment of the clinical efficacy of its oral form needs long-term follow-up studies.

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