The Turkish Journal of Pediatrics 32:85-92, 1990

EXPERIENCE WITH PROPAFENONE FOR THE TREATMENT OF CARDIAC ARRHYTHMIAS IN CHILDREN*

*Alpay Çeliker MD***, Sema Özer MD**, Şencan Özme MD***
*Süheyla Özkutlu MD***, Öz Kahramanyol MD*****

Summary: Çeliker A, Özer S, Özme S, Özkutlu S, Kahramanyol O. (Hacettepe University Institute of Child Health, Ankara, Turkey). Experience with propafenone for the treatment of cardiac arrhythmias in children. Turk J Pediatr 32: 85-92, 1990.

The aim of this prospective study was to evaluate the efficacy of propafenone in suppressing various arrhythmias in a group of children who were patients in the Pediatric Cardiology Unit of Hacettepe University Children's Hospital. Seven of the 13 children (53.8%) with ventricular ectopics, all three children with paroxysmal re-entry atrioventricular tachycardia, and two of the three children with paroxysmal atrial tachycardia were treated successfully with propafenone. The drug did not cause any side effects or arrhythmogenesis. The median dosage of propafenone at discharge was 300 mg/m^2/day (range 250-400 mg/m^2/day) every eight hours. Our findings confirm the efficacy and safety of propafenone for the treatment of childhood arrhythmias. *Key words: propafenone, arrhythmia, child.*

Propafenone, a drug with a membrane stabilizing effect, local anesthetic properties, and weak beta-blocking and calcium antagonist effects, has proven to be successful in the treatment of supraventricular and ventricular arrhythmias in adults[1-3]. However, experience with the administration of this drug in children is limited[4,5]. The aim of this study was to assess the antiarrhythmic effects, clinical efficacy and safety of propafenone in the short and long-term management of children with various arrhythmias.

Material and Methods

The prospective study included eighteen children aged between five years and 18 years (median age: 12 years) who had been treated with propafenone for various

* From the Hacettepe University Institute of Child Health, Ankara.
** Associate Professor of Pediatrics and Pediatric Cardiologist, Hacettepe University Institute of Child Health.
*** Professor of Pediatrics and Pediatric Cardiologist, Hacettepe University Institute of Child Health.
**** Associate Professor of Pediatrics and Pediatric Cardiologst, S.S.K. Hospital, Ankara.

arrhythmias. There were ten females and eight males. The arrhythmias were documented by 12-lead ECG, exercise testing and 24-h Holter monitoring in three children. Electrophysiologic studies were performed in two children (Cases 7 and 13).

Thirteen children had frequent ventricular ectopic activity. Three children had paroxysmal re-entry atrioventricular tachycardia, one with the Wolff-Parkinson-White (WPW) syndrome. One child had paroxysmal atrial tachycardia with frequent supraventricular ectopic activity, and one had paroxysmal atrial flutter or fibrillation. In two children (11.1%) there was associated structural heart disease (Table I). In 13 children (72.2%) up to three (median: 2) conventional anti-

TABLE I: Clinical Details of the Patients

Case	Age (Yrs)	Sex	Arrhythmia	Structural defect	Previous treatment
1	10	F	VES	no	no
2	12	F	VES	no	Epd, Prop, Quin
3	11	F	VES	no	Met, Epd, Quin
4	13	M	VES	no	no
5	15	F	VES	no	Epd, Prop, Dis
6	8	M	VES (intermittent WPW)	no	Epd, Aj, Quin
7	18	F	PRAVT	no	Dig, V, Pind
8	10	M	PRAVT (WPW)	no	no
9	6	M	VES (AES)	no	no
10	13	M	VES	no	Epd
11	13	F	VES	no	Proc
12	11	M	VES	Small VSD	Epd
13	17	F	AFL/FIB	Repaired ASD	Prop, Dig
14	12	M	VES	no	Epd, Quin
15	5	M	VES	no	Epd, Quin, Met
16	14	F	PRAVT	MI-MS	no
17	14	M	VES	no	Epd, Quin
18	6	F	PAT (AES)	no	Dig

VES–ventricular ectopics; WPW–Wolff-Parkinson-White syndrome; PRAVT–paroxysmal re-entry atrioventricular tachycardia; AES–atrial ectopics; PAT–paroxysmal atrial tachycardia; AFL/FIB–paroxysmal atrial flutter or fibrillation; Epd–epdantoin; Prop–propranolol; Quin–quinidine; Met–methoprolol; Dis–disopyramide; Aj–ajmaline; Dig–digoxin; V–verapamil; Pind–pindolol; Proc–procainamide; VSD–ventricular septal defect; ASD–atrial septal defect; MI–mitral insufficiency; MS–mitral stenosis.

arrhythmic drugs had failed to control the arrhythmias. The frequency of paroxysmal tachycardia was assessed prospectively by the use of an incidence score. Improvement in the incidence score by two or more points was considered significant.

Treatment with propafenone was introduced according to the results of previous research. The initial dose of 300 mg/^{2}/day orally or 1 mg/kg intravenously was followed by an oral maintenance dose of 300 mg/m^2/day every eight hours. Treatment was initiated in the hospital or at home, with frequent monitoring. Propafenone was used initially in three patients (16.6%); in one patient (Case 16) during spontaneous tachycardia, and in two patients (Cases 7 and 13) during electrophysiologic studies. Five children had three to five-day periods of continuous ECG monitoring. The dose of propafenone was increased up to 400 mg/m^2/day in order to control the arrhythmias.

Out-patient reassessments were at one, three, and six months and then at appropriate intervals for each patient. These included a review of symptoms, a standard 12-lead ECG, and in some cases, 24-h Holter monitoring.

Results

In-patient treatment

Sinus rhythm was achieved in all three children who had been given propafenone during their episodes of tachycardia. There was no clinically apparent negative inotropic effect in these children. All the children treated for tachycardias were free of arrhythmias on the day of discharge. Antiarrhythmic agents were continued in the four children already on treatment at the time of inclusion in the study. Propafenone was discontinued in one patient.

Ventricular ectopics were recorded daily in thirteen children and in seven patients their frequency decreased by more than 75 percent.

The median daily dose of propafenone at discharge was 300 mg/m^2/day (range: 250-400 mg/m^2/day; Table II).

Ventricular ectopics (thirteen children)

Seven patients (Cases 4, 6, 11, 12, 14, 15, 17) had total suppression of ventricular ectopic activity at their last review. These patients were not on any additional antiarrhythmic agents (Fig. 1). The other six children with ventricular ectopics continued to experience frequent ectopic activity, and they were withdrawn from propafenone treatrnent.

TABLE II: Follow-up of the Patients

VES case	Dose ($mg/m^2/day$)	Other Drugs	Outcome	Follow-up (mo.)
1	300	no	Failure	10 (W/D)
2	350	no	Failure	12 (W/D)
3	300	no	Failure	8 (W/D)
4	250	no	Success	12
5	400	no	Failure	4 (W/D)
6	275	no	Success	16
9	250	no	Failure	2 (W/D)
10	300	no	Failure	3 (W/D)
11	250	no	Success	4
12	300	no	Success	6
14	350	no	Success	7
15	250	no	Success	8
17	300	no	Success	10
PRAVT case	**Dose ($mg/m^2/day$)**	**Other Drugs**	**Outcome**	**Follow-up mo.**
7	350	no	Success	7
8	300	no	Success	6
16	250	no	Success	4
PAT or AFL/FIB case	**Dose ($mg/m^2/day$)**	**Other Drugs**	**Outcome**	**Follow-up mo.**
13	400	Dig	Failure	4 (W/D)
18	300	no	Partial	3

VES–ventricular ectopics; PRAVT–paroxysmal re-entry atrioventricular tachycardia; PAT–paroxysmal atrial tachycardia; AFL/FIB–paroxysmal atrial flutter or fibrillation; Dig–digoxin; W/D–withdrawn.

Paroxysmal re-entry atrioventricular tachycardia (three children)

Treatment with propafenone was successful in all three children. They were not on any additional antiarrhythmic agents. 24-h Holter-monitoring was planned to reassess the suppression of the arrhythmia. One case with the WPW syndrome (Case 8) continues to have anterograde conduction via the accessory pathway. Intravenous propafenone was successful in one patient (Case 16) during the episodes of tachycardia (Fig. 2).

Paroxysmal atrial tachycardia, flutter or fibrillation (two children)

One child (Case 13) responded poorly to treatment, and despite the addition of digoxin to the regimen due to troublesome episodes of tachycardia, was withdrawn from the study after four months. Another child (Case 18) in which partial suppression of arrhythmia was observed at follow-up also demonstrated,

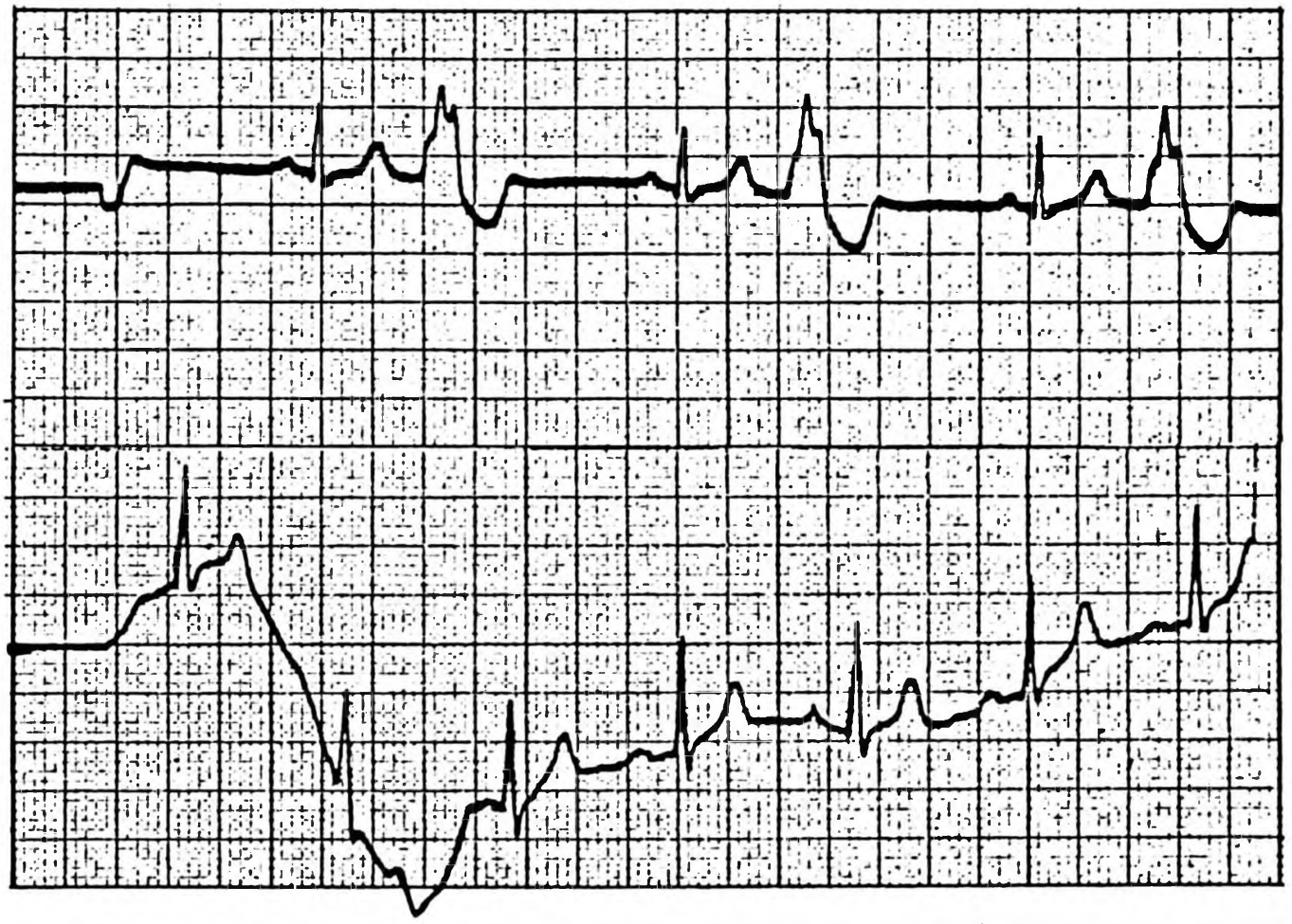

Fig. 1. The recording demonstrates a ventricular bigeminy (Lower III b). After treatment with propafenone, ventricular ectopic activity disappeared.

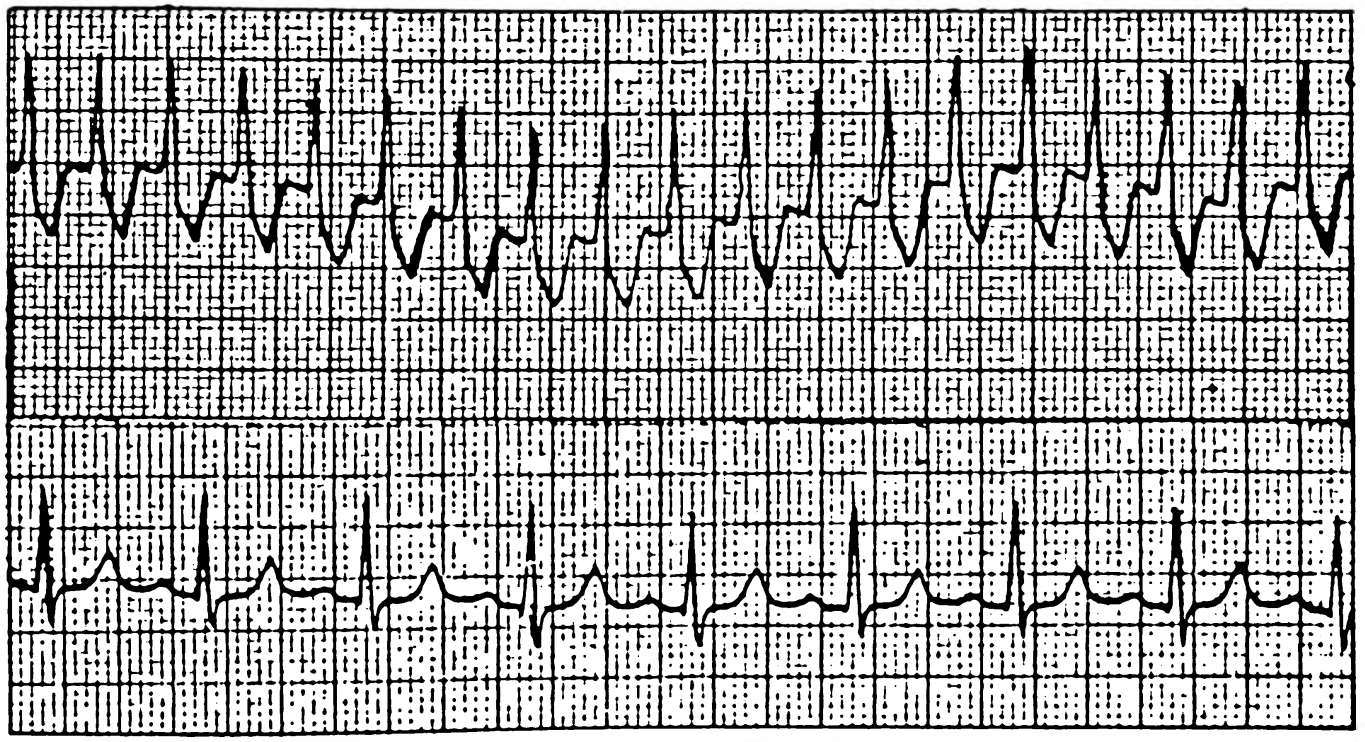

Fig. 2. Paroxysmal re-entry atrioventricular tachycardia (Case 16) terminated in a few minutes time by the administration of intravenous propafenone.

to some degree, disappearance of premature atrial contractions during 24-h Holter monitoring and recently total suppression of the tachycardia.

Side Effects and withdrawals

Treatment with propafenone did not cause major arrhythmogenesis or side effects. Seven children were withdrawn from the study because they had failed to respond to treatment (Table II).

Discussion

Propafenone is a new antiarrhythmic agent with Vaughan Williams Class Ic action[1-3]. This drug has various effects on the cardiac system and ventricular myocardium[6]. The treatment of arrhythmias in children raises particular problems related to pharmacokinetics, the nature of arrhythmias, growth, drug administration and compliance. There is always a need for new, effective and safe antiarrhythmic agents which can be used in children. Experience has shown propafenone to be an effective agent in the management of adult arrhythmias since it is effective in the control of ventricular arrhythmias and those associated with preexcitation syndromes[7-10].

In this study, we report the use of propafenone in children, in whom it was most effective against supraventricular arrhythmias when used alone. Propafenone therapy was successful in seven of thirteen (53.8%) children with ventricular ectopic activity who had a long-term follow-up. In the other six cases, no significant reduction of ventricular ectopic activity was observed. The use of propafenone has been evaluated in adult patients with frequent ventricular ectopics who responded to therapy[6,7,9]. Various studies report that suppression of ventricular ectopic activity by more than 85 percent was achieved in 60 to 80 percent of cases[6,7]. Our six patients who were withdrawn from propafenone treatment had no symptoms, and dose increments had not been considered. In six of the seven children in whom suppression of ventricular ectopic activity was achieved with propafenone, conventional antiarrhythmic drugs had failed to control the arrhythmias. This result shows the efficacy of propafenone on clinically significant ventricular ectopic activity.

The administration of propafenone alone controlled the paroxysmal re-entry atrioventricular tachycardia in three of the children in our study. Two children were difficult to manage because they had been previously resistant to conventional arrhythmic agents. Musto et al[5] reported the electrophysiologic effects and clinical efficacy of propafenone in children with supraventricular tachycardia and found that propafenone prolonged retrograde conduction in all their patients and blocked or prolonged anterograde conduction in 11 of 18 patients with accessory connections. Musto et al[6] also reported the long-term results of propafenone

therapy which was successful in three of four children with paroxysmal re-entry atrioventricular tachycardia[5]. In this study, the dosage of propafenone given in two or three divided doses was 14.3±3.8 mg/kg/day. In the study reported by Dressler et al[4], propafenone in a dose of 300 mg/m^2/day was administered three to four times a day and was effective in 85.7 percent of 35 patients[4]. This recent finding, together with ours, emphasizes the efficacy of propafenone in treating children with paroxysmal re-entry atrioventricular tachycardia.

In one child with paroxysmal atrial flutter or fibrillation that we studied, treatment failed despite the combination with digoxin. Coumel et al[9] found that as an anti-arrhythmic agent, propafenone was less effective than quinidine or amiodarone, but Connolly and Hoffert[11] reported the successful use of propafenone in the treatment of atrial flutter or fibrillation in their long-term studies. In another child in our study with paroxysmal atrial tachycardia, the episodes disappeared with the administration of this drug but complete suppression of atrial ectopic activity could not be achieved.

Intravenous propafenone was effective in controlling supraventricular tachycardia in three children (Cases 7, 13 and 16). Recent studies have shown the efficacy of propafenone in controlling supraventricular tachycardias which were no longer inducible or nonsustained during electrophysiological study[5,10].

The lack of observed side effects in our study indicates that propafenone is a promising anti-arrhythmic agent which has been evaluated in recent reports. Despite this finding, some studies have revealed a negative inotropic effect of propafenone, a fact that should be considered when this drug is used in patients with depressed left ventricular function[1-3].

In conclusion, the administration of propafenone is effective and safe in children and may be used in the management of supraventricular and ventricular arrhythmias for which a Class 1 anti-arrhythmic drug is required.

REFERENCES

1. Somberg JC, Clinical use of Class Ic antiarrhythmic drugs. In Williams EM (ed). *Anti-Arrhythmic Drugs*, New York: Springer-Verlag, 1989, pp. 235-265.
2. Somberg JC, Tepper D, Landau S. Propafenone: a new antiarrhythmic agent. *Am Heart J* 115:1274, 1988.
3. Siddoway LA, Roden DM, Woosley RL. Clinical pharmacology of propafenone: pharmacokinetic, metabolism and concentration-response relations. *Am J Cardiol* 54:9D, 1984.
4. Dressler F, Grävinghoff L, Grütte E, et al. Herzrhythmusstörungen mit Propafenon bei säuglingen und kindern. *Monatsschr Kinderheilkd* 133:154, 1985. (Eng. Abstr).
5. Musto B, D'Onofrio A, Cavallaro C, et al. Electrophysiologic effects and clinical efficacy of propafenone in children with recurrent paroxysmal supraventricular tachycardia. *Circulation*, 78:863, 1988.

6. Friedman PL, Antman EM, Singh BM. Propafenone: a new Class Ic antiarrhythmic drug for the management of ventricular arrhythmias. *Hosp Formul* 23:531, 1988.
7. Salerno DM, Granrud G, Sharkey P, et al. A controlled trial of propafenone for treatment of frequent and repetitive ventricular premature complexes. *Am J Cardiol* 53:77, 1984.
8. Prystowsky EN, Heger JJ, Chilson DA, et al. Antiarrhythmic and electrophysiologic effects of oral propafenone. *Am J Cardiol* 54:26D, 1984.
9. Coumel P, Leclercq J, Assayag P. European experience with the antiarrhythmic efficacy of propafenone for supraventricular and ventricular arrhythmias. *Am J Cardiol* 54:60D, 1984.
10. Dubuc M, Kus T, Campa MA, et al: Electrophysiologic effects of intravenous propafenone in Wolff-Parkinson-White syndrome. *Am Heart J* 117:370, 1989.
11. Connolly SJ, Hoffert DL. Usefulness of propafenone for recurrent paroxysmal atrial fibrillation. *Am J Cardiol* 63:817, 1989.