

Original Article

Pharmacological treatment of young children with permanent junctional reciprocating tachycardia

Margriet van Stuijvenberg,¹ Gertie C. M. Beaufort-Krol,¹ Jaap Haaksma,² Margreet Th. E. Bink-Boelkens¹

¹Beatrix Children's Hospital, Division of Pediatric Cardiology; ²Department of Cardiology, Thoraxcenter, University Hospital Groningen, The Netherlands

Abstract Our objective was to assess the efficacy of pharmacological treatment in reducing the incidence of permanent junctional reciprocating tachycardia in young children, or to bring the mean heart rate over 24 h to a normal level.

We included 21 children with a median age of 0.05 year seen with permanent junctional reciprocating tachycardia over the period 1990 through 2001. Of these children, two had abnormal left ventricular function. Follow-up visits were made at least every 6 months. We registered the presence of the tachycardia over 24 h, the mean heart rate over 24 h, and cardiac function. Treatment was started with propafenone alone, or in combination with digoxin as the first choice. Treatment was effective in 14 cases (67%), with either complete disappearance of the tachycardia after discontinuation of medication, or continuation in sinus rhythm with medication; partially effective in 4 cases (20%) when the mean heart rate over 24 h on the last Holter recording was less than 1 standard deviation above the normal for age; but was not effective in the remaining 3 cases (14%). In 3 patients treated with propafenone, or 13 given propafenone and digoxin, treatment was effective in 12 (75%), partially effective in 2 (13%), and ineffective in the other 2 (13%).

All 21 children had a normal left ventricular function at the end of follow-up. The median duration of follow-up was 2.4 years. Permanent junctional reciprocating tachycardia had disappeared spontaneously in one-third of the children, 5 being less than 1 year old. Adverse effects, seen in 5 cases, were mild or asymptomatic. No signs of proarrhythmia were registered.

Pharmacological treatment, either with propafenone alone, or in combination with digoxin, is safe and effective in young children with permanent junctional reciprocating tachycardia. The mean heart rate is normalized, and cardiac function is restored and preserved. Radiofrequency ablation may be delayed to a safer age, with the arrhythmia disappearing spontaneously in one-third.

Keywords: Arrhythmia; catheter ablation; drug treatment; propafenone

PERMANENT JUNCTIONAL RECIPROCATING tachycardia is a relatively rare variant of re-entry tachycardia, with retrograde conduction over a slow-conducting accessory pathway. The arrhythmia is generally incessant, often resulting in reversible cardiomyopathy.^{1,2} Treatment consists of radiofrequency ablation. In small children, however, ablation is

associated with a higher risk of severe complications, including death.^{3–8} Furthermore, studies of the natural history have revealed spontaneous disappearance of the tachycardia in some cases.⁹ Pharmacological therapy with antiarrhythmic drugs, therefore, might be a better first option, although the risk of proarrhythmia and decreased left ventricular function should be taken into account.¹⁰ It has been suggested that the tachycardia may be refractory to pharmacological treatment,^{11–13} but data published to date concerning efficacy are limited and varied. We hypothesized that, if pharmacological therapy sufficiently reduces the incidence of the tachycardia, or normalizes

Correspondence to: Margriet van Stuijvenberg, Beatrix Children's Hospital, University Hospital Groningen, PO Box 30001, 9700 RB Groningen, The Netherlands. Tel: +31 50 3612800; Fax: +31 50 3614235; E-mail: m.van.stuijvenberg@bkk.azg.nl

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the mean heart rate over 24 h, without producing important side effects, cardiac function may improve or be preserved in young children with this tachycardia, thus delaying or avoiding the need for radiofrequency ablation.

Patients and methods

In this retrospective study, we included all 21 patients seen with permanent junctional reciprocating tachycardia between 1990 and 2001. The tachycardia was defined as incessant or frequently recurring supraventricular tachycardia with a 1 to 1 atrioventricular relationship, a negative P-wave in leads II, III and aVF which occurs closer to the succeeding QRS-complex rather than the preceding one, so that the ratio RP'/RR ranges from 0.50 to 0.75.¹ The presence of the tachycardia over 24 h as assessed using Holter recording was registered at diagnosis and during follow-up. The tachycardia was deemed incessant if present over half of the time, episodic if present from one-tenth to half the time, and sporadic if present less than one-tenth of the time. If no Holter recording had been made at diagnosis before the start of medication, the presence of the tachycardia over 24 h was estimated based on the first subsequent Holter recording. The mean heart rate over a period of 24 h that included registration of the tachycardia on the Holter recording was calculated at diagnosis and during follow-up. Mean heart rate was stratified in 3 categories according to age-specific reference values. These were normal, between 1 and 2 standard deviations above normal, and equal or more than 2 standard deviations above normal.

Cardiac function was assessed by echocardiography at diagnosis and during follow-up. Left ventricular function was considered abnormal if either the end-systolic and/or end-diastolic diameter of the left ventricle exceeded the 95th centile for body weight, or the shortening fraction was below 0.28. Pharmacological treatment was started with propafenone alone, or in combination with digoxin as the first choice. Digoxin was given partly as a positive inotrope, and partly as an antiarrhythmic drug. If ineffective, treatment was switched to sotalol alone, or in combination with digoxin. Follow-up visits were made at least every 6 months. Medication was adjusted, or changed, according to growth and efficacy. The doses were registered. We did not use individual doses to assess the influence on efficacy. We did register all side effects. The electrocardiogram was used to assess bradycardia, defined as more than 2 standard deviations below normal, PR and QRS-duration, and QT_c , this being considered prolonged if more than 0.44 s. Holter recordings were used to assess the presence of the tachycardia, the mean heart rate, and signs of proarrhythmia. Follow-up ended at the last Holter recording made before April 1, 2002, or at the time of radiofrequency ablation, the latter being performed electively in our department in children older than 4 years of age, preferably with a bodyweight of 30–40 kg. Outcome was defined according to the criteria given in Figure 1. Pharmacological treatment was considered effective if the tachycardia disappeared completely after discontinuation of medication, or the patient continued in sinus rhythm with medication. It was deemed partially effective if the mean heart rate over 24 h on the last Holter recording

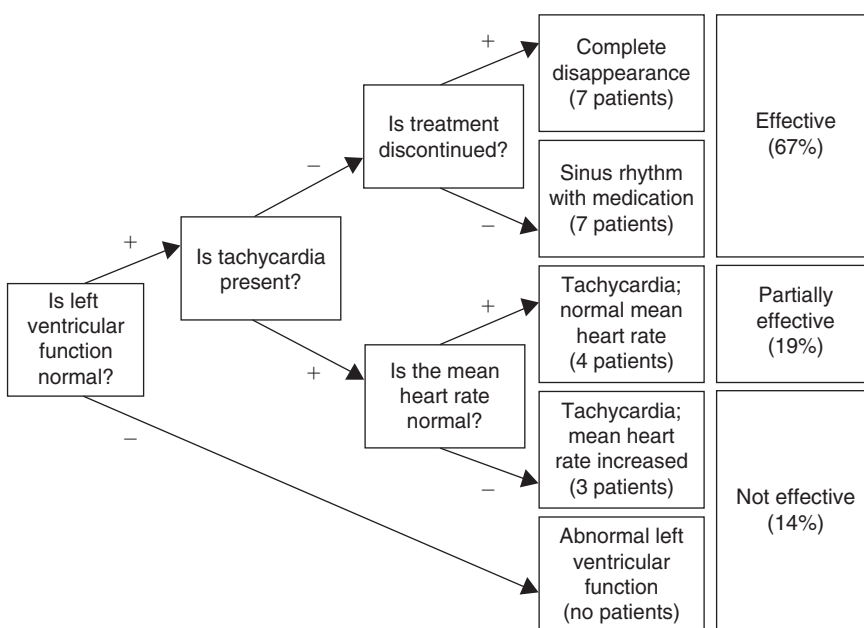


Figure 1. Definition of outcome of 21 patients treated for permanent junctional reciprocating tachycardia. At the end of follow-up, left ventricular function was normal in all the children.

was less than 1 standard deviation above normal. It was considered ineffective if these conditions were not achieved. Continuous data were given in median values and 25 and 75 percentiles. Logistic regression analysis was used to test for statistically significant differences between the mean heart rate of the study population over 24 h during follow-up and the reference group.

Reference group

Reference values for 24 h mean heart rate were estimated per age-group of 1 year, according to the distribution of mean heart rates on Holter recordings achieved in a group of 1004 children of the same age, making 1960 Holter recordings, who had visited our Holter recording ward for another reason. We excluded all children using medication, along with technical failures, recordings of less than 20 h, and recordings with third degree atrioventricular block. Only recordings with a basic sinus rhythm were included.

Results

The baseline characteristics of the 21 patients are given in Table 1. Incessant tachycardia was seen in 15 of the children (71%). Clinical and echocardiographic signs of abnormal left ventricular function were seen in 2 children. In addition, two children had a structurally abnormal heart. The tachycardia was sporadic in four children. Treatment was started because of symptoms and syncope in one case each, and because of early postoperative tachycardia in two

children with concordant atrioventricular and discordant ventriculo-arterial connections ("transposition").

At the end of follow-up, all 21 children had a normal left ventricular function. Pharmacological treatment (Fig. 1) had proved effective in 14 (67%), partially effective in 4 (19%), and ineffective in 3 children (14%). The 3 children in whom treatment was ineffective had a mean heart rate between 1 and 2 standard deviations above normal. None had a mean heart rate more than 2 standard deviations above normal. During follow-up, we performed elective radiofrequency ablation, at the age of 4.8 years, in 1 patient who had a mean heart rate between 1 and 2 standard deviations above normal.

Pharmacological treatment was effective in 8 (53%) of the 15 children with incessant tachycardia, and in all the 6 children with episodic or sporadic tachycardia (Table 2).

During follow-up, we made 205 Holter recordings. Logistic regression analysis showed no statistically significant difference between the mean heart rate over 24 h of the group studied after the initiation of pharmacological treatment and the reference group adjusted for age. The overall median duration of follow-up was 2.4 years, with 25 and 75 percentiles of 0.9 to 4.9 years. The duration of follow-up was 2.2 years, with 25 and 75 percentiles of 1.3 to 3 years, in the 7 children in whom the tachycardia disappeared completely after discontinuation of medication, 1.0 year, with 25 and 75 percentiles of 0.7 to 4.9 years, in the 7 patients remaining in sinus rhythm with medication; and 4.4 years, with 25 and 75 percentiles of 0.7 to 5.9 years, in the remaining 7 patients.

The tachycardia disappeared spontaneously in 7 of the children (33%), this occurring at a median of 0.2 year, and with 25 and 75 percentiles of 0.1 to 3.8 years. Of the 7 children, 5 were less than 1 year old. The period free from tachycardia was 0.9 year, with 25 and 75 percentiles of 0.7 to 1.2 years, before the medication was stopped. The period of follow-up free from tachycardia after cessation of medication was 0.6 year, with 25 and 75 percentiles of 0.2 to 1.5 years.

Of the 7 children in whom the tachycardia disappeared completely, 3 had incessant, 1 episodic, and 3 sporadic forms at diagnosis. The two children with episodic tachycardia, and the four with the sporadic variant, were all in sinus rhythm with or without medication at the end of the period of follow-up (Table 2).

The tachycardia disappeared in only one of the 8 children in whom it had been diagnosed before birth, in comparison to 6 of the 13 in whom it was diagnosed later. There were no other clinically relevant differences in baseline characteristics between those with the tachycardia diagnosed prenatally as opposed to postnatally.

Table 1. Baseline characteristics.

	n = 21
Age at diagnosis (years)	0.05 (0.0–0.5)
Gender (males)	11 (52%)
Birth weight (g)	3360 (3071–3805)
Gestational age (weeks)	39 (38–40)
Antenatal diagnosis	8 (38%)
Gestational age at diagnosis (weeks)	35 (32–38)
Antenatal intervention necessary	7 (88%)
Induction of labour	2
Caesarean section	3
Maternal digoxin prescription	2
Clinical symptoms	
Tachycardia only	18 (86%)
Cardiac failure	2 (10%)
Other (hepatomegaly)	1 (5%)
Rate of tachycardia on ECG at diagnosis	245 (196–273)
Rate of tachycardia on Holter at diagnosis	229 (193–253)
Presence of tachycardia at diagnosis	
Incessant	15 (71%)
Episodic	2 (10%)
Sporadic	4 (19%)

Abbreviation: ECG: electrocardiogram

Table 2. Presence of permanent junctional reciprocating tachycardia per 24 h at diagnosis versus rate at the end of follow-up.

At diagnosis	End of follow-up			0% of PJRT n = 14	
	Incessant n = 2	Episodic n = 3	Sporadic n = 2	Complete disappearance n = 7	Sinus rhythm with medication n = 7
Incessant n = 15	2	3	2	3	5
Episodic n = 2				1	1
Sporadic n = 4				3	1

Abbreviation: PJRT: permanent junctional reciprocating tachycardia

Table 3. Medication versus outcome.

Medication	Outcome		
	Effective	Partially effective	Not effective
Propafenone	3		
Digoxin and propafenone	9	2	2
Digoxin, propafenone and propranolol		1	
Sotalol	1		
Digoxin and sotalol		1	
Digoxin, sotalol and verapamil			1
Digoxin and verapamil	1		
Total	14 (67%)	4 (20%)	3 (14%)

In 5 children, the ratio of RP' to RR was 0.50. They had been diagnosed at 0.1 year, with 25 and 75 percentiles of 0.1 to 0.2 year. After a follow-up of 1.3 years, with 25 and 75 percentiles of 0.9 to 1.9 years, the tachycardia had disappeared in 4. The other one had sinus rhythm with medication.

At the end of follow-up, or before discontinuation of treatment, we had used propafenone alone in 3 cases, or propafenone in combination with digoxin in 13 cases. In these 16 patients (Table 3), treatment was effective in 12 (75%), partially effective in 2 (13%), and ineffective in the other 2 (13%).

In milligrams per kilogram body weight per day, digoxin was prescribed at a dose of 0.007 mg, with 25 and 75 percentiles of 0.006 to 0.008; propafenone at 14.7 mg, with 25 and 75 percentiles of 12.4 to 16.7; propranolol at 1.1, with 25 and 75 percentiles of 0.9 to 1.4; sotalol at 5.5, with 25 and 75 percentiles of 4.7 to 6.0; and verapamil at 5.0, with 25 and 75 percentiles of 4.2 to 6.0. The dosage of propafenone, in milligrams per square meter body surface area per day, was 306, with 25 and 75 percentiles of 257 to 373. Mild or asymptomatic adverse effects were reported in 5 patients: prolongation of the PR-interval in 4 cases; bradycardia in 2 cases; bronchial constriction in 1 case; and second-degree Wenckebach atrioventricular

block during sleep at night, normal for his age, in another case. PR-intervals did not exceed 0.20 s, and the bradycardias were asymptomatic. No signs of proarrhythmia were registered.

Discussion

Considering its low prevalence, our study of 21 children with permanent junctional reciprocating tachycardia represents a relatively large series of patients treated according to a uniform protocol. Of the children, three-quarters were treated with propafenone alone, or in combination with digoxin, this proving effective or partially effective in almost nine-tenths. Abnormal left ventricular function seen at diagnosis in 2 patients resolved shortly after initiation of treatment, and remained normal during follow-up, confirming that normalization of the mean heart rate over 24 h by pharmacological treatment is associated with restoration and preservation of cardiac function. Thus, abnormal left ventricular function at diagnosis does not justify radiofrequency ablation as the first choice of treatment in all cases.^{12,13} The low incidence of left ventricular dysfunction in our series might reflect the young age of our patients. On the other hand, prolonged periods of rapid heart rate are less tolerated by the very young. One-third of our young children showed spontaneous disappearance of the tachycardia, 5 being less than 1 year old. No recurrence was seen over 0.6 year of follow-up after discontinuation of treatment, which we consider long enough to conclude that the abnormal rhythm has disappeared. We found a higher frequency of spontaneous disappearance in those with episodic or sporadic episodes of tachycardia compared to those in whom the abnormal rhythm was incessant at diagnosis. This may suggest a more benign natural history for the episodic and sporadic forms. Still, in 3 out of the 15 patients with the incessant form, the arrhythmia disappeared completely (Table 2). Postnatal diagnosis, and a relative short RP'/RR interval, were also in favour of spontaneous disappearance. Due to

the limited numbers in our series, however, we cannot draw definite conclusions.

Lindinger et al.⁹ treated 25 patients with permanent junctional reciprocating tachycardia. In their patients, either propafenone or flecainide had the highest efficacy, in approximately two-thirds. Drago et al.¹⁴ had shown the most effective treatment to be the combination of antiarrhythmic drugs class IC or III with beta-blockers and digoxin. All of their 14 patients treated in this fashion had normal sinus rhythm at the end of follow-up. Perry et al.¹⁵ treating seven patients with flecainide, showed the drug to be effective in 6, and partially effective in the other. Pharmacological treatment with class IC or III antiarrhythmic drugs, therefore, is effective, although different protocols have been used, which makes it difficult to compare the reported efficacies. The abnormal rhythm disappeared completely in one-third of our patients, this being higher than the rate of one-fifth reported in other series.^{9,16} This may reflect the young age of our patients.

Adverse effects were either mild, or asymptomatic. This is in line with the other studies discussed.^{9,14,15} Although the numbers of our patients are small, our findings show that the proarrhythmic risk of propafenone alone or in combination with digoxin is low. Only 2 children had left ventricular dysfunction. This might have caused the low incidence of side effects of propafenone. Although the risk of proarrhythmia is higher in children with structural defects compared with those having structurally normal hearts, propafenone is a relative safe drug, probably on account of its beta-blocking capacities.¹⁷

We conclude that pharmacological treatment with propafenone, either alone or in combination with digoxin, is safe and effective in children with permanent junctional reciprocating tachycardia. The mean heart rate is normalized, and cardiac function is restored and preserved. It enables disease to progress naturally, with spontaneous disappearance in one-third of young children. If the tachycardia does not disappear, radiofrequency ablation can safely be delayed until the risks of complication have decreased.

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