The Turkish Journal of Pediatrics 1997; 39: 61-67

ADENOSINE – SENSITIVE RIGHT VENTRICULAR TACHYCARDIA IN CHILDREN*

*Alpay Çeliker MD***, *Dursun Alehan MD****, *Gülendam Koçak MD*****
*Şencan Özme MD******, *Sema Özer MD*******

SUMMARY: Çeliker A, Alehan D, Koçak G, Özme Ş, Özer S. (Cardiology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Adenosine-sensitive right ventricular tachycardia in children. Turk J Pediatr 1997; 39: 61-67.

Right ventricular outflow tachycardia is a distinct subgroup of idiopathic ventricular tachycardia (VT) with characteristic clinical and electrophysiologic properties. This study was planned to evaluate the effects of adenosine on idiopathic right ventricular tachycardia in children, and to assess the long-term efficacy of verapamil treatment. Diagnostic tests including electrocardiogram, chest roentgenogram, echocardiogram, exercise stress test and 24-hour ambulatory electrocardiographic monitoring were performed in each patient. Adenosine was administered in increasing amounts until an effective dose or a maximal dose of 300 μg/kg was reached. In adenosine-sensitive patients verapamil was given orally (3-10 mg/kg/day) for long-term suppression of arrhythmia.

Seven patients with a mean age of 10.2 ± 4.7 years were enrolled in the study. There were five male and two female patients. Six patients had VT, and one patient had frequent ventricular ectopic beats. Arrhythmia originated from the right ventricle in all patients. Adenosine was effective in terminating the arrhythmia in all patients, with a mean effective dose of 183 ± 75 μg/kg. Favorable long-term results (mean follow-up period 17 ± 8 months) were obtained with verapamil treatment at an average dose of 6.3 ± 2.2 mg/kg.

In conclusion, adenosine can be used effectively for termination of VT originating from the right ventricular outflow tract in children. In these patients verapamil may be considered as the drug of choice for long-term therapy. *Key words: adenosine, right ventricular tachycardia, children.*

Ventricular tachycardia (VT) in the absence of apparent structural heart disease is an uncommon but well-recognized entity[1]. Various descriptive terminologies, including benign, repetitive, functional, and idiopathic, have been used for this form of VT. The mechanisms underlying VT in patients with no demostrable cardiac abnormality are still not clear, and may involve triggered activity, reentry, or catecholamine-sensitive automaticity[2]. One form of idiopathic VT is characterized by a right bundle branch block morphology, suppressed by verapamil, and is considered to be caused most commonly by reentry. The second type of idiopathic VT typically originates from the right ventricle, has a left bundle branch

* From the Cardiology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.

** Associate Professor of Pediatrics and Pediatric Cardiologist, Hacettepe University Faculty of Medicine.

*** Pediatrician and Fellow in Pediatric Cardiology, Hacettepe University Faculty of Medicine.

**** Pediatrician, Hacettepe University Faculty of Medicine.

***** Professor of Pediatrics and Pediatric Cardiologist, Hacettepe University, Faculty of Medicine.

block morphology, requires adrenergic stimulation for initiation and can be terminated by adenosine and verapamil administration. Suppression or termination of the arrhythmia with adenosine suggests a cyclic adenosine monophosphate (c-AMP)-mediated, triggered activity as the arrhythmia mechanism[3].

Several studies have demonstrated the effects of adenosine on idiopathic VT in adult patients, however there is little information concerning pediatric patients. The purpose of this study was to evaluate the effects of adenosine on idiopathic right ventricular tachycardia in children and to examine the long-term results of verapamil treatment in these patients.

Material and Methods

The study population comprised seven consecutive patients with recurrent episodes of idiopathic, monomorphic, right ventricular tachycardia or frequent ventricular ectopic beats originating from the right ventricle, admitted to Hacettepe University Pediatric Cardiology Unit between March 1993 and April 1995.

After a thorough physical examination, several diagnostic tests including 12-lead surface electrocardiogram (ECG); chest roentgenogram; M-mode, two-dimensional and Doppler echocardiogram; exercise stress test with modified Bruce Protocol; and 24-hour ambulatory electrocardiographic monitoring were performed in each patient.

During VT, adenosine was administered as a rapid bolus through a peripheral vein, followed by a rapid flush of normal saline solution. The initial dose was 100 µg/kg, with each subsequent dose increased by 50 µg/kg until the desired effect was obtained or a maximal dose of 300 µg/kg was reached. Surface ECG monitoring was used for continuous recording of three leads during adenosine administration. If VT was terminated by adenosine administration, verapamil was given orally to asses its efficacy in the suppression of ventricular arrhythmia.

Results

There were five male and two female patients with a mean age of 10.2 ± 4.7 years. Four patients had sustained incessant VT, two patients (Cases 1 and 7) had short runs of VT, and one patient (Case 6) had frequent ventricular ectopic beats (Table I). Ventricular arrhythmia originated in the right ventricle (a left bundle branch block configuration and an inferior axis) in all patients (Fig. 1). Physical examination, chest roentgenogram and echocardiogram were normal in each patient, and no one had evidence of structural heart disease. VT was associated with chest pain in five patients, four of whom had palpitations as well. Two patients were asymptomatic and none of the patients experienced syncope. Previous antiarrhythmic therapy had been given to three patients for several months without success. Two patients had received propranolol or propafenone, and one patient had been treated with propafenone and mexiletine.

Table I: Clinical and Laboratory Findings of Patients

Patient	Age/Sex (year)	Symptom	QRS morphology	Exercise	Effective adenosine dose	Effective verapamil dose	Prior drug therapy	Holter
1	6/M	chest pain, palpitation	LBBB, inferior axis	VEB (+)	300 µg/kg	10 mg/kg	Propranolol	VT (nonsustained)
2	7/M	chest pain, palpitation	LBBB, inferior axis	VEB (+)	200 µg/kg	8 mg/kg	–	VT (sustained)
3	4/M	chest pain, palpitation	LBBB, inferior axis	VEB (+)	200 µg/kg	5 mg/kg	–	VT (sustained)
4	12/F	–	LBBB, inferior axis	VEB (+)	100 µg/kg	6 mg/kg	Mexiletine Propafenone	VT (sustained)
5	16/F	–	LBBB, inferior axis	VEB (+)	100 µg/kg	3 mg/kg	Propafenone	VT (sustained)
6	16/M	chest pain, palpitation	LBBB, inferior axis	VEB (-)	200 µg/kg	5 mg/kg		Frequent VEB's (couplets)
7	11/M	chest pain	LBBB, inferior axis	VEB (-)	100 µg/kg	8 mg/kg		VT (nonsustained)

F : Female.
M : Male.
LBBB : Left bundle branch block.
VEB : Ventricular ectopic beat.
VT : ventricular tachycardia.

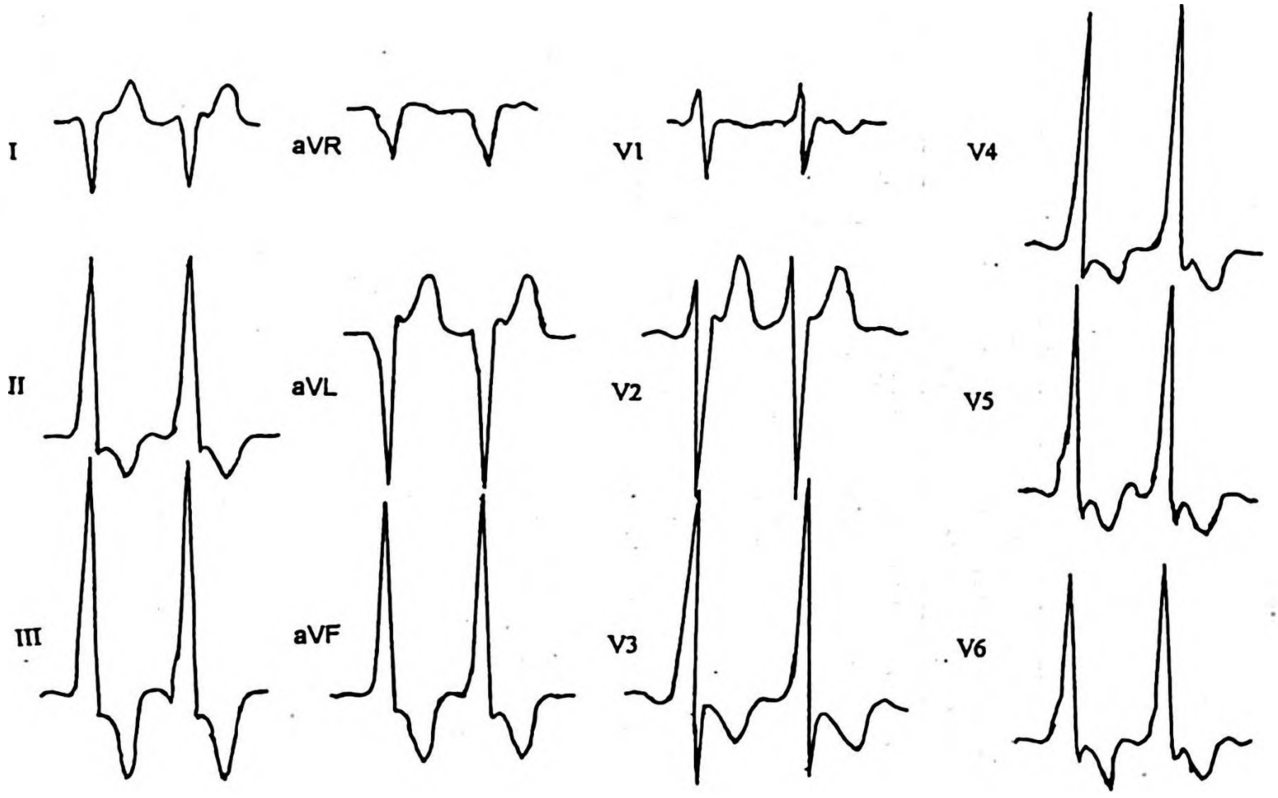

Fig. 1: Surface electrocardiogram recorded during ventricular tachycardia. The typical left bundle branch block-inferior axis morphology suggests that ventricular tachycardia originates from the right ventricular outflow tract.

Five patients had exertion-related VT, and tachycardia could be induced with an exercise stress test. However, in two patients (Cases 6 and 7) episodes of tachycardia were unrelated to exercise, and could not be initiated with an exercise stress test. Twenty-four-hour ambulatory electrocardiographic monitoring demonstrated repetitive monomorphic VT in six patients, and spontaneous ventricular premature complexes with a similar QRS configuration in all patients, usually increasing during periods of exercise.

Drug Therapy: Adenosine was effective in terminating the arrhythmia in all seven patients (Fig. 2). The mean effective dose was 183 ± 75 μg/kg (range 100-300 μg/kg), and the average time to terminate VT after a rapid bolus through a peripheral vein was 20 seconds. Afterwards, oral verapamil was given to all patients. Verapamil was effective in the suppression of arrhythmia in each patient with an average dose of 6.3 ± 2.2 mg/kg (range 3-10 mg/kg), proved with 24-hour ambulatory ECG monitoring.

Follow-up: During a mean follow-up period of 17 ± 8 months (range 5-31 months), no patient had sustained palpitations or chest pain. Verapamil-related side effects were not observed in any patient. Repeated control electrocardiograms and ambulatory monitoring revealed significant improvement of arrhythmia, with occasional premature ventricular complexes.

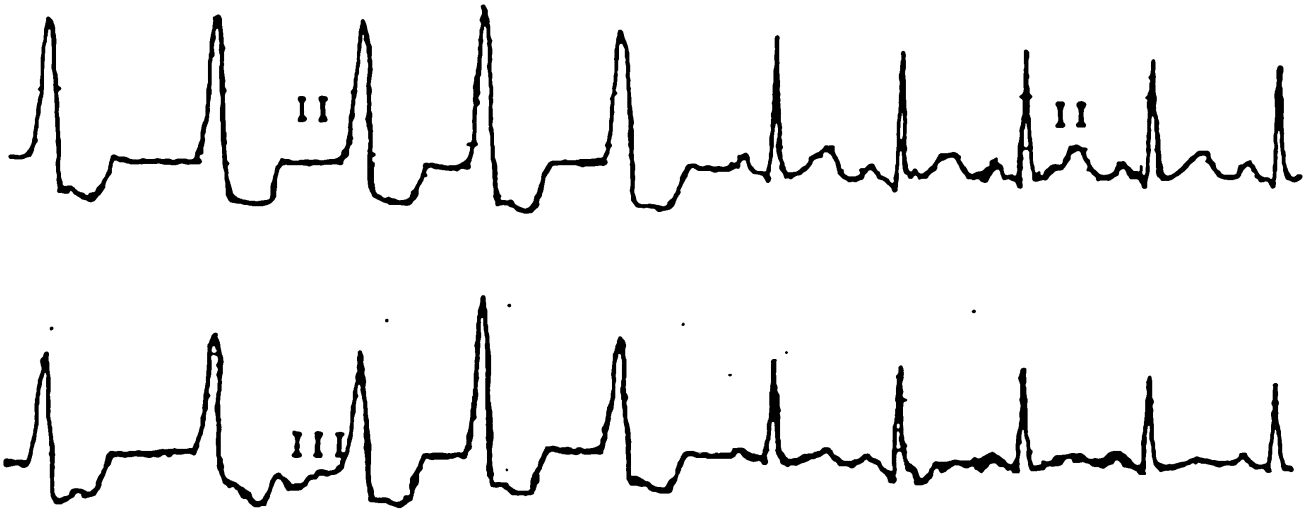

Fig. 2: Termination of ventricular tachycardia with adenosine administration. After a bolus injection of adenosine, ventricular tachycardia terminates and sinus rhythm is restored.

Discussion

Ventricular tachycardia in children, although uncommon, has received increasing attention in recent years. In the absence of structural heart disease, VT could be either right ventricular or left ventricular in origin. Right ventricular outflow tract tachycardia is a distinct subgroup of idiopathic VT, with characteristic clinical and electrophysiologic properties. Recently Lerman et al.[3] demonstrated that this form of VT is nonreentrant, nonautomatic, catecholamine-mediated, and sensitive to exogenous adenosine.

Based on the cellular mechanism of adenosine and other related electrophysiologic findings, it has been suggested that the mechanism of VT is triggered activity dependent on delayed afterdepolarizations (DADs). DADs arise during phase 4 of the action potential and are dependent on intracellular calcium (Ca^{++}) overload. Elevated Ca^{++} activates the oscillatory release of Ca^{++} from the sarcoplasmic reticulum that alters cell membrane permeability, allowing for a transient inward current responsible for afterdepolarization and triggered activity[4]. Adenosine, which inhibits the formation of c-AMP through inhibition of adenylate cyclase, prevents intracellular calcium overload, afterdepolarizations and triggered activity, and thereby terminates VT. Although controversies exist, this effect was suggested to be specific to VT but caused by c-AMP-mediated, triggered activity[5, 6].

In adult patients the efficacy of adenosine in terminating idiopathic VT originating from the right ventricle has been well defined, however there is limited information concerning pediatric patients[7, 8]. Our series is the largest to date on the use of adenosine in children with idiopathic right ventricular tachycardia. In our cases, VT attacks were suppressed in all patients by intravenous adenosine administration, suggesting that c-AMP-mediated, triggered activity is the probable cause of idiopathic right ventricular tachycardia.

Some studies on this subject have indicated that various antiarrhythmic agents, including beta blockers and verapamil, could be effective in adenosine-sensitive VT. The latter, by blocking the slow-inward calcium current, prevents intracellular calcium overload and hence can terminate triggered activity without producing direct effect on intracellular c-AMP[2, 9]. In our patients verapamil was found to be extremely effective in long-term suppression of VT and related symptoms without any significant side effects.

Cardiac catheterization, angiography and electrophysiologic studies were not performed in our patients, which may be regarded as limitations of the study. Nonetheless, examination of the electrophysiologic effects of adenosine on right ventricular tachycardia, which have been well documented in various studies, was not the aim of the study. Furthermore, the favorable clinical results obtained with drug therapy prevented us from considering invasive electrophysiologic studies in these patients.

In some cases long-term success in preventing recurrences of VT attacks may be achieved by catheter ablation[10, 11]. Because of the relative risks associated with this technique, this method of treatment was not suggested as the first-line therapy[12]. However, for those symptomatic patients whose arrhythmias cannot be controlled with antiarrhythmic drugs, catheter ablation is a reasonable alternative choice.

In conclusion, because of the antiadrenergic effects of adenosine on the ventricular myocardium and Purkinje fibers, termination of VT with adenosine may prove to be a sensitive and specific method for identifying VT caused by c-AMP-mediated, triggered activity in childhood and adolescence. In these patients verapamil is safe, highly effective and may be considered as the drug of choice for long-term therapy.

REFERENCES

1. Bhadna K, Marchlinski FE, Iskandrian AS. Ventricular tachycardia in patients without structural heart disease. Am Heart J 1993; 126: 1194-1198.
2. Lauer MR, Liem LB, Young C, Sung RJ. Cellular and clinical electrophysiology of verapamil-sensitive ventricular tachycardias. J Cardiovasc Electrophysiol 1992; 3: 500-514.
3. Lerman BB, Belardinelli L, West GA, Berne RM, DiMarco JP. Adenosine-sensitive ventricular tachycardia: evidence suggesting cyclic AMP-mediated triggered activity. Circulation 1986; 74: 270-280.
4. Lerman BB, Belardinelli L. Cardiac electrophysiology of adenosine: basic and clinical concepts. Circulation 1991; 83: 1499-1509.
5. DeLacey WA, Nath S, Haines DE, Barber MJ, DiMarco JP. Adenosine and verapamil-sensitive ventricular tachycardia originating from the left ventricle: radiofrequency catheter ablation. PACE 1992; 15: 2240-2244.
6. Lerman BB. Response of nonreentrant catecholamine-mediated ventricular tachycardia to endogenous adenosine and acetylcholine. Circulation 1993; 87: 382-390.
7. Ng K, Wen M, Yeh S, Lin F, Wu D. The effects of adenosine on idiopathic ventricular tachycardia. Am J Cardiol 1994; 74: 195-197.

8. Griffith MJ, Garratt CJ, Rowland E, Ward DE, Camm AJ. Effects of intravenous adenosine on verapamil-sensitive "idiopathic" ventricluar tachycardia. Am J Cardiol 1994; 73: 759-764.
9. Sung RJ, Shapiro WA, Shen EN, Morady F, Davis J. Effects of verapamil on ventricular tachycardias possibly caused by reentry, automaticity, and triggered activity. J Clin Invest 1983; 72: 350-360.
10. Wilber DJ, Baerman J, Oishansky B, Kall J, Kopp D. Adenosine-sensitive aventricular tachycardia: clinical characteristics and response to catheter ablation. Circulation 1993; 87: 126-134.
11. Morady F, Kadish AH, DiCario L, et al. Long-term results of catheter ablation of idiopathic right ventricular tachycardia. Circulation 1990; 82: 2093-2099.
12. Stevenson WG, Nademanee K, Weiss JN, Wiener I. Treatment of catecholamine-sensitive right ventricular tachycardia by endocardial catheter ablation. J Am Coll Cardiol 1990; 16: 752-755.