Accelerated Idioventricular Rhythm in Children: Adenosine Sensitivity and the Effects of Verapamil on Arrhythmias and QT Dispersion

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ABSTRACT

Objectives: Accelerated Idioventricular Rhythm (AIVR) is a distinct subgroup of idiopathic ventricular tachycardia (VT) with characteristic clinical and electrophysiologic properties that have not been studied extensively in children. This study was designed to assess the efficacy of adenosine and verapamil in children with this rhythm disorder and to determine the effects of verapamil on QT dispersion in these patients.

Methods: Eight patients (6 male, 2 female) with a mean age of 9.6 ± 4.8 years were enrolled in the study. QT interval analysis was performed on 12 lead surface electrocardiogram. During AIVR, intravenous adenosine was administered with increasing amount (100–300mcg/kg). If arrhythmic episode was terminated with adenosine administration, verapamil was given orally (3–10mg/kg/day) to assess its efficacy in suppression of ventricular arrhythmias and to examine its efficacy on QT dispersion.

Results: Adenosine was effective in terminating arrhythmia in all patients with a mean dose of 162 ± 74 mcg/kg. During a mean follow-up period of 17 ±8 months, verapamil was effective in suppression of arrhythmia with an average dose of 6.2 ± 2.2 mg/kg. QT dispersion decreased significantly from 81.2 ± 8.3 ms to 36.3 ± 6.0 ms (p<0.001) in patients whose arrhythmia was suppressed by verapamil therapy.

Conclusion: Idiopathic VT attacks can be suppressed by intravenous adenosine administration. For a long term therapy verapamil is a safe and highly effective drug. Moreover, verapamil decreases QT dispersion.

Keywords
Adenosine, verapamil, accelerated idioventricular rhythm, QT dispersion, children
Introduction

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. But the mechanisms underlying VT occurring in children with no demonstrable cardiac abnormality are still not clear, and may involve triggered activity, reentry, or catecholamine-sensitive automaticity (2). One form of idiopathic VT, termed slow ventricular tachycardia or accelerated idioventricular rhythm (AIVR), is thought to be benign in children but it can be association with several conditions. Suppression or termination of the arrhythmia with adenosine may occur and this suggests a cyclic adenosine monophosphate (c-AMP)–mediated triggered activity as the arrhythmia mechanism (3).

Recently increased differences in durations of QT intervals (QT dispersion) in individual electrocardiographic leads are believed to reflect increased inhomogeneity in myocardial repolarization, which is a substrate for the development of ventricular arrhythmias (4). Consequently, measurement of QT dispersion has shown to have clinical application as a method of assessing both arrhythmia risk (increased
dispersion), and antiarrhythmic drug efficacy (decreased dispersion) (5-7).

Although several studies have demonstrated the effects of adenosine on idiopathic VT, there is not much information about AIVR concerning pediatric patients and we are unaware of any previous report investigating the effects of verapamil on QT dispersion in these patients. Therefore this study was designed: 1) to investigate the effects of adenosine on AIVR children, 2) to assess the efficacy of long term verapamil treatment in suppression of ventricular arrhythmia, and 3) to ascertain whether verapamil affects QT dispersion in these patients.

Methods

The study population comprised of eight consecutive patients with recurrent episodes of AIVR, 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 testing with modified Bruce Protocol, and 24-hour ambulatory ECG monitoring were performed in each patient. QT interval analysis was performed on 12-lead surface electrocardiograms, recorded simultaneously at 25 mm/sec speed. QT interval was taken from the onset of the QRS to the end of the T wave (return to the T/P baseline). If U waves were present the QT interval was measured to the nadir of the curve between the T and U waves. For each lead, wherever possible, three consecutive cycles were measured and an average QT interval was calculated. Measurements were performed manually by a single investigator (D.A). QT dispersion, defined as the difference between maximum and minimum QT intervals, was calculated in ECGs in which at least 10 leads were measurable.

During AIVR, adenosine was administered as a rapid bolus through a peripheral vein, and was followed by a rapid flush of normal saline solution. The initial dose was 100 g/kg with each subsequent dose increased by 50 g/kg until desired effect was obtained or maximal dose of 300 g/kg was reached. Surface ECG monitoring was used for continuous recording of three leads during adenosine administration. If arrhythmia was terminated by adenosine administration, verapamil was given orally (3-10 mg/kg/day) to assess its efficacy in suppression of ventricular arrhythmia and to examine its effects on QT dispersion.

The Wilcoxon signed rank test was used for statistical analysis. A p value <0.05 was considered significant.

Results

There were six male and two female patients with a mean age of 9.6 ± 4.8 years. Five patients had sustained incessant tachycardia, three patients (case 1 and 7) had short runs of AIVR. Ventricular arrhythmias had a left bundle branch block configuration and a rightward axis suggesting the right ventricular outflow tract site of origin (Fig. 1). Physical examination, chest roentgenogram and echocardiogram were normal in each patient, and no one had evidence of structural heart disease. AIVR was associated with chest pain in six patients and four of them 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 received propranolol or propafenone, and...
one patient was treated with propafenone and mexiletine.

Six patients had exertionally related AIVR, in whom tachycardia could also be induced with exercise stress test. However in two patients (case 6 and 7) episodes of tachycardia were unrelated to exercise, and could not be initiated with exercise stress test. 24-hour ambulatory ECG monitoring demonstrated repetitive monomorphic VT in all patients.

**Drug Therapy**

Adenosine was effective in terminating arrhythmia in all 8 patients (Fig. 2). The mean effective dose was 162 ± 74 g/kg (range 100-300 g/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 suppression of arrhythmia in each patient with an average dose of 6.2 ± 2.2 mg/kg (range 3-10 mg/kg), proved with 24-hour ambulatory ECG monitoring.

**QT Dispersion**

The mean QT dispersion prior to verapamil treatment was 81.2 ± 8.3 milliseconds. On verapamil therapy QT dispersion decreased to 36.3 ± 6.0 milliseconds, which was statistically significant (p<0.001) (Table 2) (Fig. 3).

**Follow-up**

During a mean follow-up 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. Repeat control electrocardiograms and ambulatory monitorings revealed significant improvement of arrhythmia, with occasional premature ventricular complexes.

**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 is sensitive to exogenous adenosine. Based on cellular mechanism of adenosine and other related electrophysiologic findings, they suggested that the mechanism of VT was due to triggered activity dependent on delayed afterdepolarizations (DAD’s). DAD’s arise during phase 4 of the action potential and are dependent on intracellular calcium (Ca++) overload. Elevated Ca++ activates 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 (8). Adenosine, which inhibits the formation of c-AMP through inhibition of adenylate cyclase, prevents intracellular calcium overload, afterdepolarizations, triggered activity, and thereby terminates VT. Although controversies exist, (9) this effect was suggested to be specific to VT only caused by c-AMP mediated triggered activity (10).

In adult patients the efficacy of adenosine in terminating idiopathic VT originating from right ventricle is well defined, (11,12) however there is limited information concerning pediatric patients. 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 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 effects on intracellular c-AMP (2,13). In our patients verapamil was found to be extremely effective in long term suppression of VT and related symptoms without any significant side effects.

In some cases long term success in preventing recurrences of VT attacks may be achieved by catheter ablation (14,15). Because of the relative risks of catheter ablation, this method of treatment was not suggested as the first line therapy (16). However, for those symptomatic patients whose arrhythmias can not be controlled with antiarrhythmic drugs, catheter ablation is a reasonable alternative choice.

One of the important findings in this study that should be emphasized was the effects of verapamil on QT dispersion. We are unaware of any previous reports evaluating this effect. To our knowledge this is the first study that demonstrates a significant reduction in QT dispersion in adenosine sensitive VT during verapamil therapy. It is proposed that increased differences in durations of QT intervals in individual electrocardiographic leads reflect inhomogeneity in myocardial repolarization, which is an arrhythmogenic factor. This has led to the idea that if QT dispersion reflects inhomogeneity of myocardial repolarization, which provides the substrate for arrhythmias, then increased QT dispersion should be associated with increased arrhythmia risk, and decreased QT dispersion with decreased arrhythmia risk (17). We think that our finding of decreased QT dispersion in patients whose arrhythmia is suppressed by verapamil therapy supports this idea.

Verapamil acts predominantly on the slow calcium current in cells of the sinoatrial and atrioventricular nodes, causing a decrease in the rate of phase 4 automaticity, a slowing of phase 0 depolarization, a slowing of phase 3 repolarization, and a prolongation of refractoriness and conducting time (18). Except for a slight decrease in plateau amplitude, its effect on the normal fast response action potential is negligible. However under pathologic conditions, verapamil can affect injured cells of ventricular or atrial tissue that may deviate from their normal fast-response characteristics (19). Apart from its effects on delayed afterdepolarization, verapamil is also effective in inhibition of calcium current, important in generating early afterdepolarization. It inhibits spontaneous automaticity, inherent to normally polarized Purkinje cells and spontaneous automaticity occurring at depolarized membrane potentials (20,21). These effects may be responsible for the reduction of QT dispersion, demonstrated in our study. However the effects of verapamil on QT dispersion and myocardial repolarization have yet to be clarified.

**Study Limitations**

Angiocardiography and electrophysiologic studies were not performed in our patients; which may be regarded as limitations of the study. But the favorable clinical results obtained with drug therapy and the presence of various studies documenting electrophysiologic effects of adenosine on right ventricular tach-
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. Although further studies are needed to identify the effects of verapamil on myocardial repolarization, our finding of decreased QT dispersion in patients treated effectively with verapamil, suggests that QT dispersion is likely to be important in the assessment of the therapeutic efficacy of antiarrhythmic strategies.

### Table 1

Clinical and laboratory findings of patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age / Sex (year)</th>
<th>Symptom</th>
<th>QRS morphology</th>
<th>Exercise</th>
<th>Effective Adenosine dose</th>
<th>Effective Verapamil dose</th>
<th>Prior drug therapy</th>
<th>Holter</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6/M</td>
<td>chest pain, palpitation</td>
<td>LBBB, rightward axis</td>
<td>VEB (+)</td>
<td>300 g/kg</td>
<td>10 mg/kg</td>
<td>Propranolol</td>
<td>VT (nonsustained)</td>
</tr>
<tr>
<td>2</td>
<td>7/M</td>
<td>chest pain, palpitation</td>
<td>LBBB, rightward axis</td>
<td>VEB (+)</td>
<td>200 g/kg</td>
<td>8 mg/kg</td>
<td>-</td>
<td>VT (sustained)</td>
</tr>
<tr>
<td>3</td>
<td>4/M</td>
<td>chest pain, palpitation</td>
<td>LBBB, rightward axis</td>
<td>VEB (+)</td>
<td>200 g/kg</td>
<td>5 mg/kg</td>
<td>-</td>
<td>VT (sustained)</td>
</tr>
<tr>
<td>4</td>
<td>12/F</td>
<td>-</td>
<td>LBBB, rightward axis</td>
<td>VEB (+)</td>
<td>100 g/kg</td>
<td>6 mg/kg</td>
<td>Mexiletine Propafenone</td>
<td>VT (sustained)</td>
</tr>
<tr>
<td>5</td>
<td>16/F</td>
<td>-</td>
<td>LBBB, rightward axis</td>
<td>VEB (+)</td>
<td>100 g/kg</td>
<td>3 mg/kg</td>
<td>Propafenone</td>
<td>VT (sustained)</td>
</tr>
<tr>
<td>6</td>
<td>16/M</td>
<td>chest pain, palpitation</td>
<td>LBBB, rightward axis</td>
<td>VEB (-)</td>
<td>200 g/kg</td>
<td>5 mg/kg</td>
<td>-</td>
<td>Frequent VEB’s (couplets)</td>
</tr>
<tr>
<td>7</td>
<td>11/M</td>
<td>chest pain</td>
<td>LBBB, rightward axis</td>
<td>VEB (-)</td>
<td>100 g/kg</td>
<td>8 mg/kg</td>
<td>-</td>
<td>VT (nonsustained)</td>
</tr>
<tr>
<td>8</td>
<td>5/M</td>
<td>chest pain</td>
<td>LBBB, rightward axis</td>
<td>VEB (+)</td>
<td>100 g/kg</td>
<td>5 mg/kg</td>
<td>-</td>
<td>VT (sustained)</td>
</tr>
</tbody>
</table>

F = female; M = male; LBBB = left bundle branch block; VEB = ventricular ectopic beat; VT = ventricular tachycardia
Accelerated Idioventricular Rhythm in Children: Adenosine Sensitivity and the Effects of Verapamil on Arrhythmias and QT Dispersion

**Table 2**

<table>
<thead>
<tr>
<th>Patient</th>
<th>QTd (before therapy)</th>
<th>QTd (after therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>78 ms</td>
<td>25 ms</td>
</tr>
<tr>
<td>2</td>
<td>84 ms</td>
<td>40 ms</td>
</tr>
<tr>
<td>3</td>
<td>82 ms</td>
<td>44 ms</td>
</tr>
<tr>
<td>4</td>
<td>75 ms</td>
<td>38 ms</td>
</tr>
<tr>
<td>5</td>
<td>82 ms</td>
<td>32 ms</td>
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<tr>
<td>6</td>
<td>76 ms</td>
<td>34 ms</td>
</tr>
<tr>
<td>7</td>
<td>92 ms</td>
<td>42 ms</td>
</tr>
<tr>
<td>8</td>
<td>80 ms</td>
<td>36 ms</td>
</tr>
<tr>
<td>Average</td>
<td>81.2±8.3 ms</td>
<td>36.3±6 ms</td>
</tr>
</tbody>
</table>

**KAYNAKLAR**


