Original Article

**Infantile Tachyarrhythmia: Management Strategy and Short-Term Results in a High-Volume Referral Center**

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**ABSTRACT**

**Background:** Arrhythmia is an uncommon but serious cause of the admission of neonates and infants to emergency wards. The rarity of the condition creates challenges in the diagnostic and therapeutic process.

**Methods:** The study was conducted in Rajaie Cardiovascular Medical and Research Center, Tehran, Iran. All infants (aged ≤ 12 mon) with tachyarrhythmias admitted within a 2-year period between September 2014 and August 2016 were included. Stepwise drug therapy based on the mechanism of the arrhythmia was selected for the whole study population. In cases refractory to drug therapy, catheter ablation was performed.

**Results:** Of 55 cases, 47 infants were treated with antiarrhythmic drugs, 3 (with atrial flutter) received cardioversion, and 3 were treated with catheter ablation. In 1 case (atrial tachycardia), the arrhythmia was eliminated after a single dose of adenosine, and in another (atrial tachycardia), the arrhythmia was eliminated spontaneously. No mortality was reported.

**Conclusions:** Most infantile arrhythmias are controllable with available antiarrhythmic drugs. Catheter ablation is a good choice for refractory cases. *(Iranian Heart Journal 2020; 21(3): 128-135)*

**KEYWORDS:** Infantile tachyarrhythmia, Ablation, Antiarrhythmic drugs

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The prevalence of arrhythmic events in infants is less clear because some of these events in this age group may be resolved spontaneously without a diagnosis. Large registries have estimated an incidence rate of about 24 per 100,000 live births. The rarity of arrhythmias in infants contributes to some challenges in the field of pediatric electrophysiology, including the lack of high-quality evidence supported by large clinical trials.
Almost all types of arrhythmias seen in adults and older children can be seen in infants. Narrow complex tachycardias are the most common type of arrhythmia in infants and encompass atrioventricular reentrant tachycardias, atrial tachycardias, atrioventricular reentrant tachycardias, and junctional ectopic tachycardias. Ventricular tachycardias may also present as narrow complex tachycardias in infancy.

The acute treatment of infantile arrhythmias includes vagal maneuvers, medical therapy, and cardioversion. Chronic medical therapy is required for most patients. Catheter ablation is another effective method for the elimination of the arrhythmia in specific conditions.

There is, however, a dearth of large clinical trials in the existing literature to guide the medical management of these patients. We conducted the present study to evaluate the efficacy of commonly used drugs in the treatment of tachyarrhythmias in infants. Definitive recognition of the mechanism of the arrhythmia was the mainstay of the selection of the antiarrhythmic drug. We also applied ablation procedures for refractory arrhythmias and evaluated the results.

**METHODS**

This prospective study was conducted after obtaining medico-legal approval at Rajaie Cardiovascular Medical and Research Center, which is the Iranian referral center for pediatric arrhythmias. All infants (aged ≤12 mon) with incessant cardiac arrhythmias admitted between September 1, 2014 and August 31, 2016 were included. Patients with ectopic beats and non-sustained arrhythmias were not included. Infants with a history of cardiac surgery were excluded from the study. Arrhythmia management was done in accordance with the available guidelines and consensus statements.

In all the patients, standard medical history was adopted, and 12-lead standard electrocardiography (ECG), simple chest radiography, and transthoracic echocardiography were done. For all regular QRS arrhythmias with stable hemodynamics, 100 μg/kg of adenosine was prescribed as a rapid intravenous injection. The mechanisms of the arrhythmias were established by an expert pediatric cardiac electrophysiologist based on the ECG pattern during the arrhythmia, baseline ECG, and response to adenosine. Further therapies were planned on the basis of the mechanisms of the arrhythmias.

In cases with atrial flutter/atrial fibrillation, direct current cardioversion (1 J/kg) was conducted. After conversion to sinus rhythm, no more antiarrhythmic agent was prescribed.

Junctional ectopic tachycardias were managed with intravenous amiodarone. Amiodarone was started with a bullous dose of 5 mg/kg and then continued with a dose of 5 μg/kg/min. In refractory cases, the infusion dose was increased up to 10 μg/kg/min. After a 24-hour sinus rhythm, oral amiodarone substituted the infusion.

Ventricular tachycardias were treated as junctional ectopic tachycardias. The initial therapy was started with amiodarone. Amiodarone was selected as the first choice due to the availability of the drug and the center’s experience as regards its long-term infusion in children. In refractory cases (no control for more than 48 hours or frequent episodes of recurrence), propranolol was added.

For regular QRS arrhythmias converted to sinus rhythm (temporarily or permanently) with adenosine, stepwise chronic therapy was conducted. The drugs used for this stepwise therapy were as follows:

**Step 1:** oral propranolol with the starting dose of 2 mg/kg/d in 3 divided doses, increased up to 4 mg/kg in refractory cases

**Step 2:** oral propranolol plus oral flecaïnide with the starting dose of 3 mg/kg in 3
divided doses, increased up to 5 mg/kg in refractory cases

**Step 3:** oral flecainide plus oral sotalol with the starting dose of 2 mg/kg in 2 divided doses increased up to 5 mg/kg in refractory cases

**Step 4:** oral flecainide plus oral sotalol plus oral propranolol with the abovementioned doses

**Step 5:** oral propranolol plus oral amiodarone with the starting dose of 5 mg/kg/d in 2 divided doses increased up to 10 mg/kg in refractory cases

**Step 6:** discontinuing all antiarrhythmic drugs and performing catheter ablation

The endpoint of the study was the completion of the period of 1 year after the first arrhythmia episode.

**Statistical Analysis**

The statistical analyses were carried out using IBM SPSS Statistics, version 19, for Windows (IBM Inc, Armonk, NY). The nominal variables were described as counts (%). These data were compared between the subgroups via the Pearson $\chi^2$ or Fisher exact test. A $P$ value of less than 0.05 was considered statistically significant.

**RESULTS**

Fifty-five infants with arrhythmias, aged between 1 day and 12 months, were included. Thirty-four (62%) patients were younger than 30 days at the time of admission. The demographic, echocardiographic, and ECG findings of the study population are summarized in Table 2.

Echocardiography revealed structural heart diseases in 21 patients, 15 of whom had simple defects such as small septal defects and patent ductus arteriosi. Six patients had complex cardiac lesions: the Ebstein anomaly of the tricuspid valve in 4, the tetralogy of Fallot in 1, and the abnormal origin of the right pulmonary artery from the ascending aorta in 1.

Orthodromic atrioventricular reciprocating tachycardias were the most common form of arrhythmias, followed by atrial tachycardias in the neonates and ventricular tachycardias in the larger infants.

In 3 patients, the injection of adenosine unmasked flutter waves. These 3 patients were successfully treated with cardioversion (direct current shock, 1 J/kg), and no chronic antiarrhythmic agent was prescribed.

Forty-five cases had focal atrial tachycardias, atrioventricular reciprocating tachycardias, or atrioventricular nodal reciprocating tachycardias. The arrhythmia was eliminated spontaneously before any antiarrhythmic therapy in 1 patient without recurrence. (The ECG characteristics of this patient indicated a focal atrial tachycardia.) There was another patient with a focal atrial tachycardia for whom permanent sinus rhythm was reestablished with adenosine. For the remaining 43 patients, the first step drug therapy (oral propranolol) was commenced. This medication, however, was successful only in 7 patients; the others suffered a recurrence of arrhythmias during the follow-up. For the patients who experienced arrhythmia recurrence, the second step drug therapy (flecainide plus propranolol) was commenced, which proved effective in 23 cases. Step 3, 4, and 5 drugs were effective in 10 patients, while the remaining 3 subjects were refractory to the combined medications. Those 3 patients refractory to the drug regimen underwent catheter ablation.

Overt ventricular pre-excitation, termed “Wolff-Parkinson–White (WPW)”, was observed in 12 cases. All these cases were admitted with regular QRS tachycardias. Propranolol alone was effective for the chronic control of the supraventricular tachycardia in only 1 case of these patients, while 9 cases were controlled by adding
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One of the remaining cases was controlled with amiodarone plus propranolol. For the other case, radiofrequency ablation was done successfully. 18

Table 1: Demographic, echocardiographic, and ECG findings of the study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ages≤30 d n (%)</th>
<th>Age 1-12 mon n (%)</th>
<th>Total n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic Data</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Male</td>
<td>20 (59)</td>
<td>16 (76)</td>
<td>36 (65)</td>
<td>0.15</td>
</tr>
<tr>
<td>Female</td>
<td>14 (41)</td>
<td>5 (24)</td>
<td>19 (35)</td>
<td>-</td>
</tr>
<tr>
<td>ECG</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Regular QRS</td>
<td>30 (88)</td>
<td>12 (57)</td>
<td>42 (76)</td>
<td>0.02</td>
</tr>
<tr>
<td>Wide QRS</td>
<td>4 (12)</td>
<td>9 (43)</td>
<td>13 (24)</td>
<td>0.02</td>
</tr>
<tr>
<td>Tachyarrhythmia Type</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FAT</td>
<td>11 (32)</td>
<td>2 (9)</td>
<td>13 (23)</td>
<td>0.10</td>
</tr>
<tr>
<td>AVRT</td>
<td>18 (53)</td>
<td>12 (57)</td>
<td>30 (55)</td>
<td>0.78</td>
</tr>
<tr>
<td>AVNRT*</td>
<td>1 (3)</td>
<td>1 (5)</td>
<td>2 (4)</td>
<td>1.00</td>
</tr>
<tr>
<td>AFL</td>
<td>3 (9)</td>
<td>0 (0)</td>
<td>3 (5)</td>
<td>0.27</td>
</tr>
<tr>
<td>JET</td>
<td>0 (0)</td>
<td>1 (5)</td>
<td>1 (2)</td>
<td>0.38</td>
</tr>
<tr>
<td>VT</td>
<td>1 (3)</td>
<td>5 (24)</td>
<td>6 (11)</td>
<td>0.02</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Simple Cardiac defects</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(ASD, VSD, PDA)</td>
<td>13 (38)</td>
<td>2 (10)</td>
<td>15 (27)</td>
<td>-</td>
</tr>
<tr>
<td>Complex cardiac defects</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(Ebstein, TOF, hemitruncus**)</td>
<td>4 (12)</td>
<td>2 (10)</td>
<td>6 (11)</td>
<td>-</td>
</tr>
<tr>
<td>No cardiac defect</td>
<td>17 (50)</td>
<td>17 (80)</td>
<td>34 (62)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* Diagnosis of AVNRT was based on very short RP intervals, response to adenosine, and no pre-excitation at the baseline ECG.

** Abnormal origin of the right pulmonary artery from the ascending aorta

SVT, Supraventricular tachycardia; FAT, Focal atrial tachycardia; AFL, Atrial flutter; AVRT, Atrioventricular reciprocating tachycardia; AVNRT, Atrioventricular nodal reciprocating tachycardia; JET, Junctional ectopic tachycardia; VT, Ventricular tachycardia; ASD, Atrial septal defect; VSD, Ventricular septal defect; PDA, Patent ductus arteriosus; TOF, Tetralogy of Fallot

Table 2: Final successful strategies in the study population

<table>
<thead>
<tr>
<th>Arrhythmia Type</th>
<th>Treatment</th>
<th>Number of Patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAT, AVRT, AVNRT</td>
<td>No drug</td>
<td>2(3.6)</td>
</tr>
<tr>
<td></td>
<td>Step 1 drugs*</td>
<td>7 (12.7)</td>
</tr>
<tr>
<td></td>
<td>Step 2 drugs *</td>
<td>23 (41.8)</td>
</tr>
<tr>
<td></td>
<td>Step 3 drugs *</td>
<td>4 (7.3)</td>
</tr>
<tr>
<td></td>
<td>Step 4 drugs *</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td></td>
<td>Step 5 drugs *</td>
<td>5 (9.1)</td>
</tr>
<tr>
<td></td>
<td>Step 6 (ablation)*</td>
<td>3 (5.5)</td>
</tr>
<tr>
<td>AFL</td>
<td>Cardioversion</td>
<td>3 (5.5)</td>
</tr>
<tr>
<td>JET</td>
<td>Amiodarone</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>VT</td>
<td>Amiodarone</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td></td>
<td>Amiodarone + Propranolol</td>
<td>3 (5.5)</td>
</tr>
<tr>
<td></td>
<td>Amiodarone + Propranolol+ Flecainide</td>
<td>2 (3.6)</td>
</tr>
</tbody>
</table>

Step 1 = Propranolol; Step 2 = Propranolol + Flecainide; Step 3 = Flecainide + Sotalol; 0
Step 4 = Flecainide + Sotalol+ Propranolol; Step 5 = Amiodarone + Propranolol; Step 6 = Ablation

WPW, Wolff–Parkinson–White; FAT, Focal atrial tachycardia; AVRT, Atrioventricular reciprocating tachycardia; AVNRT, Atrioventricular nodal reciprocating tachycardia; AFL, Atrial flutter; JET, Junctional ectopic tachycardia; VT, Ventricular tachycardia
The procedure was successful in all 3 subjects. Nevertheless, late recurrence was observed in 1 patient, who had the Ebstein anomaly of the tricuspid valve and multiple accessory pathways. This case of recurrence responded well to antiarrhythmic drug therapy with flecainide. The drug was discontinued when this patient turned 1 year old, and there was no recurrence of the arrhythmia during the following 1-year follow-up period. The responses to the different antiarrhythmic regimens are shown in Table 2.

The characteristics of the arrhythmias and the results of the ablation procedures are depicted in Table 3.

Amiodarone was effective in our only case of junctional ectopic tachycardia. There were 6 cases of ventricular tachycardias. Amiodarone alone was effective in only 1 case. Three cases were controlled with a combination of amiodarone and propranolol. The remaining 2 cases responded to a combination of amiodarone, propranolol, and flecainide.

Two significant side effects were observed; both were caused by amiodarone and in the patients with ventricular tachycardias. In 1 patient, amiodarone produced a QTc interval of more than 480 ms after 1 month’s control. In the other patient, subclinical hypothyroidism was observed after 3 months. For both of these patients, amiodarone was discontinued and replaced with propranolol.

These 2 subjects remained in sinus rhythm until the end of infancy.

In summary, of 55 cases, 47 infants were treated with antiarrhythmic drugs, 3 (with atrial flutter) received cardioversion, and 3 underwent catheter ablation. In 1 case, the arrhythmia (atrial tachycardia) was eliminated after a single dose of adenosine. In another case, the arrhythmia (atrial tachycardia) was resolved spontaneously. No mortality was observed.

**DISCUSSION**

The most common types of cardiac arrhythmias in infants are atrioventricular reciprocating tachycardias over an accessory pathway. Those pathways may disappear spontaneously during the first year of life, during which a normal anatomic growth produces a sufficient electrical barrier between the atria and ventricles. The exact rate of the spontaneous abolishment of the accessory pathways during infancy is unclear because some of them are concealed without any presentation on the surface ECG. This is the reason why most authors have recommended long-term oral antiarrhythmic agents to prevent recurrence during infancy.

Adenosine is a short-acting atrioventricular blocking agent with a significant role in terminating common arrhythmias and unmasking atrial activity during the arrhythmia. The mechanisms of a great
number of arrhythmias are definable with careful evaluations of 12-lead ECG and atrial activities when the atroventricular node is temporarily blocked with adenosine.\textsuperscript{10}

Several drugs have been proposed and tried for chronic arrhythmia prophylaxis in infants.\textsuperscript{11-17} Beta-blockers have been widely used with different success rates.\textsuperscript{5,6,14} In our study, only 7 of 40 patients did not experience recurrence on propranolol alone at a dose of 1 to 2 mg/kg/d. Higher doses may be effective, but we preferred to add oral flecainide at a dose of 3 to 4 mg/kg/d and continue low-dose propranolol (1 mg/kg/d). This strategy was successful in 23 of 33 cases and indicated the high efficacy of this drug regimen.

The permanent junctional reciprocating tachycardia is a misnomer in that it points to a type of orthodromic atrioventricular reciprocating tachycardia in which the retrograde limb of the circuit is a decremental conducting accessory pathway. Many authors have recommended ablation for permanent junctional reciprocating tachycardias because of their poor control with drugs and the high success rate of catheter ablation.\textsuperscript{15} In the present study, there were 6 cases of permanent junctional reciprocating tachycardias, all of which were converted to sinus rhythm with drugs: 4 of them with a combination of flecainide and propranolol and the other 2 with amiodarone and propranolol. Our findings suggested that the decision for ablation in infants with permanent junctional reciprocating tachycardias should be reevaluated.

Atrial flutter has been described as a benign arrhythmia in neonates and infants.\textsuperscript{9,11} In our study, there were 3 cases of atrial flutter, all of which were managed as per recommendations of many authors with DC cardioversion and without any more antiarrhythmic agent. None of the patients suffered a recurrence.

Congenital junctional ectopic tachycardias were detected in 1 of our patients. Amiodarone has been proposed as the most effective drug for this condition, and we successfully treated our patient with this drug. Ventricular tachycardias are reported in infancy, albeit with different presentations.\textsuperscript{2,8,16} There were 6 cases of ventricular tachycardias in our study population. We successfully controlled the condition by using amiodarone as a single agent or in combination with other drugs for all these patients. Two patients exhibited drug side effects (prolonged QT intervals and hypothyroidism); we discontinued the drug for them and achieved complete resolution.

Catheter ablation is a proven method for arrhythmia elimination in children. Apropos the indications for catheter ablation, the 2016 guideline of the American Heart Association (AHA) divided pediatric patients into 2 groups: large children, defined as those with a bodyweight of equal to or greater than 15 kg, and small children, defined as those with a bodyweight of less than 15 kg. Ablation is recommended for many of the larger patients with arrhythmias, but that indication is more limited in smaller ones. The indications for ablation in small children can be summarized as those for cases refractory to medical therapy and those for cases with heart failure.\textsuperscript{5} Several authors have reported high success rates of ablation in small children and in those with congenital heart anomalies.\textsuperscript{3-5} In the current study, there were 3 cases of arrhythmias refractory to multiple antiarrhythmic agents and combinations; we successfully conducted ablation in all of these 3 cases.

The majority of our study population (62%) had normal cardiac anatomies. Congenital heart diseases were observed in the other one-third of the study patients, which chimes in with other similar studies.\textsuperscript{1,14,15} A small minority of our patients (18%) had cardiac dysfunction due to tachyarrhythmias.
In summary, medical management for tachycardias in neonates and infants appears to be safe and effective with a good overall outcome. Furthermore, propranolol and flecainide have a wide margin of use, and catheter ablation is hardly necessary for neonates and infants.

CONCLUSIONS
Most infantile arrhythmias are controllable with available antiarrhythmic drugs. Flecainide plus propranolol is a widely effective regimen for chronic antiarrhythmic therapy during infancy. When indicated, catheter ablation can be performed for small infants with very good results.

Acknowledgments
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All the procedures performed in the study were in accordance with the ethical standards of Rajaie Cardiovascular Medical and Research Center and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

REFERENCES


