Rhythm disorders in neonates

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ABSTRACT
Arrhythmias are a variety of heart rhythm alterations which may occur in fetuses and neonates considered healthy. The majority are benign. The incidence reported varies from 1 to 10% in neonates in the first days of extrauterine life. Arrhythmias in the neonatal stage entail high morbidity and mortality, above all when they occur in patients with congenital heart disease or lack of response to medical treatment. Opportune pharmacological control of rhythm offers a good long-term prognosis.

The natural history of arrhythmias in the neonatal period differs from arrhythmias in other pediatric age groups; they can be classified as: sinus arrhythmia, tachyarrhythmias, long QT syndrome, and bradyarrhythmias. It is important that doctors in charge of treating this group of patients recognize the causal factors of arrhythmias, and the diagnostic and therapeutic options available.

Key words: arrhythmias, neonates, sinus dysrhythmia, tachyarrhythmias, long QT syndrome, treatment, prognosis.
The electrocardiogram (ECG) is the reference procedure to identify heart rhythm alterations in neonates; however, it is necessary to ascertain that an arrhythmia is not transitory. With the development of neonatal intensive care units and increased monitoring of patients, in both the prenatal and postnatal stages, various rhythm alterations have been identified in fetuses and neonates considered healthy. The majority of those arrhythmias are benign; however, detecting them requires a thorough evaluation of them and the risk factors for their genesis, such as maternal illnesses or infections, fetal distress, or congenital heart disease.

An incidence of heart rhythm alterations of between 1 and 10% has been described in healthy neonates in the first days of extrauterine life; notwithstanding, this figure is higher in patients admitted to neonatal intensive care units.

**PATHOPHYSIOLOGY**

Arrhythmias may occur as a result of various mechanisms; the most important are: defects in impulse generation with increase or reduction of automaticity and defects in conduction of stimulus with a simple block or one-directional block and a reentry mechanism. However, for these alterations to manifest clinically there must be a pathophysiological substrate, in the neonate, that predisposes him/her to rhythm disorders. The most common are: 1) hydroelectrolytic alterations; 2) hypoxemia; 3) immaturity of the autonomic nervous system; 4) myocarditis; 5) congenital heart disease; or 6) endovenous catheters that irritate the endocardium.

Evaluation of neonates with arrhythmias starts with the search for maternal factors, which may trigger rhythm alterations, in electrolyte intake and blood sugar. A surface electrocardiogram is sufficient to establish a diagnosis in most cases. An echocardiogram is indicated in symptomatic patients, in those with suspected congenital heart disease and with persistent arrhythmias. A 24-hour (Holter) electrocardiogram can establish a diagnosis in patients with arrhythmias which cannot be documented with a surface electrocardiogram.

**SINUS DYSRHYTHMIA**

Sinus dysrhythmia is the most common form of change in heart rhythm in neonates and is considered a normal variant; the heart rate drops during expiration and rises during inspiration. This type of rhythm is more evident during episodes of fever.

**TACHYARRHYTHMIAS**

This term means an abnormal increase in heart rate. They are considered “benign” tachycardias when there is no clinical hemodynamic repercussion and no treatment is required. This type of phenomena do not require follow up because they do not affect health.

Depending on the site where these arrhythmias are generated, they can be classified as: a) supraventricular tachyarrhythmias (when there is an ectopic focus above the bundle of His or it participates in the circuit of the arrhythmia) and b) ventricular tachyarrhythmias (when the abnormal stimulus is generated below the bundle of His).

Finally, if the start and end of the abnormal rhythm are sudden or gradual, tachyarrhythmias are classified as paroxysmal or non-paroxysmal. The most common form of non-paroxysmal tachycardia is sinus tachycardia, in which case the various factors that triggered the tachycardia must be corrected: anemia, hydroelectrolytic alterations, sepsis, respiratory problems, etc.
Supraventricular tachyarrhythmias

Supraventricular extrasystoles

Are premature heartbeats originating in the atria. They have been reported to exist in 5 to 30% of neonates, a figure which is higher in preterm neonates. Electrocardiographically there is premature atrial depolarization with an abnormal morphology; if depolarization is conducted to the ventricles it usually does so with a normal ventricular complex. If the supraventricular extrasystole is capable of reactivating the sinus node it will have an incomplete compensatory pause. (Figure 2). In these heart rhythm disorders patients are usually asymptomatic and they are considered benign events in patients with structurally healthy hearts.

Supraventricular extrasystoles can be triggered by several causes, among them: toxic concentrations of sympathomimetic amines such as isoproterenol or dopamine, or by central catheters which cause mechanical irritation. If supraventricular extrasystoles are frequent, a chest x-ray and an electrocardiogram are indicated to rule out congenital heart disease or cardiomyopathy. Such patients should be monitored for three or four days and a 24-hour electrocardiographic record is indicated. If there are no episodes of supraventricular tachycardia the patients do not require treatment; however, they are kept under observation for a month. Cases in which atrial extrasystoles trigger supraventricular tachycardia with alteration of ventricular function should receive treatment.

Atrial ectopy

This arrhythmia is very common in fetuses and neonates. It is produced by increased automaticity in a group of atrial cells which are not part of the normal conduction system. In the ECG they appear as tachycardias with a narrow QRS complex and an abnormal P wave with variable morphology (migratory pacemaker) or they may have a single ectopic focus. It tends to accelerate and decelerate (“heating” and “cooling” phenomenon). In most cases this arrhythmia disappears over time and does not cause further complications; however, when the ectopic atrial rhythm has a frequency above 200 bpm and accelerated ventricular conduction, it can cause heart failure and dilated cardiomyopathy.

Atrioventricular reentry tachycardia

Occurs in one of every 1,700 neonates and is the leading cause of supraventricular paroxysmal tachycardia.
tachycardia in the neonatal period in up to 50% of cases.\textsuperscript{2-5} For this arrhythmia to occur there must be an accessory pathway that can allow anterograde or retrograde conduction (Wolf-Parkinson-White WPW syndrome) or a pathway with only retrograde conduction (occult pathway). In most cases the tachycardia starts with an extrasystole which may be atrial or ventricular; it causes a one-directional block, usually in the accessory pathway, although it may also occur in the atrioventricular node and the tachycardia is initiated by a reentry mechanism.\textsuperscript{6,9} (Figures 3 and 4)

To distinguish an atrioventricular reentry tachycardia from other forms of supraventricular tachycardia, it is important to locate the P wave on the electrocardiogram during the tachycardia. In atrioventricular reentry tachycardia there is a retrograde P wave which is inscribed after the QRS complex. For these arrhythmias atrial and ventricular tissue is required to maintain the reentry circuit; therefore, there cannot be atrioventricular block or disassociation during the arrhythmia.\textsuperscript{7,8}

These arrhythmias occur more commonly in patients with structurally healthy hearts; however, WPW syndrome may be associated with Ebstein disease, corrected transposition of the great vessels, or hypertrophic cardiomyopathy.\textsuperscript{3}

It is well established that neonates with WPW syndrome have a high probability of resolution of supraventricular tachycardia in the first year of life. However, it has also been shown that up to one third of such patients with resolution of symptoms have a probability of a relapse of tachycardia at school age.\textsuperscript{3,6}

Lemler et al. conducted a study to identify risk factors for recidivism of symptoms in patients with WPW in subsequent stages of life. They analyzed the following factors: heart failure during the arrhythmia, recurrence of the arrhythmia during treatment in the first year of life, difficulty controlling the arrhythmia in the initial period, congenital heart disease and persistence of the delta wave on the electrocardiogram. They found that the only positive predictive factor for recurrence of the arrhythmia was persistence of the delta wave despite treatment.\textsuperscript{11}

\textbf{Atrial flutter}

Although it is a common rhythm disorder in fetuses (25% of tachycardias in fetuses) and in neonates, it is very rare in pediatric age and does not become common again until adult age. It is associated with congenital heart diseases: endocardial fibroelastosis or cardiomyopathies,
chromosomal alterations, and other pathological states in up to 30% of cases. Electrocardiographically it is characterized by a “sawtooth” shaped pattern of P waves with frequencies ranging from 300 to 600 beats per minute; the ventricular response may be regular or irregular, but with lower frequency (Figure 5).

This arrhythmia has high morbidity and mortality in the neonatal stage, especially if it is associated with congenital heart diseases or lack of response to medical treatment; however, if pharmacological control of the rhythm is achieved, the long-term prognosis is good.7-9,12

**Treatment of supraventricular tachyarrhythmias**

*Acute treatment.* Depends on the patient’s general condition. In cases of tachycardia with narrow QRS complex, without hemodynamic compromise, the initial treatment is to attempt to suppress the arrhythmia with vagal maneuvers like applying a cold compress on the patient’s face for 10 to 20 seconds and even facial immersion in cold water for 5 seconds. Ocular compression or carotid massage are not recommended. These maneuvers trigger the “diving reflex,” which not only causes vagal stimulation but also a drop in sympathetic activity. During the procedure, the electrocardiographic record and blood pressure should be monitored, due to the possibility of asystole at the end of the supraventricular tachycardia.7-9,13 If treatment with vagal maneuvers is ineffective intravenous adenosine is recommended in both term and preterm neonates; initial dose 50 to 150 mg/kg. The dose may be increased by 50 g/kg every minute to a maximum dose of 250 to 500 mg/kg. Side effects of large doses of adenosine are bronchoconstriction, stridor, and low blood pressure secondary to peripheral vasodilation.13 If the tachycardia persists despite treatment, with hemodynamic instability of the patient, electric cardioversion is indicated. The application of current should be synchronized with the QRS complex, starting with a dose of 0.5 joules per kilogram of body weight. In the large majority of cases cardioversion is effective to stop the supraventricular tachycardia.7-9,11,13,14

*Chronic treatment.* In neonates with a history of supraventricular tachycardia, when the acute event is resolved, chronic treatment should be initiated to prevent recurrence of the tachycardia. Digoxin and b blockers are the first-line agents for treating reentry tachyarrhythmias. Class 1A (procainamide), IC (propafenone or flecainide) and class 3 (amiodarone) antiarrhythmic drugs have also been used successfully when digoxin and b blockers are ineffective. Use of calcium antagonists in neonates should be avoided as a sudden drop in cardiac flow following their administration has been reported13,14 (Table 1).

Ablation with radiofrequency in the neonatal stage has been used in isolated cases where there is recurrence of arrhythmia with hemodynamic deterioration despite treatment which has also had the side effects of antiarrhythmic drugs.14,15

**Ventricular tachyarrhythmias**

**Ventricular extrasystoles**

Are defined as premature ventricular complexes. The following criteria are used in electrocardio-
graphic diagnosis: 1) early start of QRS complex; 2) duration of QRS complex greater than 80 ms; 3) abnormal morphology of QRS complex with alteration in the ST segment and in the T wave; and 4) no preceding P wave. Ventricular extrasystoles are common in neonates with structurally healthy hearts; their occurrence has been reported in up to 18% of healthy neonates who have undergone a 24-hour Holter in the first day of extrauterine life. Premature ventricular contractions have also been observed in patients with hypoxia, hypoglycemia, myocarditis, ventricular hypertrophy, ventricular tumors, or ventricular catheters (Figure 6).

Table 1. Antiarrhythmic drugs indicated in neonatology (continued on next page)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral Dose</th>
<th>IV Dose</th>
<th>Indications</th>
<th>Side effects</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosine</td>
<td>0.05 mg/kg. The dose may be increased every 2 minutes by 0.05 mg/kg</td>
<td></td>
<td>Reentry SVT, Diagnosis of atrial flutter</td>
<td>Dyspnea, arrhythmias, AV block, palpitations, bradycardia</td>
<td>Administer rapidly</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>10-20 mg/kg/day for 7 to 14 days and then 5 mg/kg/day</td>
<td>DL: 5 mg/kg in 1 h; DM continuous infusion 10-15 mg/kg/day</td>
<td>Refractory SVT, VT, and VF</td>
<td>Proarrhythmia, bradycardia, AV block, hypothyroidism, interstitial pneumonitis, pulmonary fibrosis, photosensitivity</td>
<td>Monitor pulmonary and thyroid functions</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Maintenance 5-10 μg/kg/day divided in 2 doses</td>
<td>DL: 15-20 μg/kg divided in 3 doses. DM: 4-8 μg/kg/day divided in 2 doses/day</td>
<td>SVT, atrial flutter</td>
<td>Bradycardia, arrhythmias, delayed conduction, lethargy, vomiting, diarrhea</td>
<td>Contraindication: VT, hypokalemia, AV block. Use with caution in WPW syndrome: may cause VF</td>
</tr>
<tr>
<td>Flecaïnide</td>
<td>1-3 mg/kg/day in 3 doses. May be increased to up to 3-6 mg/kg/day</td>
<td></td>
<td>Refractory tachycardias: SVT, VT</td>
<td>Bradycardia, AV block, arrhythmias, heart failure, blood dyscrasias, liver dysfunction, dyspnea</td>
<td>Contraindication: retarded conduction, liver or myocardial dysfunction</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>1 mg/kg/dose in 1 to 2 minutes. Infusion 20-50 μg/kg/min</td>
<td></td>
<td>VT, VF</td>
<td>Low blood pressure, bradycardia, arrhythmias, lethargy, vomiting, paresthesia, respiratory depression</td>
<td>Use after a cardioversion</td>
</tr>
<tr>
<td>Procainamide</td>
<td>15-50 mg/kg/day Divided in 4-8 doses/day</td>
<td>DL. 3-6 mg/kg/dose in 5 minutes DM. Continuous infusion 20-80 μg/kg/min</td>
<td>SVT, WPW, VT</td>
<td>Low blood pressure, bradycardia, arrhythmias, vomiting, diarrhea, blood dyscrasias, hepatomegaly, increase in liver enzymes</td>
<td>Contraindication: blockage in conduction, helical ventricular tachycardia</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.25 mg/kg/dose every 6-8 h; increase to a maximum of 5 mg/kg/day</td>
<td></td>
<td>SVT, WPW, VT</td>
<td>Low blood pressure, heart failure, arrhythmias, alterations in conduction, asystole, lethargy, hypoglycemia, hyperglycemia, bronchospasm, vomiting, diarrhea, agranulocytosis</td>
<td>Contraindication: asthma, bradycardia, heart block, cardiogenic shock</td>
</tr>
</tbody>
</table>
In neonates with ventricular extrasystoles, a chest x-ray and an echocardiogram are indicated to rule out an underlying heart disease. Patients with structurally healthy hearts and isolated ventricular extrasystoles do not require treatment. In cases of underlying heart disease and frequent ventricular extrasystoles (more than ten per hour), of polymorphic ventricular extrasystoles or when there are pairs of them, the initiation of antiarrhythmic therapy is indicated.3-6,9

Ventricular tachycardia

Is defined as the presence of three or more consecutive ventricular extrasystoles with a heart rate above 120 bpm. This tachycardia may be monomorphic, when the abnormal beats have a single morphology, or polymorphic: different morphologies in the extrasystoles, which means that there are multiple ectopic foci. It may be nonsustained (less than 30 seconds of arrhythmia) or sustained ventricular tachycardia. Incessant ventricular tachycardia is arrhythmia in more than 10% of a day.3-6,9,16 This type of arrhythmias are uncommon in the neonatal stage, and when they appear their causes should be investigated. Usually, antiarrhythmic therapy is required. Conditions to consider as possible causes of ventricular tachycardias include: myocarditis, ventricular tumors, myocardial infarction secondary to anomalies in the coronary arteries, electrolyte disorders, metabolic diseases, drug use, and long QT syndrome3-6,9,16 (Figure 7).

Neonates with sustained ventricular tachycardia suffer hard-to-control heart failure and may
develop cardiogenic shock; they have a poor prognosis given that, even with antiarrhythmic therapy, mortality near 50% has been observed.16

Treatment of ventricular tachycardias

In patients with ventricular tachycardia and hemodynamic compromise, it is indicated, initially to perform electric cardioversion or defibrillation with a dose of 2 joules per kilogram of body weight. In patients with nonsustained ventricular tachycardia, without hemodynamic deterioration, antiarrhythmic therapy with lidocaine or amiodarone should be initiated. In cases of incessant and recurrent ventricular tachycardia, despite medical treatment, an electrophysiological study is indicated to locate the origin of the ventricular tachycardia and attempt ablation with radiofrequency6-9,13 (Table 1).

LONG QT SYNDROME

Long QT syndrome (LQT) is a hereditary disease and causes sudden death in the neonatal stage; it is associated with both bradycardia and helical ventricular tachycardia (torsade de pointes)6,17,18 The diagnosis is based on a family history of sudden death and the finding of a long QT (corrected QT > 450 ms) on the surface electrocardiogram.6,17,18 (Figure 8).

Recently long QT syndrome has been associated with three molecular abnormalities in transport of electrolytes across the cell membrane: LQT 1 and LQT 2, related to potassium channels, and LQT 3, which is accompanied by alterations in sodium channels. A higher incidence of cardiovascular symptoms has been found in LQT 1 and LQT 2; there is higher mortality in LQT 3.17,18

Treatment of long QT syndrome uses propranolol at high doses to lower the adrenergic discharges involved in the genesis of arrhythmias. If such treatment proves unsuccessful, placement of a permanent pacemaker or an implantable automatic defibrillator is indicated.13,17-19

BRADYARRHYTHMIAS

In neonates a drop in cardiac rhythm may be due to alterations in impulse generation (function of the pacemaker) or in conduction of the stimulus.

Sinus bradycardia

Is defined as a heart rate below 90 beats per minute and has been described as the leading cause of rhythm disorders in the neonatal stage. This bradycardia may be primary, due to sinus
node dysfunction; it is very rare in the neonatal period and is associated with immaturity of the central nervous system, and therefore is more common in preterm neonates.\textsuperscript{10} The most common causes of pathological sinus bradycardia are hypoxia and use of medications\textsuperscript{6,20} (Figure 9).

**First degree atrioventricular block**

It is the presence of a PR interval above the normal limit for the patient’s age. The normal PR interval in the neonatal period varies from 0.06 to 0.14 s (0.17 seconds in the first day of extrauterine life). A prolonged PR interval may be due to alterations in atrial conduction, in the atrioventricular node, or in the His-Purkinje system. It is very commonly associated with congenital heart diseases or with inflammatory heart diseases. Medications that raise vagal tone can also prolong the PR interval. The majority of patients are asymptomatic and do not require treatment.\textsuperscript{3,6}

**Second degree atrioventricular block**

Is characterized by intermittent failure of conduction of stimulus to the ventricles. There are two forms: Mobitz 1, with blockage in the atrioventricular node which produces the characteristic Wenckebach phenomenon, consisting of gradual prolongation of the PR interval with eventual failure of conduction and a blocked heartbeat. This block is associated with medications or with maternal connective tissue disease. In the Mobitz 2 block the alteration is located in the distal part of the conduction system. It is characterized by normal PR intervals interrupted by a blocked heartbeat. This block has a more serious prognosis and in some cases may require placement of a pacemaker.\textsuperscript{3,6,20}

**Congenital complete atrioventricular block**

Congenital complete atrioventricular block occurs in 15 000 to 20 000 live births. It is characterized by failure of conduction of cardiac stimulus from the atrium to the ventricles. The atrial rhythm is higher than the ventricular and the P waves have no relationship with the QRS complexes\textsuperscript{2,6,21} (Figure 10).

Congenital complete atrioventricular block may occur in a structurally healthy heart or be associated with congenital heart diseases. Patients with congenital atrioventricular block and structurally healthy hearts are very commonly associated

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**Figure 9.** Female patient of 15 days’ extrauterine life, asymptomatic. With sinus arrhythmia and sinus bradycardia with ventricular heart rate of 80 bpm during sleep.

**Figure 10.** Male patient of 40 days’ extrauterine life with Holt-Oram syndrome. Interatrial communication with signs of heart failure. 12-lead electrocardiogram showing complete atrioventricular block, with atrioventricular disassociation. P waves with heart rate of 150 bpm and QRS complexes with heart rate of 75 bpm.
with exposure to anti-Ro (SS-A) and anti-La (SS-B) antibodies. Such antibodies are common in women with connective tissue disease, especially systemic lupus erythematosus and Sjögren syndrome. These antibodies cause tissue damage and fibrous degeneration of conductive tissue.\textsuperscript{20,22} Congenital heart block in patients with heart disease is associated with complex congenital anomalies such as L-transposition of the great vessels, left isomerism, and also in patients with trisomy 18.\textsuperscript{6,20-22}

Patients with congenital atrioventricular block may be asymptomatic or develop left ventricular dysfunction and heart failure in early stages of life and even in the prenatal stage. In such cases an unstable ventricular escape rhythm is observed, with heart rate below 50 bpm, and a permanent pacemaker is indicated. Eronen et al. studied 91 patients with congenital atrioventricular block. They observed that despite early placement of permanent pacemakers in asymptomatic neonates, they developed heart failure and dilated cardiomyopathy; risk factors for this torpid evolution were hydrops, fetal and neonatal bradycardias, low birth weight, male patients with neonatal problems associated with “prematurity” or with neonatal lupus.\textsuperscript{23,24}

CONCLUSIONS

Arrhythmias in neonates are not common events. However, the natural history of arrhythmias in the neonatal period differs greatly from that of arrhythmias in other pediatric age groups. It is important for physicians who attend to this group of patients to know how to recognize rhythm disorders, the factors for development of arrhythmias, and the available diagnostic and therapeutic options.

REFERENCES


