

Ten Years of Experience in The Diagnosis and Treatment of Neonatal Arrhythmias

On Yıllık Neonatal Aritmi Tanı ve Tedavi Deneyimimiz

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Abstract

Introduction: Neonatal arrhythmias (NA) are rare in the neonatal period but cause mortality and morbidity. NA often occurs as a continuation of arrhythmias in the fetal period. The aim of this study is to retrospectively evaluate the incidence, prenatal diagnosis rate, clinical features and treatment outcome of NA in our neonatal intensive care unit.

Materials and Methods: The data of neonates with atrial or ventricular extrasystole, conduction system abnormality, hereditary arrhythmia, bradyarrhythmia and tachyarrhythmia treated in the Neonatal Intensive Care Unit of Uludağ University Faculty of Medicine for ten years were retrospectively reviewed and included in the study. Patients with sinus tachycardia and sinus bradycardia were excluded from the study.

Results: NA was detected in a total of 39 of 3703 patients. The most common arrhythmia was supraventricular tachycardia (n=15, 38.5%). Fourteen patients were diagnosed in the prenatal period, while seven patients had multiple arrhythmias. The most common etiologic cause (n=20, 51.2%) was congenital heart disease, while two patients had a history of maternal systemic lupus erythematosus. Antiarrhythmic treatment was required in 25 (64.1 %) patients. Cardioversion or defibrillation was performed in three patients. In 16 patients, the arrhythmia was under control at follow-up, and 5 patients continued antiarrhythmic therapy.

Conclusion: Cardiac arrhythmias can already begin in the prenatal period and be accompanied by various underlying cardiac or systemic diseases. These patients usually do not respond to first-line drug therapy and are controlled by second-line or multi-medication therapy. Cardioversion, on the other hand, is rarely necessary. Appropriate treatment initiated in a timely manner is of great importance for neonates.

Öz

Giriş: Yenidoğan aritmileri (NA) yenidoğan döneminde nadirdir olup mortalite ve morbidite ile sonuçlanabilir. NA genellikle fetal aritmilerin devamı olarak ortaya çıkar. Bu çalışmanın amacı; yenidoğan yoğun bakım ünitemizde NA'nın insidansının, prenatal tanı oranının, klinik özelliklerinin ve tedavi sonuçlarının retrospektif olarak değerlendirilmesidir.

Gereç ve Yöntem: Uludağ Üniversitesi Tıp Fakültesi Yenidoğan Yoğun Bakım Ünitesi'nde on yıl boyunca tedavi gören atriyal veya ventriküler ekstrasistol, iletim sistemi anormalliği, kalıtsal aritmi, bradiaritmi ve taşiaritmi olan yenidoğanların verileri retrospektif olarak incelenerek çalışmaya dahil edildi. Sinüs taşikardisi ve sinüs bradikardisi olan hastalar çalışma dışı bırakıldı.

Keywords

Neonatal arrhythmia, prenatal diagnosis, antiarrhythmic treatment

Anahtar kelimeler

Neonatal aritmi, prenatal tanı, antiaritmik tedavi

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Bulgular: Toplam 3703 hastanın 39'unda NA tespit edildi. En sık görülen aritmi supraventriküler taşikardiydi idi (n=15, %38,5). On dört hastaya prenatal dönemde tanı aldı, yedi hastada ise multipl aritmi saptandı. En sık etyolojik neden (n=20, %51,2) konjenital kalp hastalığı iken, iki hastada maternal sistemik lupus eritematozus öyküsü mevcuttu. Hastaların 25'ine (%64,1) antiaritmik tedavi başlandı. Üç hastaya kardiyoversiyon veya defibrilasyon uygulandı. Takipte 16 hastada aritmi kontrol altına alınabildi, 5 hastada ise antiaritmik tedaviye devam edildi.

Sonuç: NA prenatal dönemde başlayabilir. Altta yatan çeşitli kalp hastalığı veya sistemik hastalıklarla birlikte olabilir. Hastalar tek ilaç tedavisine yanıt vermediğinde aritmi çoklu ilaç tedavisi ile kontrol altına alınmaya çalışılmaktadır. Nadiren kardiyoversiyon tedavisi gerekmektedir. Yenidoğanlar için uygun tedavinin zamanında başlatılması büyük önem taşımaktadır.

Introduction

Although neonatal arrhythmias (NA) are rare in the neonatal period, they are accompanied by various clinical conditions and cause mortality and morbidity (1). In neonates, cardiac arrhythmias occur in 1-5% of cases (2). NA often occurs as a continuation of arrhythmias in the fetal period. Therefore, prenatal diagnosis is important for the early diagnosis and treatment of NA (1). Although life-threatening arrhythmias are rare, their diagnosis is important (3). Many benign arrhythmias are detected during routine monitoring in neonatal intensive care units without prenatal diagnosis (4). The type of treatment depends on many factors, e.g. the type, duration and frequency of the arrhythmia, the patient's clinical condition, tolerance and cardiac function. For all types of arrhythmias, the first step is to determine whether the patient is hemodynamically stable; aggressive treatment strategies should be used for arrhythmias that present with hemodynamic instability (5). The intrauterine treatment of fetal arrhythmias is an interesting topic on which research is ongoing. Studies on the development of modified technologies for the diagnosis and treatment of fetal arrhythmias are currently being conducted in the literature (6). The aim of this study is to retrospectively evaluate the incidence, prenatal diagnosis rate, clinical characteristics and response to treatment of NA in our neonatal intensive care unit.

Materials and Methods

The study included newborns diagnosed with arrhythmia by routine electrocardiography (ECG) between January 2011 and July 2021 in the neonatal intensive care unit of Uludag University Faculty of Medicine and followed up with a diagnosis of NA by 24-hour rhythm Holter monitoring. Patients were divided into four groups according to their arrhythmia types: premature complex and extrasystoles (premature atrial or ventricular contraction and extrasystoles), tachyarrhythmias [supraventricular tachycardia (SVT), ectopic atrial tachycardia (EAT), atrial flutter, ventricular tachycardia], bradyarrhythmias [second-degree and complete atrioventricular (AV) block],

hereditary arrhythmias (long QT syndrome, short QT syndrome). The diagnosis was confirmed by genetic testing in patients with hereditary cardiac arrhythmias. Patients with isolated sinus tachycardia, sinus bradycardia and arrhythmias due to secondary causes such as electrolyte disturbances and sepsis were excluded from the study. The demographic characteristics of the patients (sex, gestational age, birth weight, APGAR score, maternal and gestational diseases) and clinical characteristics (prenatal diagnosis, prenatal treatment, concomitant cardiac pathologies, type of arrhythmia, condition of presence of multiple arrhythmias, treatment methods) were retrospectively collected and approved by the Ethics Committee of Uludag University Faculty of Medicine for Clinical Research.

Statistical Analysis

For statistical analysis, SPSS software, version 19 was utilized. $P < 0.05$ were regarded as significant for all analyses.

Results

NA was detected in 39 out of 3703 patients who were hospitalized and followed up during the study. Of the patients, 17 were girls and 22 were boys, the average gestational age was 38 weeks, 9 babies were preterm, and 30 were term babies (Table 1). A prenatal diagnosis was made in 14 (35.9%) patients, and 6 of these patients were treated during the prenatal period. Seven patients had multiple cardiac arrhythmias, and 13 patients had congenital cardiac pathology.

Two mothers had a history of systemic lupus erythematosus (SLE), and three mothers had a history of diabetes (Table 2).

Looking at the distribution of arrhythmias in order of frequency, SVT was the most common, ventricular extrasystole (VES) was the second most common, followed by atrial extrasystole (AES), EAT, complete AV block, supraventricular extrasystole, respectively (Table 3). The clinical characteristics of patients diagnosed with SVT, the most common type of arrhythmia, are given in Table 4.

The most common etiologic cause (n=20, 51.2%) was congenital heart disease, while the most common concomitant cardiac pathology (n=3, 7.6%) was dilated cardiomyopathy. Genetic testing was performed on three patients. Genetic testing revealed long QT syndrome type 2 in only one patient. Mutations in genes associated with 22q11 deletion were detected in one patient with Di George syndrome and another patient with dilated cardiomyopathy (BAG3, MYPN, FLNC, SYNE1).

Twenty-five (64.1%) patients required antiarrhythmic therapy in the postnatal period, 9 received a single drug and 16 responded to dual or multidrug treatment (Table 5). Adenosine was the most preferred drug as the first treatment option in 9 (23%) patients in the acute treatment. Propranolol was used second in the treatment of chronic periods in 9 patients (23%) (Table 6).

Cardioversion or defibrillation was performed in a total of 3 patients. While 1 of these patients had an SVT attack, 1 patient had ventricular tachycardia and ventricular fibrillation, and 1 patient had atrial flutter. Cardioversion was performed in 2 patients with SVT and atrial flutter, and 1 patient with ventricular fibrillation with ventricular tachycardia was defibrillated. When evaluating the prognosis of the patients, it was found that the arrhythmia was controlled in 16 patients during follow-up, while 5 patients continued antiarrhythmic therapy. The age of the 5 patients who continued treatment was determined to be 1 to 5 years. Complete AV block was observed in two patients in the control Holters, WPW was observed in three patients and long QT syndrome was continued in one patient.

Discussion

Neonatal arrhythmias are rare in neonatal intensive care units, but different rates of their incidence are reported in the literature. Jones et al. (7) reported an incidence of NA of 4.8% based on ECG results obtained in the first two days of life in 1028 healthy newborns. In another study, cardiac arrhythmias were detected in 33 cases using the standard ECG technique in 3383 healthy term infants and the incidence was 0.1% (8). In contrast, Turner and Wren (9) found a frequency of NA of 24.4 per 100,000 live births. In our study, the frequency of NA was reported as 1%. In a study conducted in our country, NA was shown to be more common in girls than in boys (10). However, in our study, 56.4% of the patients were male. In preterm infants, the incidence of NA has been reported to be 23.6-38.5% (1,10-12). The incidence of NA in preterm infants in our neonatal intensive care unit was 23%, similar to that reported in the literature.

NA usually occurs as a continuation of cardiac arrhythmias in the fetal period (1). Therefore, prenatal diagnosis is important for early diagnosis and treatment of NA. Fetal arrhythmias can be observed in 2% of pregnancies, and pregnant women referred to pediatric cardiologists for fetal echocardiography with a provisional diagnosis of NA account for 10-20% of referrals (6). In studies conducted in our country, the prenatal diagnosis rate of NA was reported to be 34-52.9% (1,12,13). In our study, the prenatal diagnosis rate was 35.9%. In 6 patients with a prenatal diagnosis, treatment began in the prenatal period. In the intrauterine period, sotalol was administered to one patient with fetal

Table 1. Demographic and clinical characteristics of patients with neonatal arrhythmia

Birth weight (g) (mean±standard deviation)	3310±679
Gestational age, med (min - max)	38 (26-42)
Prematurity, n (%)	9 (23)
Male gender, n (%)	22 (56.4)
Caserean rate, n (%)	36 (92.3)
APGAR (1 st minute), med	8
APGAR (5 th minute), med	9
Prenatal diagnosis, n (%)	14 (35.9)
Gestational age in prenatal diagnosis, med (min - max)	36.5 (25-39)
Prenatal treatment, n (%)	6 (15.4)
Fetal echocardiography, n (%)	23 (59)
Congenital cardiac pathology, n (%)	13 (33.3)
Multiple arrhythmias, n (%)	7 (17.9)
Mortality, n (%)	1 (2.6)
The parameters showing normal distribution were given as mean ± SD, and the parameters not showing normal distribution were given as median (25%-75%)	

SVT and two patients with fetal tachycardia, salbutamol was administered to two patients with fetal complete AV block and digoxin was administered to another patient with fetal tachycardia. Especially in cases of congenital heart disease, heart failure, hydrops fetalis and persistent cardiac arrhythmias, intrauterine administration of pharmacologic agents or insertion of pacemakers should be considered in cases with heart block (6). One of the patients treated pharmacologically during the intrauterine period who was included in our study had non-immune hydrops fetalis, none of them had structural congenital heart disease on

Table 2. Distribution of maternal gestational or chronic diseases

Maternal gestational or chronic diseases	n (%)
Maternal diabetes	3 (7.6)
Chronic hypertension	1 (2.6)
Hypothyroidism	1 (2.6)
Epilepsy	1 (2.6)
Sinus vein thrombosis	1 (2.6)
Maternal SLE, n (%)	2 (5.1)
Tetralogy of Fallot	1 (2.6)

SLE: Systemic lupus erythematosus

Table 3. Distribution of arrhythmia types

Arrhythmia	n (%)
SVT	15 (38.5)
VES	4 (10.3)
WPW	1 (2.6)
Complete AV block	2 (5.1)
AES	3 (7.7)
EAT	3 (7.7)
Supraventricular extrasystole	2 (5.1)
Short QT syndrome	1 (2.5)
Atrial flutter	1 (2.5)
SVT + WPW	2 (5.1)
EAT+ VES	1 (2.5)
SVT + VES	1 (2.5)
VES + AES	1 (2.5)
AES + ventricular tachycardia + ventricular fibrillation	1 (2.5)
AES with block + long QT syndrome	1 (2.5)

SVT: Supraventricular tachycardia, VES: Ventricular extrasystole, WPW: Wolff Parkinson White syndrome, AV: Atrioventricular, AES: Atrial extrasystole, EAT: Ectopic atrial tachycardia

fetal echocardiography, and antiarrhythmic medication was started because of persistent arrhythmias.

NA may be accompanied by congenital heart disease. The literature reports that 15-47% of newborns with cardiac arrhythmias have structural congenital heart disease (1,13,14). Similar to the literature, cardiac pathology was considered the etiologic cause in 50.2% of patients in our study, while structural complex cardiac pathology was found in 33.3% of patients. Maternal diseases may also be a predisposing factor for NA. Systemic diseases such as gestational diabetes and SLE in the mother are among the known risk factors for NA (13). In two of our patients, the mother had a history of SLE and a complete AV block was diagnosed in the prenatal period. Congenital AV block is a rare condition that presents clinically in the prenatal, natal or postnatal period and is characterized by transplacental passage of maternal anti-Ro/SSA and anti-La/SSB antibodies. In the literature, treatments with maternal sympathomimetics, digoxin and salbutamol have been tried in the prenatal period. There is a lifelong pacemaker requirement of more than 60% in the postnatal period (15,16). Our patients with a history of maternal SLE and AV block were treated with maternal salbutamol in the antenatal period and followed up in the postnatal period without the need for a pacemaker. All types of arrhythmias can be observed in the fetus and neonate. The most common are sinus tachycardia and bradycardia, SVT and, less commonly, atrial flutter, ventricular arrhythmias and complete heart block (1). In our study, patients with sinus tachycardia and bradycardia were excluded. SVT is the most common, followed by VES, AES, ectopic atrial tachycardia, complete AV block and other arrhythmias. The incidence of SVT, the most common type of arrhythmia in our study, ranged from 1/250 to 1/1000 in infancy (17). Twenty-three percent of SVT patients are diagnosed during the neonatal period. The literature reports that SVT accounts for 30-40% of NA (1,18). In our study, the frequency of SVT was 38.4%. Sotalol was started as fetal treatment in two patients and digoxin in one patient. Hinkle et al. (19) suggested a combination of digoxin as the first choice for fetal treatment, sotalol as the second choice and sotalol together with digoxin as the third choice. In the acute postnatal period, adenosine was the most common first choice.

Hereditary arrhythmias are rare. They arise as a result of the development of cardiac channelopathy, which is associated with mutations in genes that code for important ion channels of the heart. They arise due to the development of cardiac channelopathy, which is associated with gene mutations that code for important ion channels of the heart. Congenital long QT

Table 4. Clinical features of patients with supraventricular tachycardia

Arrhythmia Type	Fetal Echo	Prenatal Diagnosis	IU anti-arrhythmic	Postnatal Echo
SVT	-	-	-	VSD, TAPVR, left atrial izomerism, PFO
SVT	+ (TR, SVT)	+	+ (sotalol)	PFO
SVT	+ (normal)	+	-	Normal
SVT + WPW	+ (normal)	+	+ (sotalol)	Moderate MR, moderate TR, mild AR
SVT	Inlet VSD	-	-	Inlet VSD, large PDA, IAS aneurysm
SVT	-	-	-	PFO, mild MR
SVT	+ (normal)	+	-	PFO
SVT	+ (normal)	+	-	Dilated CMP
SVT	+ (normal)	+	+ (digoxin)	Small PDA, PFO, mild MR, mild TR
SVT	-	-	-	Small PDA, mild TR, PFO
SVT + VES	-	-	-	PFO
SVT	-	-	-	PFO
SVT	-	-	-	Mild systolic dysfunction
SVT	+ (normal)	-	-	Minimal AR
SVT	Tetralogy of Fallot	-	-	Tetralogy of Fallot
SVT	-	-	-	Pulmonary HT, HF, severe TR, minimal AR, ASD
SVT	Right atrial dilatation	-	-	Severe TR, VSD, large PDA, deformity of the tricuspid valve
SVT + WPW	-	-	-	PDA; PFO, physiological dilatation of right cavities

SVT: Supraventricular tachycardia, VES: Ventricular extrasystole, TAPVR: Total anomalous pulmonary venous return, PFO: Patent foramen ovale, TR: Tricuspid regurgitation, WPW: Wolff Parkinson White syndrome, MR: Mitral regurgitation, AR: Aort regurgitation, VSD: Ventricular septal defect, PDA: Patent ductus arteriosus, IAS: Interatrial septal, CMP: Cardiomyopathy, HT: Hypertension, HF: Heart failure, ASD: Atrial septal defect

Table 5. Types of arrhythmia according to the state of treatment

	Without Treatment n (%)	Single Drug Therapy n (%)	Multipl Drug Therapy n (%)	Cardioversion or Defibrillation n (%)
SVT	1 (2.5)	4 (10.2)	9 (23)	1 (2.5)
VES	2 (5.1)	1 (2.5)	1 (2.5)	0
WPW	1 (2.5)	0	0	0
Complete AV block	2 (5.1)	0	0	0
Atrial extrasystole	3 (7.6)	0	0	0
Ectopic atrial tachycardia	1 (2.5)	1 (2.5)	1 (2.5)	0
Supraventricular extrasystole	2 (5.1)	0	0	0
Short QT syndrome	1 (2.5)	0	0	0
Atrial flutter	0	0	0	1 (2.5)
SVT + WPW	0	1 (2.5)	1 (2.5)	0
EAT + VES	0	0	1 (2.5)	0
SVT + VES	0	0	1 (2.5)	0
VES + AES	1 (2.5)	0	0	0
AES + ventricular tachycardia + ventricular fibrillation	0	0	0	1 (2.5)
AES with block + long QT syndrome	0	1 (2.5)	0	0

SVT: Supraventricular tachycardia, VES: Ventricular extrasystole, WPW: Wolff Parkinson White syndrome, AV: Atrioventricular, EAT: Ectopic atrial tachycardia, AES: Atrial extrasystole

Table 6. The first choice antiarrhythmic drug according to the type of arrhythmia

	Adenosine n (%)	Propranolol n (%)	Digoxin n (%)	Sotalol n (%)	Amiodarone n (%)	Esmolol n (%)
SVT	7 (17.9)	4 (10.2)	3 (7.6)	-	-	-
VES	-	2 (5.1)	-	-	-	-
EAT	1 (2.6)	-	-	1(2.6)	-	-
AF	-	-	-	-	1 (2.6)	-
SVT + WPW	1 (2.6)	1 (2.6)	-	-	-	-
EAT + VES	-	-	-	-	1 (2.6)	-
SVT + VES	-	1 (2.6)	-	-	-	-
AES + VT + VF	-	-	-	-	-	1 (2.6)
AES + long QT	-	1 (2.6)	-	-	-	-

SVT: Supraventricular tachycardia, VES: Ventricular extrasystole, EAT: Ectopic atrial tachycardia, AF: Atrial fibrillation, WPW: Wolff Parkinson White syndrome, AES: Atrial extrasystole

syndrome, short QT syndrome, catecholaminergic polymorphic VT and Brugada syndrome are examples of genetic cardiac arrhythmias (19). In our study, long QT syndrome was detected in a patient with blocked atrial extrasystole whose genetic study is currently underway, and the diagnosis of another patient with short QT syndrome was genetically confirmed.

While many benign arrhythmias do not require treatment in the neonatal period, some types of arrhythmias with clinical signs should be treated with antiarrhythmic therapy (20). In the study conducted by Naumburg et al. (21), 72.2% of patients with fetal arrhythmias received antiarrhythmic therapy in the postnatal period. In our study, 25 (64.1%) patients required antiarrhythmic therapy in the postnatal period; 9 patients received a single drug and 16 responded to dual or multidrug treatment. The choice of first-line or acute medication for treatment depends on the type of arrhythmia. In our study, adenosine was the most commonly used drug as a first-line acute treatment, as SVT was the most common in 9 (23%) patients. In life-threatening tachyarrhythmias, apart from drug treatment, cardioversion or defibrillation must be performed urgently and without delay. Synchronized cardioversion is performed for SVT and ventricular tachycardia, while defibrillation is used for ventricular fibrillation (22). In our study, cardioversion with AES was performed in 2 patients with SVT and atrial fibrillation, ventricular tachycardia and ventricular fibrillation, and defibrillation was performed in our hemodynamically unstable patient, and the arrhythmia was controlled.

Return to sinus rhythm was achieved in 75-96% of pediatric patients receiving adenosine with a diagnosis of SVT (19). In our study, 16 of the 25 patients treated with medication responded to treatment and their medication could be discontinued during follow-up. In five patients, a

return to sinus rhythm was achieved by adenosine therapy in the acute phase, and in 10 patients who did not respond to adenosine therapy in the acute phase and required chronic antiarrhythmic treatment. Two of the 5 patients still being treated with SVT, one patient with SVT, one patient with WPW, one patient with VES and one patient with long QT syndrome are currently being followed up with antiarrhythmic medical treatment. A return to sinus rhythm was achieved in 83.3% of our drug-treated patients with SVT and their treatment was completed after an average of 19.5 ± 16.8 months.

Study Limitations

Major limitation of this study is that it is retrospective. This was a retrospective, descriptive study and the number of patients was not sufficient to clarify etiological issues. Secondly, although drug-induced arrhythmias were underestimated, prospective observations with a larger number of patients could have been performed to obtain a clearer picture of the drug of first choice in neonatal arrhythmias and the response to the drug. Despite these limitations, we believe that our current data will be useful in increasing awareness about NA.

Conclusion

In conclusion, arrhythmias are rare in the perinatal period but are among the most important cardiac problems. They can occur together with various underlying cardiac or systemic diseases. Prenatal diagnosis is very important for treatment in the postnatal period. It is important to start treating affected patients in the prenatal period. Patients who do not respond to single-drug therapy in acute treatment may require a high level of second-line treatment with chronic medication. Patients with hemodynamic instability

or resistant arrhythmias may require cardioversion or defibrillation. Careful examination and continuous cardiac monitoring in the postnatal period as well as good prenatal monitoring and fetal echocardiography are important for early diagnosis if required. Careful examination, continuous cardiac monitoring in the postnatal period, good prenatal monitoring and fetal echocardiography, if needed, are essential for early diagnosis.

Ethics

Ethics Committee Approval: The study received approval from the institution's ethics committee Bursa Uludağ University Faculty of Medicine Clinical Research Ethics Committee (decision no: 2011-KAEK-26, date: 08.11.2021).

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

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