www.jpnim.com Open Access eISSN: 2281-0692
Journal of Pediatric and Neonatal Individualized Medicine 2016;5(2):e050212
doi: 10.7363/050212
Received: 2016 Mar 20; revised: 2016 Apr 24; accepted: 2016 Apr 28; published online: 2016 Oct 31

Original article

Neonatal arrhythmias – morbidity and mortality at discharge

Ariana Silva[1], Paulo Soares[1,2], Filipa Flor-de-Lima[1,2], Cláudia Moura[1,3], José Carlos Areias[3], Hercília Guimarães[1,2]

[1]Faculty of Medicine of Porto University, Porto, Portugal

[2]Neonatal Intensive Care Unit, Department of Pediatrics, Centro Hospitalar de São João, Porto, Portugal

[3]Pediatric Cardiology, Department of Pediatrics, Centro Hospitalar de São João, Porto, Portugal

Abstract

Introduction: Cardiac arrhythmias are often diagnosed in fetuses and newborns. In the neonatal period, the incidence varies between 1% and 5%. There are three main types of rhythm disturbance: irregular heart rhythm, tachycardia and bradycardia. The prognosis changes with the nature of the arrhythmias and with timely diagnosis and management, but the majority have benign course, either spontaneously or after brief treatment, with life-threatening arrhythmias occurring rarely.

Aim: To evaluate the morbidity and mortality of neonates with cardiac arrhythmia, at discharge from the Neonatal Intensive Care Unit (NICU).

Methods: The study population included all newborns who were admitted with the diagnosis of cardiac arrhythmia between January 1, 2005 and December 31, 2014 at the NICU of "Centro Hospitalar de São João" (CHSJ), a level III unit. Data were collected retrospectively by reviewing patient's clinical records.

Results: Of a total of 66 patients with cardiac arrhythmia, at discharge from the NICU, 3% died and 9% showed sequelae. Adverse outcome was associated with preterm delivery, 1st and 5th minutes Apgar score < 7, resuscitation at birth, earlier prenatal diagnosis, gestation complications, postnatal therapy with electrical cardioversion, other reasons for hospitalization besides arrhythmia, inotropic support, longer hospital stay, oxygen therapy and mechanical ventilation and duration of both, transfusion support, parenteral nutrition and central vascular access. No arrhythmia type was associated to differences in outcome.

Conclusion: Our study reports an overall good prognosis of neonates with cardiac arrhythmia at discharge from NICU. Nevertheless, we identified some factors related to the perinatal period and to NICU stay that were associated with adverse outcome.

Keywords

Arrhythmia, newborn, Neonatal Intensive Care Unit, morbidity, mortality, congenital heart defect.

Corresponding author

Ariana Silva, Faculty of Medicine of Porto University. Alameda Professor Hernâni Monteiro, 4200-319 Porto, Portugal; email: mimed10173@med.up.pt.

How to cite

Silva A, Soares P, Flor-de-Lima F, Moura C, Areias JC, Guimarães H. Neonatal arrhythmias – morbidity and mortality at discharge. J Pediatr Neonat Individual Med. 2016;5(2):e050212. doi: 10.7363/050212.

Introduction

Cardiac arrhythmias are often diagnosed in fetuses and newborns, occurring in 2% of the pregnancies and, in the neonatal period, the incidence varies between 1% and 5%. Arrhythmias are a common reason of referral to fetal cardiology and pediatric cardiology units, and they are more frequent in the presence of congenital heart defects (CHD) [1-3].

Neonatal arrhythmias can be a continuation of an arrhythmia diagnosed prenatally, or can be discovered only incidentally after birth, during evaluation for other conditions, some of which nonspecific, such as irritability and feeding difficulties, or present as heart failure (HF) [4-6].

Electrocardiographic findings are the basis of diagnosis of arrhythmias in newborns. There are three main types of rhythm disturbance: irregular heart rhythm, tachycardia and bradycardia [7]. The first one includes premature atrial contractions (PACs) and premature ventricular contractions (PVCs). PACs are the main type of neonatal arrhythmias, but they are usually benign and self-limited, disappearing in weeks after birth. PVCs are less frequent and require more cautious evaluation in order to exclude an underlying heart disease. Nevertheless, they also present a benign course in most patients [1, 3, 4].

Transient bradycardia is a common condition in the first hours of life, tending to resolve within 2 to 3 days after birth [3]. Sustained sinus bradycardia is generally secondary to multiple cardiac or systemic conditions, and the only treatment required is the one necessary to solve the underlying disease [4]. Congenital complete atrioventricular (AV) block is the most relevant cause of sustained neonatal bradycardia and it occurs in isolation or in relation to either maternal autoantibodies, associated with connective tissue disease (CTD), or CHD [1, 5, 8].

About tachycardia, the most frequent origin is supraventricular and it is the most commonly associated with significant clinical impact in the neonatal period. The major mechanism of supraventricular tachycardia (SVT) in neonates is a re-entry circuit through an AV accessory pathway. Ventricular tachycardia (VT) is rare and is often consequence of an underlying heart abnormality [1, 3-6].

The prognosis changes with the nature of the arrhythmia and with timely diagnosis and management, but the majority have benign course, either spontaneously or after brief treatment, with life-threatening arrhythmias occurring rarely [1, 9]. Generally, mortality is higher if comorbidities exist, mainly CHD [7].

The purpose of this study is to evaluate the morbidity and mortality of neonates with cardiac arrhythmia, at discharge from the Neonatal Intensive Care Unit (NICU).

Methods

This retrospective observational study was conducted at the NICU of "Centro Hospitalar de São João" (CHSJ), a level III unit. The study population included all the newborns who were admitted with the diagnosis of cardiac arrhythmia between January 1, 2005 and December 31, 2014.

Data were collected retrospectively by reviewing patient's clinical records. Neonatal information included gender, birth weight, Apgar scores, need for resuscitation at birth, associated CHD and other congenital major malformations, karyotype abnormalities, type of arrhythmia and time of diagnosis, treatment received, admission and evolution in the NICU, total length of hospital stay, neurological exam and treatment at discharge and guidance to pediatric cardiology consultation. Maternal data included age, chronic diseases and previous abortions. Pregnancy and prenatal data included the occurrence of multiple pregnancy and gestational complications, drugs used during pregnancy, type and week of delivery.

Sequelae at discharge were defined as follows: bronchopulmonary dysplasia (BPD) of any severity according to classification by National Institutes of Health consensus criteria, periventricular leukomalacia (PVL) of any grade according to Murgo et al. grading system, and HF at any class as stated by Modified Ross Heart Failure Classification [10-12].

The statistical analysis was performed using IBM SPSS® statistics 22. Categorical variables were characterized by absolute and relative frequencies and continuous variables by mean (± standard deviation) if they had symmetric distribution or by median (minimum-maximum) if they had asymmetric

distribution. Fisher's exact test and Chi-squared test were used to compare categorical variables. Independent t test and Mann-Whitney U test were used for continuous variables with symmetric and asymmetric distribution, respectively. A multivariate analysis by logistic regression was performed to evaluate predictive factors of morbidity and mortality. A p-value inferior to 0.05 was considered statistically significant.

This study was approved by the Ethics Committee of CHSJ.

Results

Of a total of 66 patients with cardiac arrhythmia, at discharge from the NICU, there were 2 (3%) patients who died and 6 (9%) patients alive with sequelae. Of these, 2 presented PVL alone, 2 had BPD plus PVL and 2 had HF.

Tab. 1 describes demographic and clinical characteristics of patients. Approximately 70% of the newborns were delivery by C-section. The majority of arrhythmic patients had a term delivery, but preterm delivery was significantly more frequent among patients deceased or alive with sequelae.

Newborn Apgar scores at 1st and 5th minutes were < 7 in 9 (13.6%) and 8 (12.1%) patients, respectively, both with significant impact on the outcome. The need for resuscitation at birth was also significantly different between groups. Mean week of prenatal diagnosis was significantly lower in the adverse outcome group.

Fetal therapy was administered in 4 (9.5%) patients, 2 of which with atrial flutter treated with digoxin plus sotalol or digoxin alone, 1 with SVT that received digoxin, and 1 with complete AV block who was given betamethasone. In all these cases transplacental way was used. 62.1% of neo-

Table 1. Demographic and clinical characteristics according to outcome.

	Total (n = 66)	Deceased or alive with sequelae (n = 8)	Alive without sequelae (n = 58)	p
Gender, n (%)				
Male	44 (66.7)	7 (87.5)	37 (63.8)	0.252[b]
Female	22 (33.3)	1 (12.5)	21 (36.2)	
Gestational age (weeks), mean (± SD)	37 (± 2.8)	34 (± 3.8)	37.4 (± 2.4)	0.486[c]
Preterm delivery, n (%)	21 (31.8)	6 (75)	15 (25.9)	**0.010**[b]
Birth weight (grams), mean (± SD)	2,934.7 (± 605.2)	2,755.6 (± 847.3)	2,959.5 (± 569.5)	0.376[c]
C-section, n (%)	46 (69.7)	8 (100)	38 (65.5)	0.094[b]
Apgar score at 1st minute < 7, n (%)	9 (13.6)	4 (50)	5 (8.6)	**0.009**[b]
Apgar score at 5th minute < 7, n (%)	8 (12.1)	4 (50)	4 (6.9)	**0.005**[b]
Resuscitation at birth, n (%)	12 (18.2)	5 (62.5)	7 (12.1)	**0.004**[b]
Age at admission (days), mean (± SD)	3.5 (± 6.6)	2 (± 4.5)	3.7 (± 6.9)	0.496[c]
CHD, n (%)	9 (13.6)	2 (25)	7 (12.1)	0.298[b]
ASD, type ostium secundum	5 (55.6)	0	5 (71.4)	0.167[b]
VSD	3 (33.3)	1 (50)	2 (28.6)	0.999[b]
HLH	1 (11.1)	1 (50)	0	0.222[b]
Coarctation of the aorta	1 (11.1)	0	1 (14.3)	0.999[b]
Prenatal diagnosis, n (%)	42 (63.6)	6 (75)	36 (62.1)	0.700[b]
Prenatal diagnosis (weeks), mean (± SD)	35.5 (± 3.2)	32.7 (± 3.6)	36 (± 2.9)	**0.016**[c]
Diagnosis at birth, n (%)	1 (1.5)	0	1 (1.7)	0.999[b]
Postnatal diagnosis, n (%)	23 (34.8)	2 (25)	21 (36.2)	0.703[b]
Postnatal diagnosis (days), mean (± SD)	10.1 (± 9.5)	22 (± 8.5)	9 (± 8.9)	0.063[c]
Fetal therapy, n (%)	4 (9.5)	1 (16.7)	3 (8.3)	0.474[b]
Postnatal therapy, n (%)	41 (62.1)	6 (75)	35 (60.3)	0.700[b]
Drugs[a]	38 (92.7)	5 (83.3)	33 (94.3)	0.386[b]
Electrical cardioversion	7 (15.9)	3 (50)	4 (10.5)	**0.042**[b]
Pacing	2 (4.4)	0	2 (5.1)	0.999[b]

[a]Adenosine, amiodarone, flecainide, propranolol, digoxin.
[b]Fisher's exact test; [c]independent t test.
CHD: congenital heart defects; ASD: atrial septal defect; VSD: ventricular septal defect; HLH: hypoplastic left heart.

nates received postnatal therapy, 92.7% in the form of drugs. The use of electrical cardioversion was significantly higher in the adverse outcome group. This therapeutic approach was used in 4 cases of atrial flutter, in 1 case of atrioventricular re-entrant tachycardia (AVRT), in 1 patient with SVT without other specification and in 1 neonate with VT. Pacing was used in only 2 (4.4%) newborns, both having complete AV block and belonging to the alive without sequelae group.

CHD occurred in 9 (13.6%) patients, tending to be more common in patients deceased or alive with sequelae, but significant difference was not observed. The most frequent CHD was atrial septal defect (ASD), type ostium secundum, and the arrhythmias diagnosed in these newborns were: 1 case with sinus tachycardia, 2 cases of AVRT and 2 cases of SVT without other specification. Three newborns had ventricular septal defect (VSD), and 2 of them had a muscular septal defect, while 1 had a perimembranous septal defect. In these patients sinus tachycardia, atrial flutter and complete AV block were diagnosed. One patient had a mixed defect with ASD and VSD. Second-degree AV block was found in a patient with hypoplastic left heart (HLH), one of the dead neonates, and SVT without other specification was diagnosed in the case of coarctation of the aorta.

Another major congenital malformation was registered in just 1 case, under the form of superior labial cleft. One baby was diagnosed with tuberous sclerosis, the same disease that his mother had. These two patients were part of the group with positive outcome. Karyotype was normal in 10 (15.2%) newborns and unknown in the remainders.

Tab. 2 shows data on maternal and pregnancy features. Maternal chronic diseases were verified in 14 (21.2%) neonates, and the more common were

Table 2. Maternal and pregnancy features of patients.

	Total (n = 66)	Deceased or alive with sequelae (n = 8)	Alive without sequelae (n = 58)	p
Maternal age (years), mean (± SD)	30 (± 5.4)	29.4 (± 6.8)	30.6 (± 5.2)	0.566[b]
Maternal chronic diseases, n (%)	14 (21.2)	0	14 (24.1)	0.187[a]
Asthma	2 (14.3)	0	2 (14.3)	0.999[a]
Tuberous sclerosis	1 (7.1)	0	1 (7.1)	0.999[a]
CTD	5 (35.7)	0	5 (35.7)	0.999[a]
Hypothyroidism	3 (21.4)	0	3 (21.4)	0.999[a]
Congenital adrenal hyperplasia	1 (7.1)	0	1 (7.1)	0.999[a]
Hereditary spherocytosis	1 (7.1)	0	1 (7.1)	0.999[a]
Schizophrenia	1 (7.1)	0	1 (7.1)	0.999[a]
Previous abortions, n (%)	6 (9.5)	0	6 (10.9)	0.999[a]
Multiple pregnancy, n (%)	3 (4.5)	1 (12.5)	2 (3.4)	0.326[a]
Gestation complications, n (%)	11 (16.7)	4 (50)	7 (12.1)	**0.022**[a]
Oligo/anydramnios	2 (18.2)	1 (25)	1 (14.3)	0.999[a]
Preeclampsia	1 (9.1)	0 (0)	1 (14.3)	0.999[a]
Gestational diabetes	5 (45.5)	1 (25)	4 (57.1)	0.545[a]
Urinay tract infection	2 (18.2)	1 (25)	1 (14.3)	0.999[a]
Cytomegalovirus infection	1 (9.1)	1 (25)	0	0.364[a]
Chorioamnionitis	1 (9.1)	0	1 (14.3)	0.999[a]
Drugs during pregnancy, n (%)	10 (15.2)	1 (12.5)	9 (15.5)	0.999[a]
Levothyroxine	3 (30)	0	3 (33.3)	0.999[a]
Insulin	2 (20)	0	2 (22.2)	0.999[a]
Carbamazepine	1 (10)	0	1 (11.1)	0.999[a]
Risperidone	1 (10)	0	1 (11.1)	0.999[a]
Hydrocortisone	1 (10)	0	1 (11.1)	0.999[a]
Hydroxychloroquine sulphate	1 (10)	0	1 (11.1)	0.999[a]
Acetylsalicylic acid	1 (10)	0	1 (11.1)	0.999[a]
Antibiotics	2 (20)	1 (100)	1 (11.1)	0.200[a]

[a]Fisher's exact test; [b]Independent t test.
CTD: connective tissue disease.

CTD, hypothyroidism and asthma. Of mothers with CTD, 3 had systemic lupus erythematosus (SLE) and 2 had Sjogren's syndrome. None of the mother's pathologies had any statistically significant association with each group of patients. The occurrence of gestation complications was significantly higher in the adverse outcome group. There were no statistically significant differences in drugs consumption during pregnancy between the two groups.

Tab. 3 is related to types of arrhythmias. Among the three main classes of rhythm disturbance, tachyarrhythmias were the most widely found, followed by bradyarrhythmias, and finally premature beats. All second-degree AV block were Mobitz type II. One case of variable AV block, with alternance between periods of second-degree and complete AV block, was reported. Only one mother of neonates with complete or variable AV block did not show known CTD. Of patients with complete AV block, 3 were anti-SSA/Ro and anti-SSB/La antibodies positive, and 2 were only anti-SSB/La antibodies positive.

In half of cases of SVT, it was not possible to know the mechanism by reviewing the patient's clinical records. In 5 babies, two different kinds of arrhythmia were identified, namely, sinus bradycardia added to PACs, SVT alternating with periods of sinus bradycardia, SVT plus PACs, PVCs and brief episodes of VT, and atrial flutter combined with second-degree AV block. All these patients were part of the good outcome group.

None of the types of arrhythmias had significant difference between groups.

Data in **Tab. 4** refers to evolution during NICU stay. All patients deceased or alive with sequelae presented other reasons for admission besides arrhythmia. Neonates with adverse outcome stayed longer in the NICU, had greater need of oxygen therapy and mechanical ventilation and longer duration of both. They also showed greater use of inotropic and transfusion supports, parenteral nutrition and central vascular access.

At discharge from the NICU, all alive newborns presented neurological exam according to age, with the exception of 1 patient in whom this data was unknown. There was no statistically significant difference in antiarrhythmic drugs at discharge between groups. Propranolol was the most required drug, mainly added to flecainide (n = 18). Isolated flecainide was used in 1 patient and another patient was medicated with flecainide and digoxin.

With multivariate analysis, none of the studied variables was predictive of adverse outcome.

Table 3. Types of arrhythmias.

	Total (n = 66)	Deceased or alive with sequelae (n = 8)	Alive without sequelae (n = 58)	p
Premature beats, n (%)	15 (22.7)	0	15 (25.9)	0.182[a]
PAC	13 (86.7)	0	13 (86.7)	0.999[a]
PVC	2 (13.3)	0	2 (13.3)	0.999[a]
Bradyarrythmias, n (%)	18 (27.3)	2 (25)	16 (27.6)	0.999[a]
Sinus bradycardia	10 (55.6)	1 (50)	9 (56.3)	0.999[a]
Second-degree AV block	2 (11.1)	1 (50)	1 (6.3)	0.216[a]
Complete AV block	5 (27.8)	0	5 (31.3)	0.999[a]
Variable AV block	1 (5.6)	0	1 (6.3)	0.999[a]
Tachyarrhythmias, n (%)	39 (59.1)	6 (75)	33 (56.9)	0.455[a]
Sinus tachycardia	1 (2.6)	0	1 (3)	0.999[a]
SVT	35 (89.7)	5 (83.3)	30 (90.9)	0.502[a]
Atrial flutter	6 (17.1)	3 (60)	3 (10)	0.268[a]
Ectopic atrial tachycardia	1 (2.9)	1 (20)	0	0.999[a]
AVRT	10 (28.6)	0	10 (33.3)	0.152[a]
WPWS	3 (30)	0	3 (30)	0.999[a]
Without other specification	18 (51.4)	1 (20)	17 (56.7)	0.658[a]
VT	2 (5.1)	0	2 (6.1)	0.999[a]
Tachyarrhythmia without other specification	1 (2.6)	1 (16.7)	0	0.999[a]

[a]Fisher's exact test.
PAC: premature atrial contraction; PVC: premature ventricular contraction; AV: atrioventricular; SVT: supraventricular tachycardia; AVRT: atrioventricular re-entrant tachycardia; WPWS: Wolff-Parkinson-White Syndrome; VT: ventricular tachycardia.

Table 4. Evolution during Neonatal Intensive Care Unit (NICU) stay.

	Total (n = 66)	Deceased or alive with sequelae (n = 8)	Alive without sequelae (n = 58)	p
Hospitalization due to arrhythmia, n (%)	57 (86.4)	6 (75)	51 (87.9)	0.999[d]
Other reasons for hospitalization, n (%)	31 (47)	8 (100)	23 (39.7)	0.001[b]
Prematurity	21 (67.7)	6 (75)	15 (62.2)	0.999[b]
Fetal hydrops	5 (16.1)	3 (37.5)	2 (8.7)	0.093[b]
Infectious risk	6 (19.4)	1 (12.5)	5 (21.7)	0.999[b]
Complex heart disease[a]	4 (12.9)	2 (25)	2 (8.7)	0.268[b]
Cardiogenic shock	1 (3.2)	1 (12.5)	0	0.258[b]
Respiratory failure	3 (9.7)	0	3 (13)	0.545[b]
Food refusal	1 (3.2)	0	1 (4.3)	0.999[b]
Oxygen therapy, n (%)	25 (37.9)	8 (100)	17 (20.7)	< 0.001[b]
Days, median (min-max)	4 (1-45)	6.5 (2-45)	3 (1-9)	0.043[c]
Mechanical ventilation, n (%)	18 (23.7)	6 (75)	12 (29.3)	< 0.001[b]
Days, median (min-max)	5.5 (1-33)	11.5 (2-33)	5 (1-14)	< 0.001[c]
Inotropic support, n (%)	13 (19.7)	6 (75)	7 (12.1)	< 0.001[b]
Transfusion support, n (%)	12 (18.2)	5 (62.5)	7 (12.1)	0.004[b]
Central vascular access, n (%)	18 (23.7)	8 (100)	10 (17.2)	< 0.001[b]
Days, median (min-max)	10 (2-25)	10.5 (2-25)	9 (4-19)	0.965[c]
Parenteral nutrition, n (%)	18 (23.7)	7 (87.5)	11 (19)	< 0.001[b]
Days, median (min-max)	7.5 (1-26)	11 (1-26)	7 (3-20)	0.596[c]
Hospital stay (days), median (min-max)	4 (1-56)	12.5 (2-56)	3.5 (1-50)	0.018[c]
Antiarrhythmic drugs at discharge, n (%)	33 (51.6)	2 (33.3)	31 (53.4)	0.419[b]
Propranolol	31 (93.9)	2 (100)	29 (93.5)	0.999[b]
Flecainide	20 (60.6)	2 (100)	18 (58.1)	0.508[b]
Digoxin	1 (3)	0	1 (3.2)	0.999[b]
Pediatric cardiology consultation, n (%)	64 (100)	6 (100)	58 (100)	-

[a] Suspected/confirmed.
[b] Fisher's exact test; [c] Mann Whitney-U test; [d] Chi-squared test.

Discussion

Our results show that neonatal cardiac arrhythmias have an overall good prognosis, with a mortality rate at discharge from the NICU of 3%. Sequelae occur in 9% of patients, although most arrhythmias are clinically benign, with no significant impact on child development. This is consistent with results of other authors [9, 13].

One of the deceased patients was prenatally diagnosed, at gestational age of 30 weeks, with atrial flutter and secondary fetal hydrops. Fetal therapy was delivered without successful results. Thus, delivery was decided at 32 weeks of gestation. After electrical cardioversion at birth, sinus rhythm was restored. On the second day of life, cardiac arrest was registered. Another case of death occurred on the third day of life, in a patient with HLH in whom second-degree AV block was verified postnatally. In both two obits cases, autopsy was not authorized by parents.

Badrawi et al. found that, regardless of the severity, occurrence of arrhythmia in NICU was significantly greater in males [2]. In our study, differences in gender distribution between different outcome groups were not statistically significant.

Earlier prenatal diagnosis was made in neonates with increased morbidity and mortality, which may be explained by a greater fetal impact of arrhythmias in this group of patients, making them more easily detected. Gestation complications were associated with a worse prognosis.

Cardiac arrhythmias are more regularly found in neonates with CHD, particularly if the source of the disturbance is in a supraventricular location, according with the fact that ASD is the CHD most frequently diagnosed [1, 13]. The concomitant existence of CHD is predictive of worse prognosis, with mortality risk increased [7]. In our sample, CHD were more frequent in the adverse outcome group, occurring in a quarter of them,

although statistically significance has not been established.

Premature beats are referred as the most frequent neonatal arrhythmias [1, 9]. In our study the rhythm disturbance most often diagnosed was SVT. PACs and PVCs are generally asymptomatic and occur in healthy patients, however metabolic and biochemical problems, hypoxia and pharmacological causes may be an underlying factor. Their detection varies largely with the duration of heart rhythm evaluation [1]. Our study is conducted in a NICU, where is expected that arrhythmias with more significant clinical impact are diagnosed more frequently. On the other hand, most of neonates are diagnosed with premature beats without need of NICU admission.

Premature beats were verified solely in patients alive without sequelae, which is compatible with the literature. In the absence of other pathologies, the prognosis of PACs is very good and no further management is necessary, with most cases being spontaneously resolved after the first weeks after birth [1, 3, 4]. PACs are associated with a risk lower than 1% of SVT development. Despite being similarly benign, PVCs may warrant a more careful approach in order to exclude myocarditis, Long QT Syndrome (LQTS), and their complications [4].

In our results, sinus bradycardia represents more than half of total bradyarrhythmias diagnosed. This is really the more common form of bradyarrhythmia and may be related with several causes, namely, increased vagal tone, myopathies and inflammatory diseases, LQTS, medication (including antiarrhythmic drugs), central nervous system abnormalities (tumours, increased intracranial pressure and meningitis), metabolic conditions (hypoxia, hypothermia, hypothyroidism, acidosis), obstructive jaundice and sepsis [1, 3, 4].

All registered cases of AV block are considered high-degree (Mobitz type II second-degree AV block and complete AV block). These forms of neonatal AV block may have a significant clinical impact, as they may be associated with CHD and more frequently lead to symptomatic bradycardia and HF [1, 3]. According to literature, the CHD most commonly related to heart block is left atrial isomerism [7]. However, in our study VSD and HLH were found in newborns with complete AV block and Mobitz type II second-degree AV block, respectively. There is an association between neonatal congenital heart block (CHB) and maternal CTD with circulating maternal anti-SSA/Ro and anti-SSB/La antibodies [5, 7, 8, 14]. In our study, this happened in one case. Several fetal therapeutic approaches have been tried, namely sympathomimetics, plasmapheresis, steroids and intravenous immunoglobulin, but the effectiveness of these options remains controversial [8, 14]. In our patients, although all cases of AV block were diagnosed prenatally, only one patient with complete AV block received fetal therapy with betamethasone, without demonstrated efficacy.

CHB implies a significant risk of morbidity and mortality (15-30%), particularly in fetal, neonatal and infant periods [15]. In our results, only 1 neonate with second-degree AV block belongs to the group of deceased or alive with sequelae, probably due to severity of associated CHD, HLH.

Most patients with CHB do not need pacemaker in the newborn period. However, most of them will require pacing therapy during childhood or adolescence [3]. Two of our patients with CHB required pacemaker in the neonatal period. In presence of failure o thrive, symptomatic bradycardia, low cardiac output, resting heart rate < 55 bpm, complex ventricular arrhythmias and associated CHD, early pacemaker implantation is advocated [4, 7, 16].

In our study, SVT was the most commonly diagnosed type of tachycardia and even the commonest kind of arrhythmia observed, as previously mentioned. Except for the case in which mechanism of SVT was not specified, AVRT was the most frequent type of SVT. These results are compatible with the literature [1, 3, 6].

Wolff-Parkinson-White Syndrome (WPWS) is a condition in which electrical impulse can be directed forwards and backwards through the accessory pathway [3, 6]. This is reported in 34-70% of babies of less than three months with SVT [17, 18]. In our study, WPWS pattern was verified in 8.6% of neonates with SVT and, at discharge from the NICU, all of them received prophylactic anti-arrhythmic treatment with propranolol, given the risk of recurrence of SVT.

Treatment of SVT is generally done by drugs, being adenosine mostly effective in acute management. Around 40% of SVTs treated in the neonatal period do not recur if anti-arrhythmic drugs are given for at least 6 to 12 months after the first episode. Recurrence rate of SVT is inversely related to age of onset, being lowest for cases with prenatal diagnosis [1, 4, 9, 18].

Atrial flutter is common in newborns, usually in structurally normal hearts, and long term medical therapy besides initial conversion to sinus rhythm is usually not needed, given the low probability of recurrence [3, 6, 7]. However, in our study, all

survivor patients with this arrhythmia were given flecainide plus propranolol at discharge.

VT is extremely rare in the neonatal period, in half of cases is seen in apparently healthy babies and is related with a positive outcome [19]. This is consistent with our results.

If hemodynamic instability exists, electrical cardioversion is the choice therapy for SVT, including atrial flutter, and VT [1, 3]. In our study, its use was associated with adverse prognosis.

Other authors emphasize the following factors linked to a high risk of mortality and morbidity in neonatal arrhythmias: shock or circulatory failure, or antenatal hydrops; comorbidities, especially prematurity or CHD; inadequate monitoring or resuscitation; wrong choice of drugs; metabolic alterations or polypharmacy [7]. In accordance to this, our results showed that preterm delivery, resuscitation at birth and low Apgar score, comorbidities and hemodynamic instability were significantly more common in the group with adverse outcome. However, fetal hydrops and CHD appeared not to influence the prognosis. Furthermore, in our study, longer hospital stay, greater need of oxygen therapy and mechanical ventilation, transfusion support, parenteral nutrition and central vascular access were related to increased morbidity and mortality.

In our results, none of the arrhythmia types had significant difference between groups. This suggests that, rather than the type of arrhythmia, the outcome is more influenced by other factors related to perinatal period and to NICU stay.

Limitations of our study are inherent to its retrospective design and related to the low number of included patients that may limit statistical power.

Conclusion

Our study reports an overall good prognosis of neonates with cardiac arrhythmia at discharge from the NICU, with a mortality rate of 3% and with sequelae occurring in 9% of patients.

Nevertheless, we identified some factors, related to the perinatal period and to NICU stay, that were associated with adverse outcome. These factors should be known in the management of these newborns, given that some of them can be preventable.

Further research on the outcome of cardiac arrhythmias in neonates is needed, mainly with prospective studies and with longer follow-up to evaluate the long-term prognosis of these patients.

Declaration of interest

The Authors declare that no conflicts of interest exist.

References

1. Sekarski N, Meijboom EJ, Bernardo SD, Ksontini TB, Mivelaz Y. Perinatal arrhythmias. Eur J Pediatr. 2014;173:983-96.
2. Badrawi N, Hegazy RA, Tokovic E, Lotfy W, Mahmoud F, Aly H. Arrhythmia in the neonatal intensive care unit. Pediatr Cardiol. 2009;30(3):325-30.
3. Stacy AS, Killen M, Frank A, Fish M. Fetal and Neonatal Arrhythmias. Neoreviews. 2008;9:e242-52.
4. Strasburger JF, Cheulkar B, Wichman HJ. Perinatal arrhythmias: diagnosis and management. Clin Perinatol. 2007;34(4):627-52, vii-viii.
5. Wren C. Cardiac arrhythmias in the fetus and newborn. Semin Fetal Neonatal Med. 2006;11(3):182-90.
6. Kothari DS, Skinner JR. Neonatal tachycardias: an update. Arch Dis Child Fetal Neonatal Ed. 2006;91(2):F136-44.
7. Skinner JR, Sharland G. Detection and management of life threatening arrhythmias in the perinatal period. Early Hum Dev. 2008;84(3):161-72.
8. Ho A, Gordon P, Rosenthal E, Simpson J, Miller O, Sharland G. Isolated Complete Heart Block in the Fetus. Am J Cardiol. 2015;116(1):142-7.
9. Moura C, Vieira A, Guimarães H, Areias JC. Perinatal Arrhythmias – Diagnosis and Treatment. Rev Port Cardiol. 2002;21:45-55.
10. Ehrenkranz RA, Walsh MC, Vohr BR, Jobe AH, Wright LL, Fanaroff AA, Wrage LA, Poole K; National Institutes of Child Health and Human Development Neonatal Research Network. Validation of the National Institutes of Health consensus definition of bronchopulmonary dysplasia. Pediatrics. 2005;116(6):1353-60.
11. Murgo S, Avni EF, David P, Muller MF. Golzarian J, Baleriaux D, Struyven J. [Periventricular leukomalacia in premature infants: prognostic role of ultrasonography and MRI]. [Article in French]. J Radiol. 1999;80(7):715-20.
12. Hsu DT, Pearson GD. Heart failure in children. Part I: history, etiology, and pathophysiology. Circ Heart Fail. 2009;2(1):63-70.
13. Binnetoglu FK, Babaoglu K, Turker G, Altun G. Diagnosis, treatment and follow up of neonatal arrhythmias. Cardiovasc J Afr. 2014;25(2):58-62.
14. Yildirim A, Tunaoolu FS, Karaaoac AT. Neonatal congenital heart block. Indian Pediatr. 2013;50(5):483-8.
15. Friedman DM, Rupel A, Buyon JP. Epidemiology, etiology, detection, and treatment of autoantibody-associated congenital heart block in neonatal lupus. Curr Rheumatol Rep. 2007;9(2):101-8.
16. Brugada J, Blom N, Sarquella-Brugada G, Blomstrom-Lundqvist C, Deanfield J, Janousek J, Abrams D, Bauersfeld U, Brugada R, Drago F, de Groot N, Happonen JM, Hebe J, Yen Ho S, Marijon E, Paul T, Pfammatter JP, Rosenthal E; European Heart Rhythm Association; Association for European Paediatric and Congenital Cardiology. Pharmacological and non-pharmacological therapy

for arrhythmias in the pediatric population: EHRA and AEPC-Arrhythmia Working Group joint consensus statement. Europace. 2013;15(9):1337-82.

17. Lupoglazoff JM, Denjoy I. [Practical attitude toward arrhythmia in the neonate and infant]. [Article in French]. Arch Pediatr. 2004;11(10):1268-73.
18. Gilljam T, Jaeggi E, Gow RM. Neonatal supraventricular tachycardia: outcomes over a 27-year period at a single institution. Acta Paediatr. 2008;97(8):1035-9.
19. Levin MD, Stephens P, Tanel RE, Vetter VL, Rhodes LA. Ventricular tachycardia in infants with structurally normal heart: a benign disorder. Cardiol Young. 2010;20(6):641-7.