Follow-up studies in prenatal medicine

Nagel, H.T.C.

CHAPTER 8

Fetal arrhythmia and long-term outcome

HTC Nagel

MI Aziz

NA Blom

L Rozendaal

HHH Kanhai

FPHA Vandenbussche

Submitted

Abstract

Objective To evaluate perinatal mortality, morbidity, long-term neurodevelopmental and cardiologic outcome of fetuses with severe tachy- or bradyarrhythmia.

Methods Follow-up study of 44 fetuses diagnosed with fetal cardiac arrhythmia between January 1990 and December 2005. Neurodevelopmental assessment included neurologic evaluation and assessment of developmental status by the Snijders-Oomen Non-Verbal Intelligence Test-Revised or the Dutch version of the Bayley Scales of Infant Development- Second Edition according to age. Cardiological assessment included clinical evaluation and electrocardiography.

Results Between January 1990 and December 2005, 44 fetuseses were diagnosed with sustained fetal tachy- or bradyarrhythmia: 28 with supravenricular tachycardia (SVT), 7 with atrial flutter (AF) and 9 with atrioventricular block (AVB). The incidence of cardiac anomalies was 18%. Hydrops was seen in 42-50%. Direct or transplacental fetal antiarrhythmic medication was given in 76% of cases. In the SVT group, 19 children needed medication postpartum. In 14/22, the arrhythmia ceased within the first year of life. In the SVT and AF group mortality was 6%. In 21% of these cases, Wolff Parkinson White (WPW) syndrome was diagnosed. Mental scores were normal in all survivors. Of the seven cases of AVB included in the follow-up there is no survivor. The other two cases were lost for long-term follow-up, but their medical records noted pacemaker therapy in one and mental retardation in the other.

Conclusion In conclusion, mortality in SVT and AF patients in our study was 6%, but mental scores were normal in all survivors. Twenty-one per cent of survivors had WPW syndrome. Prognosis in AVB patients was poor.

Introduction

Fetal cardiac arrhythmia is best defined as an irregular cardiac rhythm that results in a fetal heart rate outside the normal range (100-160 beats/minute).
Fetal arrhythmias are common in clinical practice, with a frequency ranging from 1% to 3% of all pregnancies. Most of these arrhythmias reflect transient, isolated ectopic beats. However, sustained episodes of tachy- or bradyarrhythmia do occur and, if not treated appropriately, these can lead to congestive heart failure, hydrops, fetal or neonatal demise, or severe neurologic morbidity in survivors.[1-7]

The most common forms of fetal tachycardias are supraventricular tachycardia (SVT), atrial flutter (AF), or sinus tachycardia. The majority of fetal SVTs are atrioventricular re-entrant tachycardias (AVRT) involving an accessory atrioventricular myocardial pathway. Other mechanisms of SVT, including atrial and junctional ectopic tachycardia, or ventricular tachycardia are rare, each constituting less than 1% of fetal arrhythmias. More than three quarters of cases of fetal bradycardia is caused by complete atrioventricular block (AVB). AVB in the absence of structural heart disease is mostly autoimmune mediated by maternal anti SS-A/SS-B antibodies. In general, complete AVB with complex congenital heart disease such as left isomerism has a very poor prognosis. Other, less frequent causes of bradycardia include sinus bradycardia, advanced second-degree AVB, prolonged QT interval syndrome, and fetal toxicity.

Ultrasound diagnosis of fetal arrhythmia offers the possibility of prenatal therapy. If indicated, antiarrhythmic drugs can be given directly to the fetus or via the mother in order to obtain a therapeutic plasma concentration in the fetus. In SVT, digoxin is the most commonly used drug. There is no consensus regarding second line antiarrhythmic treatment if digoxin therapy fails. In first and second degree AVB, transplacental steroid treatment may reduce the effects of inflammation and fibrosis of the conduction system caused by maternal antibodies. In AVB cases with extremely low ventricular rates transplacental treatment with sympathomimetic agents such as terbutaline or salbutamol can be given to increase atrial and ventricular rates. Elective delivery by cesarean section can be performed in the third trimester of pregnancy to start direct neonatal therapy (antiarrhythmic drugs, radiofrequency catheter ablation or pacemaker therapy).

The goal of pre- and postnatal treatment of fetal tachycardia is to achieve sinus rhythm or to reduce the fetal heart rate in order to prevent heart failure or death. In several reports, neurological morbidity has been linked to fetal tachycardia. Neurologic morbidity may result from dysfunction of cerebrovascular autoregulation in hemodynamically compromised fetuses.[8] In most cases of fetal tachycardia, medication can be stopped within months after delivery. However, in cases of fetal SVT, particularly involving accessory atrioventricular pathways, recurrences can be expected later in life. In the literature, we found strikingly little information regarding

long-term follow-up of major fetal arrhythmias.

The aim of this study was to evaluate perinatal mortality and morbidity as well as long-term neurolodevelopmental and cardiologic outcome of fetuses with severe tachy- or bradyarrhythmia diagnosed at our center.

Methods

Patients

Leiden University Medical Center is a tertiary fetal referral center. We searched both our antenatal and neonatal databases for infants with in utero cardiac arrhythmia, diagnosed between January 1990 and December 2005. In this time period the management protocol included complete work up with ultrasound examination and consultation of the pediatric cardiologist. Fetal ultrasound included detailed anatomic imaging of the fetal heart to diagnose or exclude cardiac defects. For the assessment of the cardiac rhythm and the origin of the ectopic beats we used M-mode evaluation of the atrial and ventricular walls, as well as visualization of blood flow within the cardiac chambers and the outflow tract with pulsed Doppler flow.

Fetal Diagnosis and Therapy

Supraventricular tachycardia (SVT) as a result of atrioventricular reentrant tachycardia (AVRT) was diagnosed if there was a 1:1 atrioventricular conduction observed with a short VA interval at a rate of 200 to 300 beats/min. Atrial flutter (AF) was diagnosed when the atrial rate was 300-450 beats/min. Ventricular rates in AF depended on the degree of AV conduction block, usually 200-300 beats/min. The highest (peak) fetal heart rate was noted to give an indication of the severity of the tachycardia. Tachycardias that were present more than 50% of the time during the ultrasound examination were defined as "persistent", and if tachycardia lasted less than 50% of the time it was classified as "intermittent". AVB was classified as 2nd degree or complete AVB based on M-mode registrations. Fetal hydrops was defined as a fluid collection visible on ultrasound in two or more cavities of the fetal body (generalized edema, ascites and pleural or pericardial effusions).[9] Maternal serum antibody titers (anticardiolipin antibodies, anti SS-A/Ro and anti SS-B/La) were obtained in case of a heart block.

Antiarrhythmic therapy was started when arrhythmias were sustained or associated with hemodynamic compromise at <34 weeks of pregnancy. After 34 weeks, such cases were delivered. A baseline electrocardiography of the mother was obtained before the treatment started and maternal cardiac monitoring was conducted during the loading period to detect early signs of toxicity. During the study period, the following drugs were used: digoxin, sotalol, flecainide, amiodarone and adenosine. Digoxin was administered to the mother in adjusted doses to

maintain a maternal serum therapeutic level of 1 to 2 ng/mL (loading dose 2 x 0.75 mg, maintenance 0.25-0.5 mg, maximum 0.75 mg/daily). Flecainide (200 mg to 400 mg daily) and sotalol (dose: 2 times daily 80-160 mg) were used as secondary agents. Amiodarone was administered by combined direct fetal intravenous and maternal oral and intravenous route. Direct fetal amiodarone therapy consisted of amiodarone on the basis of estimated fetal weight (10 mg/kg). In some cases adenosine was given intravenously as direct fetal therapy just before the amiodarone therapy (dose 0.1 mg/kg). Drugs to treat AVB were given to the mother: ritodrine (intravenously 9 mg/hour), dexamethasone (4 mg daily) and fenoterol (intravenously 150 μgram/hour).

Follow-up

Obstetric and neonatal records were reviewed. With approval of the protocol by the institutional review board of the Leiden University Medical Center, family physicians were contacted by letter to explain the aims and nature of the study. After consultation with the family physician, the parents were sent an explanatory letter asking their permission to review all medical records and their cooperation for testing the children. The neurodevelopmental and cardiological status was assessed from June - August 2006. The parents were asked to fill out the Dutch translation of the Child Behaviour Check List (CBCL), a validated questionnaire for the assessment of behavioural/ emotional problems. At the subsequent consultation the child was examined by a pediatric cardiologist and a psychologist. Neurologic examination was performed by a pediatrician. Cardiologic examination included medical history, physical examination and electrocardiography (ECG). Additional studies, i.e. 24 hour-Holter monitoring, exercise test and echocardiography were performed if children were symptomatic.

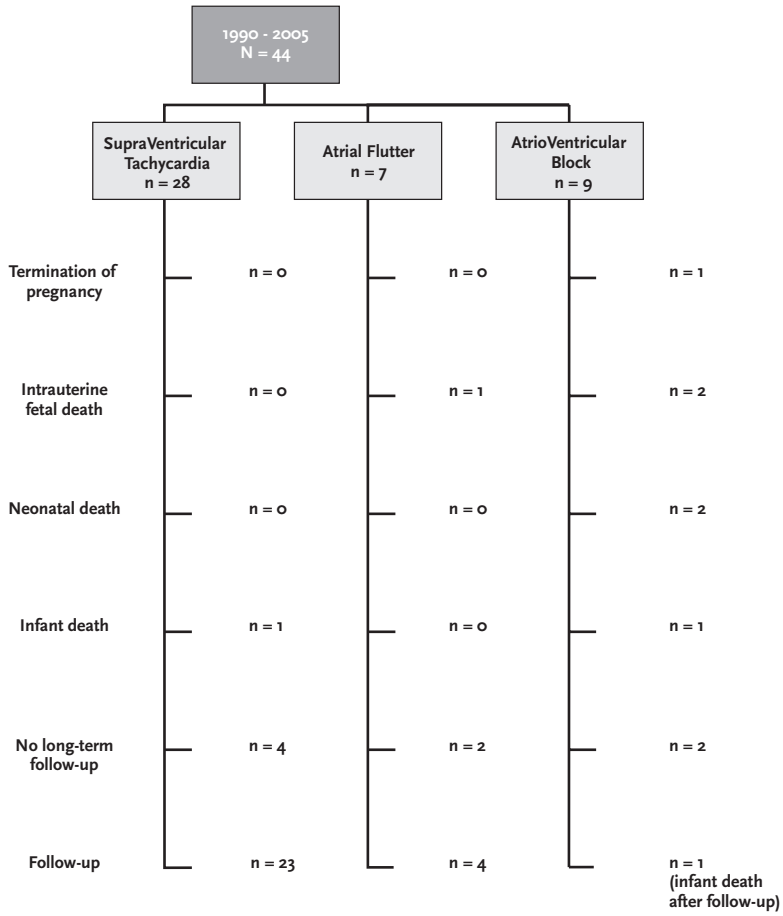
In the children aged 6 months to 30 months, the Dutch version of the Bayley Scales of Infant Development- Second Edition (BSID-II-NL) was used to test 3 scales of neurodevelopment (mental scale, motor scale and behavioral rating).[10,11] Mental scales are converted to a mental developmental index (MDI) with a mean of 100 and standard deviation of 15. Motor scales are converted to psychomotor developmental index (PDI) with mean 100 and standard deviation 15. The normal limits are defined as MDI and PDI values between 85-114. Values of 70-84 are defined as mildly delayed performance. A score of < 69 is defined as significantly delayed performance. In the children aged 2.5-16 years the intelligence scores were assessed with the Snijders-Oomen Non-Verbal Intelligence Test-Revised (SON-R 2.5-7 and SON-R 5.5-17).[12] Scores are calculated as performance scale (SON-PS) and reasoning scale (SON-R). Raw subtest scores are standardized with population and age specific scores with a mean value of 100 and a SD of 15. The SON-R has been validated for Dutch and Belgian children. Total test scores are depicted as IQ-scores with confidence intervals.

Results

Study population characteristics

During the 16-year study period, 44 pregnancies were referred to our center because of sustained fetal tachy- or bradyarrhythmia. **Figure 1** shows the overall outcome of the 44 fetuses with arrhythmia.

Figure 1. Overall outcome of 44 fetuses with arrhythmia.



Perinatal characteristics of the study population are presented in **Table 1**.

Table 1. Characteristics of the study population (N = 44), by type of arrhythmia.

Type of arrhythmia		SupraVentricular Tachycardia (n = 28)	Atrial Flutter (n = 7)	AtrioVentricular Block (n = 9)
Median maternal age in years (range)		28 (20-39) A	31 (24-39)	32 (28-36)
Median maternal gravidity (range)		2 (1-6) **A**	1 (1-4) **B**	2 (1-3)
Median maternal parity (range)		1 (0-4) **A**	0 (0-3) **B**	1 (0-1)
Median number of previous abortions (range)		0 (0-3) **A**	0 (0) **B**	0 (0-1)
Percentage of male fetuses (n)		60.7 (17)	42.9 (3)	57.1 (4) **C**
Median gestational age at diagnosis of arrhythmia in weeks (range)		29 (18-40) **B**	30 (24-38) **C**	23 (12-37) **B**
Median peak/slowest Fetal Heart Rate in beats per minute (range)		247 (200-400) **A**	237 (200-250) **B**	55 (45-70)
Percentage of fetal hydrops (n)		42.3 (11) **A**	- **C**	50.0 (4) **B**
Median duration of fetal hydrops in days since diagnosis (range)		7 (1-30) **A**	-	24 (1-50)
Percentage of antenatal therapy (n)		61.5 (16) **A**	50.0 (3) **B**	33.3 (3)
Median duration of antenatal therapy in days (range)		56 (12-95) **B**	49 (43-96)	33 (12-93)
Mode of delivery: vaginal / VE-FE / cesarean: n		19 / 1 / 7 **A**	4 / 1 / 1 **B**	7 / - / 2
Median gestational age at birth in weeks (range)		38 (30-42) **A**	37 (36-38) **C**	36 (30-40) **D**
Median birth weight in grams (range)		2993 (1547-3965) **A**	3282 (2530-4726) **B**	2704 (2300-3470) **D**
Median Apgar score (range)	**1'**	9(1-10) **B**	7 (3-9) **C**	8 (0-9) **D**
	5'	10 (7-10) **B**	9 (6-10) **C**	8 (3-10) **D**
	10'	10 (8-10) **C**	9 (6-10) **E**	8 (4-10) **F**
Median umbilical artery pH (range)		7.29 (7.10-7.43) **D**	7.29 (7.10-7.35) **C**	7.32 (7.12-7.41) **D**

VE-FE = Vacuum or Forcipal Extraction. Data are complete or % of missing or ignored values is indicated: **A**) ≤10; **B**) 10-20; **C**) 20-30; **D**) 30-40; **E**) 40-50; **F**) 50-60.

This study included no fetuses with ventricular tachycardia. The median gestational age at the time of diagnosis was 29 weeks for SVT (range 18-40), 30 weeks for AF (range 24-38) and 23 weeks for AVB cases (range 12-37). The mechanism of SVT was atrioventricular reentrant tachycardia in all cases. Hydrops at the time of diagnosis was present in 42% of SVT-cases. There were no fetal deaths in the SVT group and one termination of pregnancy (TOP) for trisomy 21 in the AF group. One infant in

the SVT group with cardiomyopathy and encephalopathy due to hydroxyglutaric aciduria died at the age of 5 months.
The AVB cases consisted of complete AVB (n=7) and 2nd degree AVB (n=2) and hydrops was present in 50% of the cases. Two of 9 cases had auto-immune associated AVB, 5 had complex congenital heart malformations and 2 had a severe form of long QT syndrome (LQTS 8 or Timothy syndrome). In the AVB group were 3 fetal deaths and 4 postnatal deaths **(Table 2)**. One case of infant death in the AVB group occurred after our follow-up.

Table 2. Details on cases of tachy- or bradyarrhythmia leading to fetal or infant death.

Type of arrhythmia	Complementary diagnosis	Outcome
SVT	D2-hydroxyglutaric aciduria induced cardiomyopathy	Died at age 5 months
AF	Trisomy 21	Intrauterine fetal death
AVB		TOP at 23 weeks
AVB	Left isomerism	TOP at 19 weeks
AVB	Corrected transposition of the great arteries, pulmonal stenosis	Intrauterine fetal death
AVB	Maternal Sjögren syndrome	Pacemaker, died at 20 months
AVB	Endocardial fibroelastosis	Pacemaker, died at age 2 days
AVB	Long QT syndrome	Pacemaker, died at age of 29 days
AVB	Long QT syndrome	Pacemaker, implantable cardioverter defibrillator, surgery, died at the age of 2 years

SVT = SupraVentricular Tachycardia; AF = Atrial Flutter; AVB = AtrioVentricular Block;
TOP = Termination of pregnancy

Drug therapy

Clinical data and details of drug therapy of all 19 cases of tachyarrhythmia in which prenatal drug therapy was applied are presented in **Table 3**. During antiarrhythmic therapy, sinus rhythm was achieved in 7/9 (77%) of non hydropic and in 6/8 (75%) of hydropic tachycardia fetuses **(Table 3)**. There is a trend towards multidrug therapy in the more recent years. Clinical data and details on drug therapy in the 3 cases of prenatally treated bradyarrhythmia are presented in **Table 4**. Pregnancies in these 3 cases were terminated by elective cesarean.

Table 3. Clinical data on cases of tachyarrhythmia in which prenatal drug therapy was applied.

Year	Type of tachyar-rhythmia	Continuous or intermittent	presence of fetal hydrops	Maternal and direct fetal drug therapy	Conversion Yes/No (after number of days of therapy)
1992	SVT	continuous	yes	D→F→D→cs	no
1994	SVT	continuous	yes	D + K	unknown
1994	SVT	intermittent	no	D	yes (66)
1997	SVT	Intermittent	no	D	unknown
2002	SVT	intermittent	no	D	yes (16)
2001	SVT	continuous	no	D	yes (4)
1996	SVT	intermittent	yes	S	yes (7)
1997	AF	intermittent	no	S	no
1997	SVT	intermittent	no	S	yes (19)
1998	AF	intermittent	no	D→D + S	yes (14)
1998	SVT	continuous	yes	S→S + D→D + F	yes (5)
1998	SVT	continuous	yes	S→D + F→F	yes (5)
1999	SVT	intermittent	yes	F→F + D	yes (5)
2000	SVT	intermittent	no	D→D + F→F	yes (4)
2002	SVT	continuous	yes	F→F + D→Ad(cc) + Am(cc) + Ad(cc) + Am(iv/o)→Am(iv) + D(iv)	yes (19)
2003	SVT	intermittent	yes	D + F→D + S →Am(cc/iv/o)→Am(cc/iv/o)→cs	no
2004	SVT	intermittent	no	F	yes (1)
2004	AF	continuous	no	F→F + D →cs	no
2004	SVT	intermittent	yes	D + F→Ad(cc) + Am(cc/iv/o)	yes (12)

SVT = SupraVentricular Tachycardia; AF = Atrial Flutter; cs = elective preterm delivery by Cesarean Section; iv = intravenous; cc = cordocentesis; o = oral; D = Digoxin; F = Flecanaide; K = Kinidine sulphate; S = Sotalol; Ad = Adenosine; Am = Amiodarone.

Table 4. Clinical data on 3 cases atrioventricular block in which drug therapy was applied.

Year	Fetal heart rate	Fetal hydrops	Maternal and direct fetal drug therapy	Outcome
1996	45 beats/ minute (3° block)	no	Dexamethasone → Dexamethasone + Ritodrine → elective delivery (37 weeks)	Died 1.5 years after delivery
2001	48 beats/ minute (3° block)	yes	Ritodrine → elective delivery by cesarean section (30 weeks)	Died 2nd day after birth
2005	45 beats/ minute (2° block)	yes	Fenoterol →elective delivery by cesarean section (34 weeks)	Mental retardation, cardiomyopathy, pacemaker

Table 5. Short term outcome of the study population (N=40)

Type of arrhythmia	Supra Ventricular Tachycardia (N=28)	Atrial Flutter (N=6)	Atrio Ventricular Block (N=6)
Neonatal arrhythmia (%)	22 (78)	4(67)	6 (100)
unknown	1 (4)	-	-
Neonatal ward admission (%)	25 (89)	6 (100)	6 (100)
[Duration in days (Standard Deviation)]	[12(15)]	[9(6)]	[21(16)]
Unknown	1	-	-
Neonatal anti-arrhythmic therapy (%)	19 (86)	4 (67)	6(100)
Medication	17	1	-
+electric cardioversion	-	2	-
+accessory pathway ablation	2	1	-
+ pacemaker implantation	-	-	5
+implantable cardioverter-defibrillator	-	-	1
Neonatal death	-	-	2
Infant death	1	-	1

Short-term follow-up

Neonatal data are presented in **table 5**. The incidence of cardiac anomalies in the study population was 18% (8/44). More details on these cardiac anomalies are given in **Table 6**. Neonatal arrhythmia was seen in all AVB fetuses and in 67% of AF-fetuses and in 78% of SVT-fetuses. Nineteen of the 28 children in the SVT group were treated with medication directly after birth. SVT was self-limiting in 14/19, and treatment could be stopped within the first year of life.

Table 6. Cardiac anomalies found during short-term follow-up.

Cardiac defects	Supra Ventricular Tachycardia (N=28)	Atrial Flutter (N=7)	Atrio Ventricular Block (N=9)	Total (N=44)
Cardiac anomalies	2	1	5	8
Congenitally corrected transposition of the great arteries			2	2
Ventricular Septal Defect	1			1
Atrial Septal Defect				
Coarctation aortae		1		1
Left atrial isomerism			1	1
Ventricular Septal Defect, Left-Right-shunt, pulmonalisstenose, cardiomyopathy			1	1
Cardiomyopathy, polyvalvular disease, pulmonary stenosis	1			1
Endocardial fibroelastosis			1	1

In 5 of 28 SVT cases preexcitation (delta wave) was present on ECG after birth (Wolff Parkinson White (WPW) syndrome). In 2 cases, radiofrequency ablation of an accessory bundle was performed in the first months of life. AF was treated with antiarrhythmic therapy (n= 4) or cardioversion (n=2). After initial conversion to sinus rhythm, AF did not recur in all 6 cases. Interestingly, in two AF cases the presence of an accessory pathway was also demonstrated. One AF case showed preexcitation on ECG after cardioversion (WPW syndrome), another AF case developed recurrent atrioventricular reentrant tachycardia that required antiarrhythmic therapy. All 4 survivors with AVB received pacemaker therapy shortly after birth.

Long-term follow-up

Informed consent for neurodevelopmental follow-up was obtained from 28 infants of the 36 survivors. Eight of the 36 surving infants could not be followed due to declined consent or lack of contact address. At the time of neurodevelopmental and cardiological assessment the median age of the children was 76 months ranging from 6 months to 15 years of age. A summary of long-term follow-up is presented in **Table 7**.

Table 7. Long-term follow-up with cardiological, neurological, motor system and psychological characteristics of the study population (N=28) by type of arrhythmia.

Type of arrhythmia	Supra Ventricular Tachycardia (N=23)	Atrial Flutter (N=4)	Atrio Ventricular-block (N=1)
Median follow-up time in months (range)	91 (6-186)	62 (21-96)	25
Abnormal cardiological examination (incl ECG)	3	1	1
Abnormal neurological and/or motor system examination	0	1	1
Mean Intelligence Quotient score (Standard Deviation)	113 (16)	102 (7)	Not performed
Mean mental Developmental Index (Standard Deviation)	99 (11)	95	62
Mean Psychomotor Developmental Index (Standard Deviation)	120 (18)	134	55
Child Behaviour Check List indicative of need for extra attention	3	0	1

In the SVT-group, 23 children, median age 91 months (range 6-186) were examined. No cases still required drug therapy and, no cases were treated with catheter ablation after the first year of life. WPW syndrome was demonstrated on ECG in 3 of 23 children. Surprisingly, the ECG showed previously unknown preexcitation (deltawave) in 1 case. One case was a six year old child with short episodes of palpitations since one year. In the neonatal period, this child had self-limiting SVT. Preexcitation was present at birth, which initially had disappeared on ECG afterward. The new case was a 9 year old asymptomatic child with WPW syndrome that had self-limiting SVT after birth. Yearly check-ups were advised and instructions were given on how to act when symptoms occur. In the SVT group, 18 children were tested with the SON–R test and five with the BSID-II-NL test. Scores were within the normal range in 14 children (14/23, 61%) and above average in 9 children (9/23, 39%). These children all had a normal neurological examination.
The CBCL was indicative of behavioral problems in 3 children. These children were offered closer attention by the hospitals psychologist.

The median age in the AF group was 62, (range 21-96), 5 of the 6 cases remained free of arrhythmia symptoms. Four of 6 underwent neurological and cardiological examination. The ECG was normal in 3 of 4. One 2 year old AF case with postnatal WPW syndrome still showed preexcitation on ECG but had remained asymptomatic. One 9 year old AF case with AVRT after birth underwent catheter ablation at the

age of 4 years and has remained asymptomatic thereafter.

One 4 year old AF child had coarctation of the aorta and a self-limiting atrial flutter. It underwent coarctectomy and remained asymptomatic after the operation. A 5 year old child (AF-group) suffered from plexus brachialis lesion due to shoulder dystocia.

In the AF group, 3 children were tested with the SON-R test and one with the BSID-II-NL test. Scores were within the normal range. The CBCL was within normal range for all children.

The group of AVB showed a very high morbidity and mortality risk. Two children had congenitally corrected transposition of the great arteries (ccTGA). One of these cases was stillborn. The other case was lost to follow-up but from his record analysis we knew that the child received a pacemaker at the age of 6 years and was in good condition at the age of 9 years. A third child in this group, who could not be followed up, showed congenital cardiac anomalies (ventricular septal defect, left to right shunt and hypertrofic cardiomyopathy) and a pacemaker was implanted. This child had been suspected for mental retardation. A fourth case survived 1.5 years after birth. She had an AVB due to maternal antibodies. A pacemaker was placed but she suffered from cardiomyopathy and died during a period with fever and pneumonia. A fifth child received immediately after birth a pacemaker because of third grade AVB. The child died the second day after birth. Postmortem analysis showed endocardial fibroelastosis. In the AVB group there were two cases of a severe form of long QT syndrome, LQTS 8, or Timothy syndrome. In one case a pacemaker was placed, but unfortunately the infant died 29 days after birth because of persistent VF. The other case also received a pacemaker and an implantable cardioverter defibrillator (ICD) afterwards. We performed follow-up of this child at the age of 2 years and he suffered from severe mental and motor retardation (MDI 62 and PDI 55). The ECG showed extreme QT prolongation and T-wave alternans. He had recurrent ICD shocks for torsade des pointes and died at the age of 2 years of ventricular arrhythmia and cardiomyopathy after stellectomy of the left ganglion stellatum.

Discussion

We studied a complete cohort of fetuses with arrhythmia. Hydrops was seen in 42% and 50% of cases with SVT/AF and AVB respectively. Fetal antiarrhythmic medication was given in 76% of cases. Fetal and postnatal mortality in the SVT and AF group was low (6%) and limited to cases with cardiomyopathy and trisomy 21. There was a high percentage of neonatal arrhythmia in our series and 21% of cases were shown to have WPW syndrome. Although 72% of SVT/AF cases have remained

free of symptoms after the first year of life, 12% had underwent radiofrequency catheter ablation at a young age. Mental scores were normal in all survivors.

The group of AVB showed very high risk of mortality and morbidity. Today, of the seven cases of AVB included in the follow-up there is no survivor. The other two cases were lost for long-term follow-up, but their medical records noted pacemaker therapy in one and severe mental retardation in the other.

If the postnatal ECG in cases of fetal SVT or AF reveals preexcitation (WPW-syndrome) long term follow-up of the child is important, even in the absence of symptoms. Complaints can arise later in life and WPW-syndrome can be a cause sudden cardiac death in older children and adults. Follow-up is necessary because curative treatment by radiofrequency ablation of the accessory pathway is indicated in older symptomatic children to prevent sudden death.[13]

The observations of Schade *et al.* 1999 indicate that patients with fetal tachycardia may develop cerebral complications already in utero.[6] These authors believe that a fetus with tachyarrhythmia and subsequent hydrops is at increased risk for the development of cerebral complications, due to the circulatory disturbances and sudden changes in heart rate which may lead to fluctuations in cerebral perfusion. Therefore, it is from the utmost importance to aim at immediate and complete control of the heart rate in the treatment of fetal tachyarrhythmia. Transplacental or direct fetal therapy of the arrhythmia is probably preferable to premature delivery because of the neonatal complications especially in cases with hydrops.

We searched the literature for follow-up studies on children born after fetal arrhythmia. In 2003, Boldt *et al.* reported on long-term outcome of 35 fetuses with SVT and 36 with AVB.[1] They conclude that fetal tachy- or bradyarrhythmias were associated with a moderately high risk for fetal distress. In their study, the survival rates were 91% in SVT and 82% in AVB. After the neonatal period the overall prognosis was good; 93% of the infants with fetal arrhythmias were still alive at a median follow-up time of 5 years. Only 3% of these children had a neurologic disorder. In concordance with our results Jaeggi *et al.* described a poor outcome in a large series (n=59) of AVB cases.[14] They compared cases of isolated AVB with cases associated with major structural congenital heart disease (CHD). Live birth and 1-year survival rates of AVB with CHD were 56% and 19% respectively when compared to cases of isolated AVB with 88% and 75% respectively ($p<0.0001$). They conclude, like in earlier reports, that AVB associated with major structural heart disease other than cc-TGA has an extremely poor outcome. Patients with LQTS 8 or Timothy syndrome with or without 2nd degree AVB have a poor postnatal outcome due to lethal ventricular arrhythmias as was also demonstrated in our series.
In 2006, Cuneo *et al.* reviewed the literature in order to summarize the outcome of fetal cardiac defects.[15] They describe that in SVT conversion rates range from 23 to 62% with standard transplacental therapy and that mortality is very low. If second-line

agents were indicated, mortality rates of 18.5% with flecainide and 25-30% with sotalol were reported. The combined mortality rate for hydropic and non-hydropic fetuses with AF was 8%. In the period 1950-2003, survival rate of fetuses with isolated atrioventricular block before dexamethasone treatment varies between 44 and 88%. Survival rate of these fetuses after dexamethasone treatment is around 88% in the period 1997-2005. Fetuses with left atrial isomerism and atrioventricular block do very poorly, survival rates were between 0 and 22%. They concluded that in utero management of tachyarrhythmia and conduction system disease has improved in utero survival.

Conclusion

In conclusion, mortality in SVT and AF patients in our study was 6% but mental scores were normal in all survivors. Twenty-one per cent of survivors had WPW syndrome. Prognosis in AVB patients was poor.

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