INCIDENCE AND POTENTIAL PREVENTION OF LIFE-THREATENING VENTRICULAR AND SUPRAVENTRICULAR TACHYARRHYTHMIAS IN CHILDREN

Ph.D. thesis

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1. INTRODUCTION

Arrhythmias in pediatric patients have the same basic arrhythmia mechanisms as arrhythmias in adults, but predisposing factors, clinical presentation, and prognosis are different. The arrhythmia substrate in children is generally congenital, whereas it is more likely to be acquired in adults. Understanding this clinical distinction is essential for preventing *life-threatening arrhythmias (LTAs) in children*. The term "life-threatening arrhythmia" is not strictly defined. Commonly, it refers to arrhythmias that can lead to cardiac arrest in a short time if no intervention is taken. Mostly it is used to describe high-frequency or polymorphic VT and VF. *Inherited arrhythmia syndrome* is the umbrella term for rare inherited heart conditions associated with a higher risk of SCD. It includes genetically determined inherited forms of ion channel disease and cardiomyopathies. Clarifying the genetic origin of SCD provides an opportunity to screen family members and prevent further tragedies. *Supraventricular tachycardia* (SVT) is often not considered an LTA; however, fatal outcomes are possible, particularly in newborns and individuals with SHD. Antiarrhythmic drugs (AADs) serve two purposes: terminate the current arrhythmia or prevent the arrhythmia from recurring. However, it should be remembered that these medications can cause the worsening of arrhythmias themselves (*proarrhythmia*).

2. OBJECTIVES

In the research projects, the central questions addressed were as follows:

1. What is the incidence of pediatric OHSCA in Hungary, and what are the most common etiologies? What is the possible role of genetic testing in diagnosing inherited arrhythmia syndromes to prevent LTAs?
2. How often is syncope the presenting symptom in pediatric channelopathies, and which clinical warning signs (red flags) help diagnose these children? Can the multivariable EGSYS score identify pediatric cardiac syncope in channelopathies?
3. What is the prevalence of complicated outcomes in neonatal SVT? What are the risk factors for complicated clinical outcomes? Does pharmacological therapy play a role in fatality? What could be the potential prevention of these fatalities?

3. METHODS

To answer the questions of my research, I carried out three studies. Study protocols were approved by the Hungarian Ethics Committee and followed Helsinki's declarations.

I. POHSCA study: To assess the incidence of pediatric OHSCA in Hungary (POHSCA) and the magnitude of inherited cardiac arrhythmias in the background, 3 databases were retrospectively analyzed.

As a first approach (I/A), Utstein data sheets of children under 18 years completed by the National Ambulance Service between 01.01.2012 – 30.06.2015 were reviewed. Utstein documentation is an anonymous data form used by the National Ambulance Service, which the rescue team should fill out in case of SCA. The study's inclusion criteria were: 1. All cases indicated „cardiac" origin as etiology. 2. „Cardiac" origin was not marked, but any of the following were present: a. Defibrillation by a witness, b. The first rhythm detected was VF or VT, c. defibrillation by the ambulance team, d. Amiodarone medication. In addition, personal data related to the anonymous form with a serial number was written out manually.

As a second approach(I/B), records of admissions to the national tertiary pediatric heart center [Gottsegen National Cardiovascular Center (GOKVI)] between 01.01.2000-01.10.2020 because of pediatric OHSCA for further investigation and implantable cardioverter defibrillator (ICD) implantation were reviewed. Demographic data, family and personal history, primary arrhythmia, clinical investigations, and presumed etiology were analyzed.

As a third approach (I/C), clinical and genetic testing results were studied in patients evaluated and followed in GOKVI between 01.10.2015-01.08.2020 with suspicion of inherited arrhythmia syndromes. Presentation symptoms, presence of cardiac arrest in the history, and genetic diagnosis without clinical symptoms were in focus. Genetic testing results in patients above 18 years and asymptomatic children of families with known arrhythmia syndromes were excluded. Genetic tests were performed with next-generation sequencing (NGS) in the laboratory of Blueprint Genetics, Helsinki.

II. SYNCOPE study: All data on children with channelopathy, followed by the single tertiary pediatric cardiac center (GOKVI) between 2000-2018 retrospectively were reviewed to study the prevalence of syncope as the presenting symptom in children with arrhythmia syndromes and if known warning signs are helpful to reveal the arrhythmic origin. Diagnosis of channelopathy was based on clinical symptoms and ECG and was supported by genetic test results when available. Children with a low probability of LQTS (Schwartz score ≤ 1) were excluded from the study. Presenting symptom was defined as the first symptom, complaint, or event which revealed the diagnosis, inducing referral for further cardiological investigations. The presence or absence of clinical symptoms and features considered typical for cardiac syncope, neurally mediated syncope, and epileptic seizures used in previous studies were examined retrospectively for presenting syncope. Additionally, the multivariable EGSYS score was also calculated retrospectively for each syncope case. This score was validated for diagnosing cardiac syncope in adults.

III. PROARRHYTHMIA study: To assess outcomes in infants and neonates with symptomatic non-post-operative SVTs and to determine risk factors for the fatal and near-fatal outcome, medical data of children treated at the single tertiary pediatric cardiac center (GOKVI) over 15 years were retrospectively reviewed with particular focus on the role of pharmacological therapy. Patients were identified by retrospective analysis of the database at the tertiary pediatric cardiac center of the GOKVI. The digital database was scanned for SVTs (BNO code: I4710, I4790, I4800, P2910), and clinical files were reviewed. Our study included all patients <1 year of age, presenting with sustained and recurrent SVT requiring therapy from January 2000 to July 2015 and receiving follow-up at our institution. Patients who had tachycardia exclusively following cardiac surgery were excluded from the analysis.

Statistical analysis: Continuous variables are presented as median (lower quartile upper quartile) and are compared among groups with Wilcoxon (Mann-Whitney) test; categorical variables are presented as frequencies (relative frequencies) and are compared among groups with Pearson chi-square test in the retrospective study of neonates with SVT.

4. RESULTS

4.1. Pediatric out-of-hospital sudden cardiac arrest (POHSCA study)

First approach: National Ambulance was alerted in 373 cases (approx. 106/year) due to cardiac arrest of patients under the age of 18 years during the 3,5 years long study period. After critical revision of Utstein data – discounting double-reported cases by different rescue teams – 84 children with pediatric cardiac arrest (approx. 24/year) were identified. „Cardiac arrest" was documented on the Utstein form in 66 cases (79%), and 18 cases (21%) were included based on other inclusion criteria detailed in the methods. The male/female ratio was 49/35 (58/42%). Return of spontaneous circulation (ROSC) was observed in 17 cases (20%), two children (2%) were transported to the hospital during continuous cardiopulmonary resuscitation (CPR), and on 3 pts (4%), CPR achieved only transient success. CPR was stopped in 3 pts (4%) and was unsuccessful in 59 cases (70%). Calculating also the case of successful resuscitation by a witness before the arrival of the National Ambulance, the rate of ROSC was 21%. Assessment of the clinical course of children after reanimation failed because identification of the patient or his general practitioner only based on the patient's residence was impossible and the location of postmortem examination was also not documented. Therefore clarification of the etiology of pediatric out-of-hospital SCD in Hungary and the planned family screening came to grief.

Second approach: During the study period of 20 years, 24 children (approx. 1/year) were admitted to the national pediatric heart center ***(GOKVI)*** after OHSCA. The male/female ratio was 14/10 (58/42%), and the median age at SCA was 13+/-4,1 years. The first documented rhythm was VF in 15/24, VT in 4/24, and asystole in 3/24, and it was not documented in 2/24 cases. An electrophysiological study was performed on 5/24, coronarography/coronary computed tomography (CT) on 6/24, cardiac magnetic resonance imaging (MRI) on 12/24, drug provocation test (ajmaline, epinephrine, isoproterenol) on 10/24, and genetic test on 12/24 cases. Drug abuse or SCD in the family history was not reported. Inherited arrhythmia syndromes in 11/24 (46%) and SHD in 4/24 (16%) cases could be identified, but the etiology remained unclear in the rest of 9/24 (38%). The inherited primary arrhythmia group consisted of

5 CPVT, 5 LQTS, and 1 BrS. The SHD group consisted of 3 HCMs and one valvular aortic stenosis. 4/9 children had mitral valve prolapse in the group classified as unknown etiology, but they were mild or minimal prolapse and considered unrelated to the clinical event. (Table 1.) The genetic tests revealed a pathological variant in 6 cases (CPVT 5, LQTS 1), a variant of uncertain significance in 1 case. A variant was not identified in 5 cases. 19/24 children were treated with ICD as secondary prophylaxis.

Table 1. Etiology of out-of-hospital sudden cardiac death in pediatric survivors based on data from Gottsegen National Cardiovascular Institute (2000-2021)

Group	Subgroup	Disease	Cases
Electric cardiac disease (46%)	channelopathy	catecholaminergic polymorphic ventricular tachycardia	5
		Long QT syndrome	5
		Brugada syndrome	1
Structural cardiac disease (16%)	cardiomyopathy	hypertrophic cardiomyopathy	3 (mild)
	congenital heart disease	valvular aortic stenosis	1 (mild)
Unknown etiology (38%)	-	-	9 (4 mild mitral valve prolapse)

Third approach: Suspicion of inherited arrhythmia syndrome emerged in 73 children in 6 years of the study period (approx. 12/year), and it was based on pathological ECG without symptoms n=23, family screening n=21, syncope n=15, successful reanimation after SCA n=14. Genetic testing revealed pathological variation in 29/73 children (approx. 5/year) and a variant of uncertain significance in 23/73 children. In 2 children, both pathological and variant of unknown significance (VUS) variants were identified. (Table 2.)

*Table 2. Primary abnormalities suggesting pediatric inherited arrhythmia syndrome based on data from Gottsegen National Cardiovascular Institute (2015-2021) Abbreviations: VUS=variant of unknown significance, ECG=electrocardiogram *Note: both pathological and VUS variants were identified in 1-1 pt.*

Primary abnormality	Patient (n)	Mutation (n)	Genetic test result
pathological ECG (without symptoms)	23	24*	pathological 11/23
			VUS 3/23
			negative 10/23
genetic family screening (without symptoms)	21	21	pathological 7/21
			VUS 8/21
			negative 6/21
syncope	15	16*	pathological 4/15
			VUS 9/15
			negative 3/15
sudden cardiac arrest	14	14	pathological 7/14
			VUS 3/14
			negative 4/14

4.2 Syncope as the presenting symptom in children with arrhythmia syndrome (SYNCOPE STUDY)

Forty-eight patients were enrolled. The median age was 10,4 yrs (IQR 6,0), and 24 patients were female. Most patients were diagnosed with LQTS, but some children were followed up with CPVT and BrS, as shown in Table 3. Inherited channelopathies caused most of the LQTS cases. The distribution of subtypes was the following: LQTS1: 11/39, LQTS2: 5/39, LQTS3: 4/39, LQTS7 (Andersen-Tawil syndrome): 4/39, LQTS8 (Timothy syndrome): 2/39. There were also 3 cases of secondary LQTS, and 10 cases were unclassified

10/39. The Schwartz score of this latter group: high probability of LQTS (score ≥3,5): 4/10, intermediate probability of LQTS (score 1.5-3.0): 6/10.

Table 3. Presenting symptoms in 48 children with primary arrhythmia syndromes.Abbreviations: LQTS = long QT syndrome, CPVT = catecholaminergic polymorphic ventricular tachycardia, Brugada=Brugada syndrome, ECG=electrocardiogram

	Cardiac syncope		Sudden Cardiac Arrest	Abnormal ECG	Family screening
	correct diagnosis	misdiagnosed as epilepsy			
LQTS n=39	**5**	**6**	**5**	**11**	**12**
CPVT n=5	**1**	**1**	**3**	**0**	**0**
Brugada n=4	**0**	**0**	**1**	**2**	**1**
Total n=48	**6 (12,5%)**	**7 (14,5%)**	**9 (19%)**	**13 (27%)**	**13 (27%)**

The diagnosis was supported by pharmacological provocation in 6 patients (four epinephrine tests for LQTS, two ajmaline tests for BrS) and by genetic testing in 35 children. However, genetic testing was not available for 9 LQTS children at the beginning of the study period. In addition, four children with BrS were not tested for genetics due to the lack of prognostic or therapeutic impact. Less than half of the patients (n=22/48, 46%) were identified by their symptoms. The presenting symptom was syncope in 13/48 [27%] and SCA in 9/48 [19%] children. In the remaining cases, abnormal ECG findings (13/48) [27%] and a positive family history of channelopathy (13/48) [27%] led to the diagnosis. (Table 3.) Most children (11/13) [77%] presenting with syncope had LQTS, but two CPVT patients were also diagnosed after a syncopal event. In addition, half of the patients presenting with syncope (7/13) [50%] were misdiagnosed as epilepsy in the initial stage of their disease. As a result, they

were followed up with „idiopathic," „therapy-resistant," or „atypical" epilepsy for 2-14 years. In three of these seven patients, the cardiac examination revealed secondary LQTS, and the syncope was related to an endocrinological crisis (Addison crisis and hypocalcemia due to hypoparathyroidism and severe vitamin D deficiency). After hormonal and electrolyte substitution, the ECG normalized, and syncope recurred in no cases. Furthermore, three patients with LQTS and one with CPVT – initially mislabelled as epilepsy – remained symptom-free on AAD therapy after cessation of antiepileptic treatment. All six patients with initially correct cardiac syncope diagnosis (LQTS 5, CPVT 1) were treated with ICD implantation. All were appropriately shocked during their subsequent clinical event while on antiarrhythmic therapy. None of the nine patients presenting with primary SCA had a syncopal history. Seven of them were also treated with ICD implantation. Unfortunately, one child died on the waiting list for an ICD implantation, and ICD was not implanted in another child with CPVT because of an unfavorable cost/benefit ratio. Abnormal ECG findings at a routine sports medicine screening examination revealed arrhythmia syndrome in 13 children. The most frequent pathological findings were the prolonged QT interval in four patients and the polymorphic premature ventricular beats in four children. The latter is characteristic of the Andersen-Tawil syndrome (LQTS7). Functional AV blocks revealed LQTS3 in two patients and Timothy syndrome (LQTS8) in one. In addition, two children had a spontaneous diagnostic Type I Brugada ECG. Positive family history was the reason for cardiological work-up in 12 LQTS patients and one child with BrS. Description of syncope by the child or an adult witness was available in 8/13 cases. The most typical cardiac warning sign/"red flag" was effort syncope. However, somewhat confusingly, warning signs considered typical for epileptic seizure or neurally mediated syncope (clonization > 15s and prodrome, respectively) were similarly frequent in this patient group of arrhythmic syncope. (Table 4.)

Table 4. Incidence of different warning signs („red flags") in cardiac syncope (n=8). Abbreviations: SCA=sudden cardiac arrest, SCD=sudden cardiac death

„red flags" for cardiac syncope	palpitation before/after syncope	2/8
	effort syncope	6/8
	syncope while supine	0/8
	syncope without a prodrome	4/8
	presence of structural heart disease	0/8
	heart disease in family history	1/8
	SCA/SCD in family history	2/8
„red flags" for neurally mediated syncope	typical predisposition	1/8
	autonomic prodromes	6/8
	avoided by sitting down	3/8
	vegetative symptoms during recovery	3/8
„red flags" for epileptic seizure	epilepsy in patient history	2/8
	epilepsy in family history	0/8
	tongue biting	0/8
	enuresis	2/8
	clonic phase duration > 15 seconds	3/8
	postictal confusion	0/8
	postictal neurological symptom	0/8
	anterograde / retrograde amnesia	1/8

Multivariable EGSYS score was calculated retrospectively for the presenting syncope, and it suggested a cardiac origin (≥3 points) in seven children (88%). One patient not identified by the score had a medium probability of having LQTS. (Table 5.)

Table 5. Multivariable EGSYS score in eight patients with syncope as presenting symptom. Abbreviations: SHD=structural heart disease, EGSYS=Evaluation of Guidelines in Syncope Study, Schwartz score=diagnostic score for long QT syndrome, LQTS=long QT syndrome, CPVT=catecholaminergic polymorphic ventricular tachycardia, ECG=electrocardiogram

Parameters	Patients							
Patient nr.	#1	#2	#3	#4	#5	#6	#7	#8
Diagnosis	LQTS	LQTS	LQTS	LQTS	LQTS	LQTS	CPVT	CPVT
SHD and/or abnormal ECG	3	3	3	3	3	3	0	3
Palpitations preceding syncope	0	0	0	0	0	0	0	0
Syncope during effort	3	3	0	3	3	0	3	3
Syncope while supine	0	0	0	0	0	0	0	0
Precipitating and/or predisposing factors	0	0	0	0	0	0	0	-1
Autonomic prodromes	-1	0	0	0	0	-1	0	0
EGSYS score	5	6	3	6	6	2	3	5
Schwartz score	5.5	5	4.5	8	6	2	-	-

4.3 Supraventricular tachycardia in neonates with fatal or near-fatal outcome (PROARRHYTHMIA study)

A total of 159 patients met the inclusion criteria. 115 (72%) patients were younger than 31 days at their first index admission for tachycardia. Body weight was 3805 +/- 1435 g. A history of intrauterine tachycardia was present in 63 patients (40%), of whom nine patients (6%) required transplacental AAD therapy, and 6 of them (4%) developed hydrops. 52 (33%) children were born after urgent Caesarian section, and 47 (30%) children were born prematurely. CHD, cardiomyopathy, or cardiac tumor was present in 34 patients (21%), and 25 children (16%) suspected systemic infection during initial therapy. On echocardiography, 90/146 (62%) had preserved left ventricular (LV) function, and 67 patients (42%) had clinical signs of heart failure. Tachycardia mechanisms were paroxysmal supraventricular tachycardia (PSVT) n=107 (67%), focal atrial tachycardia (FAT) n=27 (17%), multifocal atrial tachycardia (MAT) n=5 (3%), junctional ectopic tachycardia (JET) n=5 (3%), PJRT n=3 (2%), Aflut n=10 (6%) and Afib n=2 (1%). CHDs were present in 33 patients (20%), and SHD (1 hypertrophic obstructive cardiomyopathy) in 1 patient (1%). CHD was complex in 12 patients (Ebstein anomaly 3, double outlet right ventricle 2, coarctation of aorta 2, Fallot tetralogy 1, AV septal defect 1, tricuspid atresia 1, truncus arteriosus communis 1, double inlet right ventricle 1) and simple in 21 patients (atrial septal defect 9, ventricular septal defect 5, supravalvular pulmonary stenosis 2, bicuspid aortic valve 2, significant persistent ductus arteriosus requiring ligation 1).AAD treatment was performed with one antiarrhythmic agent (n=81) or with a combination of two (n=78) or three agents (n=6). (See Table 6) In 6 patients, more than one combination was used until treatment success. The mode of initial AAD administration was intravenous in 109 cases (69 %). One neonate underwent catheter ablation because multiple AADs or combinations of drugs could not control tachycardia.

Table 6. Antiarrhythmic drugs and combinations used for acute treatment (ineffective and final effective therapies are also included). Abbreviations: AAD=antiarrhythmic drug

Single AAD therapy (n=81)	**Double AAD therapy** (n=78)
propafenon: 43	propafenone+digoxin: 22
digoxin: 24	sotalol+ digoxin: 15
amiodarone: 11	propafenon+metoprolol: 12
metoprolol: 8	propafenon+amiodarone: 9
sotalol: 4	amiodarone+metoprolol: 7
Triple AAD therapy (n=6)	metoprolol+digoxin: 5
propafenon+amiodarone+metoprolol: 2	amiodarone+digoxin: 5
propafenon+metoprolol+digoxin: 2	amiodarone+flecainid: 2
propafenon+amiodarone+digoxin: 1	propafenon+sotalol: 1
amiodarone+flecainid+digoxin: 1	verapamil+metoprolol: 1
	amiodarone+lidocain: 2

There were five patient deaths (3%) and four complicated clinical courses with multiorgan failure or irreversible hypoxic-ischemic encephalopathy (3%). Seven of these nine patients (78%) were neonates. Clinical and demographic characteristics of the 159 patients classified after complicated (death or multiorgan failure) or uncomplicated courses are shown in Table 7.

Table 7. Comparison of complicated and non-complicated group. Abbreviations: AA=antiarrhythmic, AAD=antiarrhythmic drug, PSVT=paroxysmal supraventricular tachycardia, FAT=focal atrial tachycardia, VT=ventricular tachycardia, iv=intravenous

Clinical parameters	Fatal or near-fatal	Non-fatal	p-value
	N=9	N=150	
Body weight (g)	3385 ± 1923	3830 ± 1405	0.056
Age at treatment (days)	**37.0 ± 88.8**	**39.9 ±69.2**	**0.020**
Prenatal tachycardia	**7 (78%)**	**56 (37%)**	**0.016**
Prenatal AA therapy	**2 (22%)**	**7 (5%)**	**0.027**
Structural and congenital heart disease	2 (22%)	32 (21%)	0.95
Fetal hydrops	1 (11%)	5 (3%)	0.234
Urgent caesarian section	**8 (89%)**	**44 (29%)**	**<0.001**
Prematurity	4 (44%)	43 (29%)	0.314
Suspicion of infection	2 (22%)	23 (15%)	0.581
Circulatory failure at presentation	6 (67%)	67 (42%)	0.125
Preserved left ventricular function	3/9 (33%)	87/146 (62%)	0.549
Type of arrhythmia: PSVT	5 (56%)	102 (68%)	0,739
FAT	2 (22%)	25 (17%)	
all else	2 (22%)	23 (14%)	
Catheter ablation	0 (0%)	1 (1%)	0.806
Proarrhythmia	**4 (44%)**	**2 (1%)**	**<0.001**
ECG sign of impending proarrhythmia	1 (11%)	5 (3%)	0.234
Major adverse events of AAD	**2 (22%)**	**0 (0%)**	**<0.001**

There were significant differences between the groups regarding age, history of prenatal tachycardia and treatment, urgent cesarean section, proarrhythmia, and major adverse events (AEs). Proarrhythmia – new onset arrhythmia – was identified in 6 cases. Three of five patients (60%) died, one of four (25%) survivors with severe complications, and two of 150 (1%) survivors without complications had proarrhythmia ($p<0.001$). In three cases (50%), proarrhythmia was related to intravenous Class IC (propafenone n= 3) use, in 2 cases (33%) to digoxin use, and in 1 case (17%) to amiodarone administration. One (17%) patient in the group with fatal outcome, one patient (20%) in the group of survivors with severe complication, and 0 (0%) in the group of survivors without complication had a major AE with severe hypotension ($p<0.001$). Both AEs occurred during intravenous propafenone therapy. ECG signs of impending proarrhythmia were detected in 6 cases related to i.v. propafenone treatment (4%). In all cases, QRS duration increased by>25% from baseline. The only patient who died without proarrhythmia or major AEs had severe HCM and Afib. The combination of amiodarone and metoprolol controlled his tachycardia following electrical cardioversion, but he died subsequently due to intractable heart failure. The only patient in the complicated, non-fatal group without signs of pharmacological AEs was born with an urgent cesarean section with severe LV dysfunction and heart failure. Adenosine revealed Aflut with a high ventricular rate. He developed hypoxaemic ischemic encephalopathy despite effective arrhythmia control with amiodarone following electrical cardioversion, mechanical ventilation, and inotropic support. One patient in the complicated, non-fatal group had ECG signs of impending proarrhythmia.

5. CONCLUSIONS

Based on the results detailed above, we have drawn the following main conclusions:

1. According to the data of the National Ambulance Service, 20-25 children in Hungary yearly suffer out-of-hospital cardiac arrest. One-fifth of cases are successfully resuscitated, and one-fifth of the surviving children were subsequently referred for additional diagnosis and ICD management (5% of childhood cardiac arrests). An inherited arrhythmia syndrome was detected later in half of the surviving patients. One-fifth of children screened and followed up for inherited arrhythmia syndrome at the national center were identified after cardiac arrest. The documentation system of medical rescue in Hungary does not allow the identification of families with pediatric SCD and hinders the initiation of family screening.
2. Syncope is not a frequent symptom of channelopathy, and it does not always precede SCA. Physical examination and commonly used "red flags" of cardiac syncope alone are insufficient to identify primary arrhythmia syndromes in children. But the combination of clinical and ECG-based features, such as the multivariate EGSYS score, can reveal the arrhythmic syncope with high precision. Based on these findings, performing ECG and multivariable EGSYS-score should be considered for each child with pediatric syncope and refractory epilepsy.
3. The mortality rate in neonates and infants with non-postoperative supraventricular tachycardias is low (3%). A complicated course and outcome are associated with age, prenatal history and therapy of tachycardia, proarrhythmia of antiarrhythmic medication, and major adverse events. The increased incidence of proarrhythmia, major adverse events, and ECG signs of impending proarrhythmia in patients with fatal or near-fatal outcomes suggests that acute intravenous pharmacologic therapy of supraventricular tachycardias in neonates might pose a risk and should be used with caution. Nevertheless, detecting proarrhythmia related to Class I/C drugs in neonates might be difficult and warrants alertness.

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