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Treatment of supraventricular tachycardia in infants: Analysis of a large multicenter database

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ABSTRACT

Objective: Supraventricular tachycardia (SVT) is the most common arrhythmia in infants. Infants are typically treated with antiarrhythmic medications, but there is a lack of evidence guiding management, thus exposing infants to risks of both inadequate therapy and medication adverse events. We used data from a large clinical database to better understand current practices in SVT management, safety of commonly used medications, and outcomes of hospitalized infants treated for SVT.

Methods: This retrospective data analysis included all infants discharged from Pediatrix Medical Group neonatal intensive care units between 1998 and 2012 with a diagnosis of SVT who were treated with antiarrhythmic medications. We categorized infants by the presence of congenital heart disease other than patent ductus arteriosus. Medications were categorized as abortive, acute, or secondary prevention therapies. We used descriptive statistics to describe medication use, adverse events, and outcomes including SVT recurrence and mortality.

Results: A total of 2848 infants with SVT were identified, of whom 367 (13%) had congenital heart disease. Overall, SVT in-hospital recurrence was high (13%), and almost one fifth of our cohort (18%) experienced an adverse event. Mortality was 2% in the overall cohort and 6% in the congenital heart disease group ($p < 0.001$). Adenosine was the most commonly used abortive therapy, but there was significant practice variation in therapies used for acute treatment and secondary prevention of SVT.

Conclusion and practice implication: Significant variation in SVT treatment and suboptimal outcomes warrant future clinical trials to determine best practices in treating SVT in infants.

1. Introduction

Supraventricular tachycardia (SVT) is the most common arrhythmia in infants, with an estimated incidence of 1/250 to 1/1000 among all infants and 1/10 among infants with congenital heart disease (CHD) [1–6]. Medications used to treat SVT typically fall into one of three categories: 1) abortive therapies; 2) acute management therapies used to achieve rate control or improve the likelihood of arrhythmia abortion; and 3) secondary prevention or "prophylactic" therapies used to prevent SVT recurrence [7,8]. Across this therapeutic spectrum, over a dozen different therapies are used to treat SVT.

Although a broad armamentarium of therapies is available, there is limited evidence to guide management. Current practices are based on survey data, small clinical trials, and retrospective studies involving few (<300) infants [7,9–16]. There are no Food and Drug Administration (FDA)-labeled medications for SVT in pediatric populations, and the safety profile of commonly used medications has not been well described in infants. This is of particular importance in infants with CHD who are at high risk of adverse events and poor outcomes.

To better understand current practices in SVT management, safety of commonly used medications, and outcomes of hospitalized infants treated for SVT, we conducted a retrospective cohort study using a large database. Results of our study are useful for guiding management and identifying priorities for future clinical trials required for FDA medication labeling.

2. Methods

2.1. Database and study cohort

We performed a retrospective cohort study using data generated from electronic medical records (EMR) of infants cared for by clinicians in one of 348 neonatal intensive care units (NICUs) managed by the Pediatrix Medical Group from 1998 to 2012. The data are de-identified and stored in the Pediatrix Clinical Data Warehouse [17]. We included all infants discharged with a diagnosis of SVT who received SVT therapy during their first 120 days of life. SVT diagnosis was based on the clinical documentation of the bedside providers. The study was approved by the

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2.2. Definitions

We categorized infants by the presence of any congenital heart disease other than patent ductus arteriosus (Appendix). We defined the need for inotropic support and mechanical ventilation as exposure to any inotrope (dopamine, dobutamine, epinephrine, milrinone, norepinephrine, or phenylephrine) and any invasive mechanical ventilation on days of exposure to antiarrhythmic medications. Arrhythmias were categorized as atrial flutter if the infant ever had a diagnosis of atrial flutter, Wolff Parkinson White (WPW) syndrome if the infant ever had a diagnosis of WPW syndrome, or unspecified SVT if the infant only had a diagnosis of SVT. Note that there were no infants with a diagnosis of both atrial flutter and WPW syndrome.

We defined abortive therapy as adenosine or cardioversion used at any time. We defined acute therapy as amiodarone, esmolol, or procainamide if started on day one of diagnosis. We defined secondary prevention therapy as amiodarone or esmolol if started after day one of diagnosis, or any other beta-blocker, digoxin, flecainide, or sotalol started on day one of or any time after diagnosis. Based on this definition, in case of recurrence of arrhythmia defined as any arrhythmia observed after the first day of diagnosis, adenosine or cardioversion would be classified as abortive therapy, while the initiation of another drug would be classified as secondary prevention. We defined arrhythmia recurrence as the administration of adenosine or cardioversion (abortive therapy) after day one of diagnosis. We defined multidrug therapy as exposure to more than one secondary prevention medication concomitantly. We defined mortality as death prior to hospital discharge.

To evaluate the safety of secondary prevention medications, we assessed incidence of adverse events (AEs). The list of potential AEs was compiled by reviewing the FDA labels for the medications of interest. AEs evaluated included hypotension requiring inotropes, bradycardia, hyperkalemia, hypoglycemia, and elevated liver enzymes. We defined bradycardia as a new diagnosis of bradycardia made by the treating providers while infants were receiving secondary prevention therapies. We defined elevated liver enzymes as any elevation of aspartate transaminase (AST) >600 IU/L, alanine transaminase (ALT) >225 IU/L, or gamma glutamyl transferase (GGT) >90 IU/L. We defined hyperkalemia as a serum potassium >6 mEq/L and hypoglycemia as serum glucose <40 mg/dL. We included only AEs that occurred while the infant was exposed to secondary prevention therapies.

2.3. Statistical methods

We used standard summary statistics to describe baseline characteristics. We reported the proportion of infants on antiarrhythmic medications and used chi-square tests of association or Fisher's exact tests to compare antiarrhythmic therapy use across diagnosis groups. We described changes in secondary prevention medications over time by calculating the proportion of infants exposed to an antiarrhythmic medication in a given year. We reported hospital length of stay as median (interquartile range) and compared its distribution across diagnosis groups using Mann–Whitney U tests. We described the incidence of AEs as the number of infant-days with AE occurrence/1000 infant-days on secondary prevention therapies, and used chi-square tests of association to compare incidence of AEs between medications.

3. Results

3.1. Patient demographics

Of the 887,910 infants present in the database, 2848 (0.3%) infants met our inclusion criteria and were included in this analysis. The median (interquartile range) gestational age and birth weight of the included infants was 37 weeks (34, 38) and 2950 g (2210, 3520). Median postnatal age at diagnosis was 2 days (0, 8), and 1869/2848 (66%) were diagnosed with SVT in the first week of life. Underlying arrhythmia diagnoses included unspecified SVT (2200/2848, 77%), atrial flutter (448/2848, 16%), and WPW syndrome (200/2848, 7%). Overall, 367/2848 (13%) had CHD (Table 1).

Table 1
Patient characteristics, n (%).

	No CHD N = 2481	CHD N = 367	Overall N = 2848
Gestational age, weeks			
<32	479 (19)	74 (20)	553 (20)
33–36	774 (31)	112 (31)	886 (31)
≥37	1223 (49)	181 (49)	1404 (49)
Birth weight, g			
<1500	265 (11)	42 (11)	307 (11)
1500–2499	562 (23)	100 (27)	662 (23)
>2500–3499	1649 (67)	224 (61)	1873 (66)
Male	1577 (64)	204 (56)	1781 (63)
Postnatal age, days			
<7	1678 (68)	191 (52)	1869 (66)
7–14	484 (20)	106 (29)	590 (21)
>14	319 (13)	70 (19)	389 (14)
Type of SVT			
Unspecified SVT	1907 (77)	293 (80)	2200 (77)
Atrial flutter	395 (16)	53 (14)	448 (16)
WPW syndrome	179 (7)	21 (6)	200 (7)
Inotropic support on day of diagnosis	144 (6)	36 (10)	180 (6)
Mechanical ventilation on day of diagnosis	441 (18)	102 (28)	543 (19)

CHD, congenital heart disease; SVT, supraventricular tachycardia; WPW, Wolff Parkinson White.

3.2. SVT therapy

Nearly half of the infants received abortive therapy (1379/2848, 48%), including adenosine (1239/1379, 90%) and cardioversion (143/1379, 10%) (Table 2). Cardioversion was primarily used in infants with a diagnosis of atrial flutter (105/143, 76%). Only 3 infants received both adenosine and cardioversion. Abortive therapy was used less frequently in infants with versus those without CHD (155/367, 42%, vs. 1227/2481, 50%, p = 0.05).

Acute therapy was used in 179/2848 (6%) infants. The most commonly used acute therapy was amiodarone (81/179, 45%), followed by esmolol (73/179, 41%) and procainamide (33/187, 18%) (Table 2). Acute therapy was used more frequently in infants with versus those without CHD (34/367, 9%, vs. 145/2481, 6%, p = 0.01). Over time, the use of procainamide decreased, while esmolol and amiodarone use

Table 2
Type of SVT therapy, n (%).

	No CHD N = 2481	CHD N = 367	Overall N = 2848
Abortive therapy	1227 (50)	155 (42)	1379 (48)
Adenosine	1095 (89)	144 (93)	1239 (90)
Cardioversion	132 (11)	11 (7)	143 (10)
Acute therapy	145 (6)	34 (9)	179 (6)
Amiodarone	66 (46)	15 (44)	81 (45)
Esmolol	60 (41)	13 (38)	73 (41)
Procainamide	27 (19)	6 (18)	33 (18)
Secondary prevention therapy	2206 (89)	317 (86)	2523 (89)
Amiodarone	135 (6)	31 (10)	166 (7)
Beta-blocker	1035 (47)	147 (46)	1182 (47)
Digoxin	1382 (63)	191 (60)	1573 (62)
Flecainide	77 (3)	9 (3)	86 (3)
Sotalol	80 (4)	14 (4)	94 (4)

CHD, congenital heart disease; SVT, supraventricular tachycardia.