

# Use of intravenous sotalol in newborns with supraventricular tachycardia



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## Introduction

Supraventricular tachycardia (SVT) in the newborn population is a common arrhythmia that can at times be difficult to treat, with long-standing persistent SVT resulting in tachycardia-induced cardiomyopathy. Certain arrhythmic substrates, like ectopic atrial tachycardia (EAT), can be refractory to commonly used antiarrhythmics and may not be responsive to cardioversion. It is therefore important to identify a host of drugs that can quickly terminate arrhythmias.<sup>1–5</sup> Class III antiarrhythmics are often used in infants with SVT that is unresponsive to typical first-line agents such as beta blockers or sodium channel blockers, though oral preparations are suboptimal given the pharmacokinetics. There are limited data describing the efficacy and dosage of intravenous (IV) sotalol for the management of tachycardia in the pediatric population, with the current literature focusing on children  $\geq 2$  years old.<sup>5</sup> In this report, we describe a case series of the use of IV sotalol for the treatment of neonatal EAT and atrioventricular reentrant tachycardia.

## Case report

### Case 1

Baby C was born at 36 weeks gestational age to a 33-year-old G<sub>1</sub>P<sub>1</sub> previously healthy mother. Obstetrical assessment at 36 weeks noted the fetus to have an irregular heart rate and the family was referred to the Pediatric Cardiology Fetal Clinic at St. Louis Children's Hospital. Fetal echocardiogram demonstrated intermittent tachycardia at rates of 180–189 beats per minute (bpm) with intact 1:1 atrioventricular conduction with no evidence of hydrops or decreased cardiac function. Given these findings, the mother was admitted to

the obstetrics unit for further fetal monitoring and was not started on any antiarrhythmic medications.

Overnight, the fetus was noted to be in SVT more than 50% of the time and mother underwent urgent cesarean section at the discretion of the maternal-fetal medicine team. At time of delivery, Baby C was well-appearing, with a documented heart rate at time of delivery of 150 bpm and an irregularly irregular rhythm. Admission electrocardiogram (ECG) showed sinus rhythm with multiple premature atrial contractions (Figure 1A) and echocardiogram was normal for age. Given these findings, the team deferred initiation of antiarrhythmic medication and continued telemetry monitoring. Over the next several hours, telemetry revealed frequent, nonsustained episodes of EAT with heart rates of 193 bpm that increased in both frequency and duration as time went on. During these episodes of EAT, noninvasive blood pressures were stable, though the nursing care team noted the baby to be fussier and more irritable. Detailed conversations were had with the family regarding risks and benefits of various antiarrhythmic agents. Given the escalation on arrhythmic burden and concerns for adequate gastrointestinal absorption, the decision was made to transfer the patient to the Cardiac Intensive Care Unit to initiate IV sotalol.

After discussions between the electrophysiology team and clinical pharmacy specialist, a conservative dosing regimen was started using a  $\text{mg}/\text{m}^2$  calculation. The manufacturer-recommended oral dose of  $30 \text{ mg}/\text{m}^2/\text{dose}$  every 8 hours with an age-related dosage reduction factor (0.17) resulted in a dose of 1 mg every 8 hours. Given the 90%–100% bioavailability of oral sotalol, no further dose reductions were made to calculate the IV dosing. An infusion time of 5 hours was chosen to mimic typical adult pharmacokinetics of an oral dose.<sup>6</sup> IV sotalol was prepared using a concentration of 0.15 mg/mL in order to allow the medication to run at measurable rates on IV infusion pumps without a carrier fluid.

Baseline evaluation included an assessment of corrected QT interval (QTc) of 447 msec as calculated by Bazett's formula (Figure 1B), renal function, and blood glucose prior to initiation of therapy. Monitoring during therapy included

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## KEY TEACHING POINTS

- Intravenous sotalol can be considered as a treatment option for supraventricular tachycardia (both automatic tachycardia and atrioventricular reciprocating tachycardia) in newborn children.
- Close monitoring is required during infusion of this medication, as there was demonstrable corrected QT interval (QTc) prolongation after a 5-hour infusion with conservative dosing strategy of 30 mg/m<sup>2</sup>/dose every 8 hours (with an age-related dosage reduction factor).
- Despite initial QTc prolongation post-infusion, the QTc did return to baseline prior to hospital discharge.

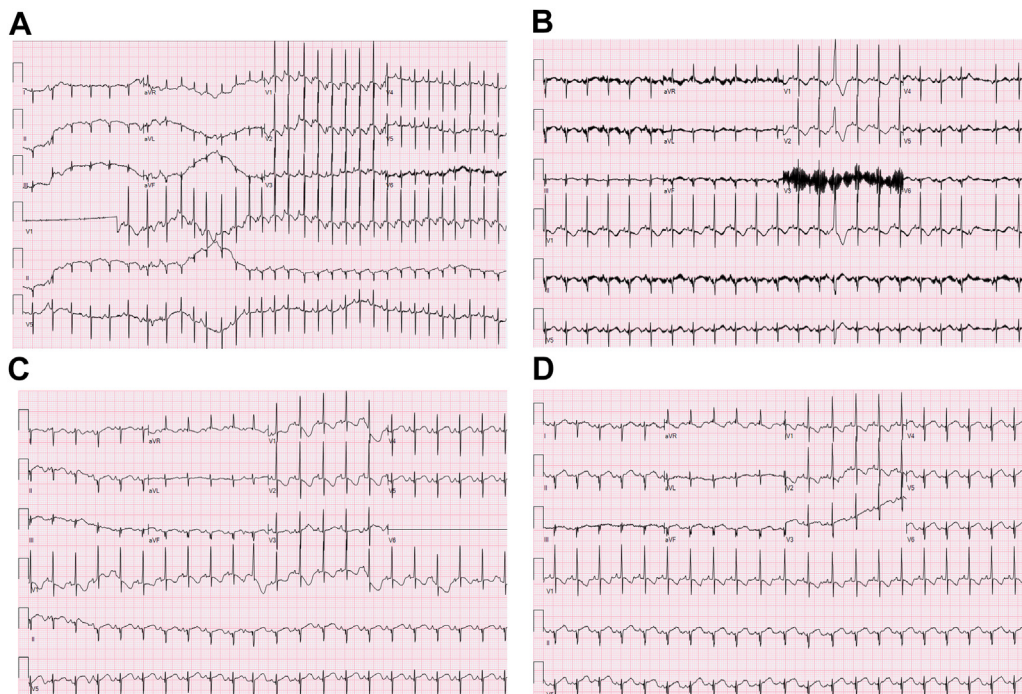
an ECG with QTc assessment after each dose, as well as blood glucose monitoring at 1 hour, 2 hours, 3 hours, and 6 hours after initiation of the infusion. After administration of the first dose, the patient's QTc measured 480 ms (Figure 1C) and she was noted to be in sinus rhythm. The patient started to have atrial ectopy and nonsustained atrial tachycardia in the 30 minutes preceding the next dose, indicating that the patient had not reached a therapeutic steady-state drug level. The next dose was increased to 1.5 mg IV every 8 hours (45 mg/m<sup>2</sup>/dose) and she remained in sinus rhythm with heart rates ranging between 100 and 140

bpm. After additional infusions (4) and maintenance of sinus rhythm, the patient was converted to oral sotalol at a dose of 2 mg every 8 hours (60 mg/m<sup>2</sup>/dose). The patient was discharged home in the following days and continues to do well on oral sotalol (Figure 1D).

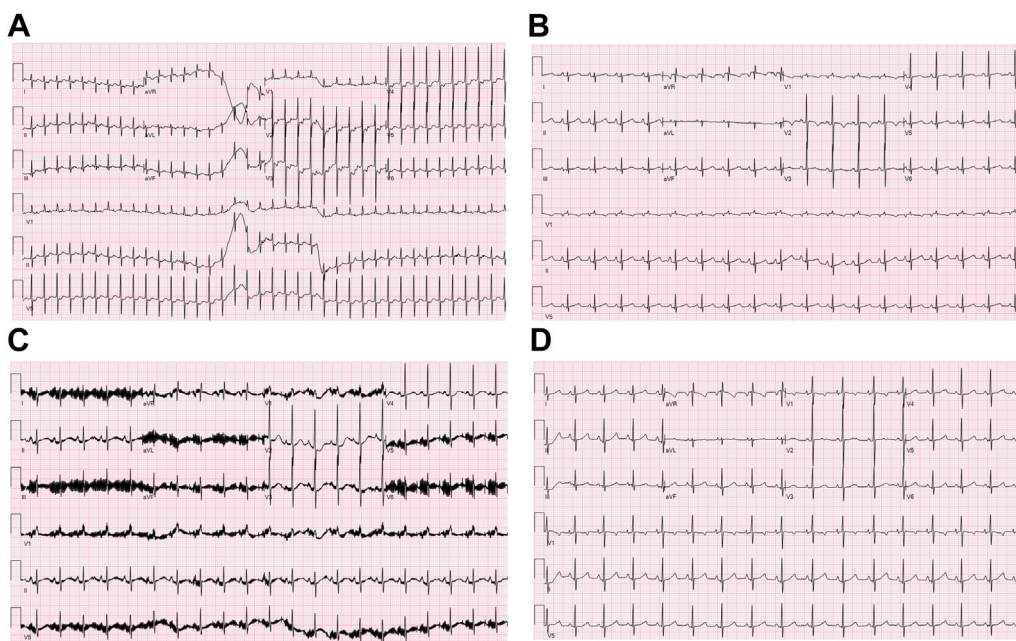
## Case 2

Baby N was a 16-day-old ex 39-week male infant who initially presented to the pediatrician's office with tachypnea and irritability at 2 days of age. In the office, he was noted to be tachycardic with a heart rate of 280 bpm. Vagal maneuvers briefly interrupted the tachycardia but the patient remained mostly in SVT. The infant was transferred to an outside Emergency Department and given intravenous adenosine 0.1 mg/kg with transient conversion to sinus rhythm. He was admitted to an intensive care unit and continued to be in SVT despite initiation of propranolol (4 mg/kg/day), esmolol (50 mcg/kg/min, up-titrated to 150 mcg/kg/min), and digoxin load (8 mcg/kg), with sporadic nonsustained conversions to sinus rhythm. At this time, the patient was transferred to the cardiac intensive care unit at St. Louis Children's Hospital for further management (Figure 2A).

Given Baby N's intractable SVT with multiple first-line therapies, a frank conversation was had with the family regarding risks and benefits of IV antiarrhythmic therapy and the baby was started on IV sotalol. After discussing dosing options, which included 30 mg/m<sup>2</sup>/dose with an age reduction factor of 0.5 (3.3 mg every 8 hours) or 2 mg/kg/day divided every 8 hours (2.4 mg every 8 hours), a dose of 3 mg IV every 8 hours was infused over 5 hours at a



**Figure 1** A: Patients' presenting rhythm, a narrow complex long RP tachycardia with an abnormal P-wave axis and heart rate of 193 beats per minute—consistent with ectopic atrial tachycardia. B: Sinus rhythm with aberrantly conducted and blocked premature atrial contractions pre-sotalol infusion with a corrected QT interval (QTc) of 447 msec. C: Postinfusion electrocardiogram (ECG) demonstrating a QTc of 480 msec. The QTc lengthened by 33 msec. D: Pre-discharge ECG on a sotalol dose of 60 mg/m<sup>2</sup>/dose every 8 hours. The QTc measured 460 msec.



**Figure 2** A: Patients' presenting rhythm, a narrow complex short RP tachycardia with a rate of 230 beats per minute, consistent with atrioventricular reentrant tachycardia. B: Sinus rhythm electrocardiogram (ECG) (no preexcitation) pre-sotalol infusion with a corrected QT interval (QTc) of 408 msec. C: Postinfusion ECG demonstrating a QTc of 465 msec. The QTc lengthened by 57 msec. D: Predischarge ECG on a stable oral sotalol dose of 45 mg/m<sup>2</sup>/dose every 8 hours with a QTc of 440 msec.

concentration of 1.5 mg/mL. Twelve-lead ECGs were performed at the initiation and termination of each dose of sotalol to monitor the QTc. Baseline QTc was 408 msec (Figure 2B), with the initial echocardiogram showing mildly dilated left ventricle with mildly reduced left ventricular systolic function. Renal function and blood glucose were monitored daily while the patient was on IV sotalol.

With the initiation of IV sotalol, Baby N returned to sinus rhythm with heart rates around 120 bpm. ECG showed a maximum QTc of 502 msec after the first dose of IV sotalol and stabilized around 480 msec after subsequent infusions (Figure 2C). Following a recurrence of SVT, sotalol was increased to 4 mg IV every 8 hours (36 mg/m<sup>2</sup>/dose). After 24 hours of sustained sinus rhythm on a stable dose of IV sotalol, the patient was converted to 4 mg oral sotalol every 8 hours. Over the next several days he had brief, self-resolving nonsustained SVT and sotalol was increased in a stepwise approach to 6 mg orally every 8 hours (45 mg/m<sup>2</sup>/dose with an age reduction factor of 0.6). QTc remained 420–440 msec (Figure 2D). After 48 hours free of tachycardia, he was discharged, with predischarge echocardiogram showing normal left ventricle size and function. Outpatient follow-up demonstrates that the infant remains in sinus rhythm with no documented breakthrough events on oral sotalol.

## Discussion

In this series, we present 2 newborns treated with IV sotalol for 2 different SVT mechanisms. To our knowledge, these are the youngest patients to have been successfully treated with IV sotalol for persistent supraventricular tachyarrhythmias. It was important to note that there was demon-

strable QTc prolongation (average 45 msec) at the end of the initial 5-hour infusion of sotalol, which shortened with time.

Sotalol produces antiarrhythmic activity through both beta-1 and beta-2 adrenergic receptor antagonism and prolongation of action potentials within the atrial and ventricular smooth muscle through potassium channel blockade (Vaughan-Williams classification III).<sup>7–9</sup> Most current literature of sotalol in pediatric patients is limited to oral therapy for treatment of supraventricular and ventricular arrhythmias, including supraventricular reentrant tachycardias, atrial flutter, atrial ectopic tachycardia, and ventricular tachycardia, in patients with postnatal age of 3 days or greater.<sup>2,3,10,11</sup> Rate of conversion to normal sinus rhythm with oral sotalol is approximately 80% and depends on the type of arrhythmia,<sup>3,9,12</sup> with reentrant SVT having the greatest response.<sup>3,12</sup> Conversion rates also vary based on dosing strategies of sotalol. At lower doses (30 mg/m<sup>2</sup>/dose), class II as well as some class III activity is noted, whereas at higher doses of 30–70 mg/m<sup>2</sup>, there is more class III activity, with a linear relationship between dose and class III activity.<sup>11</sup> QTc prolongation has also been shown to be dose dependent.<sup>12</sup>

Very limited literature has been published regarding IV sotalol in pediatric patients. Zhang and colleagues<sup>5</sup> studied IV sotalol in pediatric patients with atrioventricular reentrant tachycardias, atrial tachycardia, atrial flutter, and ventricular tachycardia. Rate of return to sinus rhythm was 69.2% in the group that received intravenous sotalol alone. Dosing consisted of a 1 mg/kg bolus over 10 minutes followed by 4.5 mg/kg/day as a continuous infusion. Two patients developed QTc prolongation that resolved with discontinuation of

therapy. As described above in our case series, there was significant QTc prolongation with relatively small doses of IV sotalol (average QTc prolongation of 45 msec) infused over 5 hours, so conservative dosing and close monitoring in neonatal patients is advisable.

Both oral and IV sotalol use has been studied in adult patient populations. A recent meta-analysis shows that sotalol is not only a good agent to maintain normal sinus rhythm in adult patients with atrial fibrillation, but is an appealing agent for conversion of atrial fibrillation to sinus rhythm as well.<sup>13</sup> Infusion rates, however, range from a bolus over 5 minutes to continuous infusion over 24 hours. The Advanced Cardiac Life Support algorithm for hemodynamically stable monomorphic ventricular tachycardia includes IV sotalol bolus over 5 minutes,<sup>14</sup> though the bolus can have negative side effects (such as hypotension, bradycardia, and torsades de pointes) and is not recommended for patients with QT prolongation or heart failure. Infusions over 5 hours produce a physiologically similar exposure to oral sotalol absorption and may limit cardiovascular adverse effects.<sup>6</sup>

## Conclusion

This is the first series to report the use of IV sotalol in 2 newborns with SVTs. The use of IV sotalol in newborns has not been well characterized in the literature. Given the lack of information, we employed a conservative approach with thoughtful discussions of dosing options, administration over 5 hours, and close monitoring to minimize the risk of hemodynamic instability. This regimen was effective in restoring sinus rhythm with transient QTc prolongation post-infusion. Larger studies are warranted to

further investigate dosing strategies and infusion times in this susceptible population.

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