Management of Fetal Supraventricular Tachycardia: Case Series from a Tertiary Perinatal Cardiac Center

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Keywords

Arrhythmia · Supraventricular tachycardia · Fetal tachycardia · Echocardiography

Abstract

Background: Fetal supraventricular tachycardia is a relatively uncommon cardiac rhythm abnormality which is often associated with adverse perinatal outcomes if untreated. Although there are several treatment modalities and protocols in use globally, there is no consensus as to the most effective antiarrhythmic to manage this condition. **Aim:** This study aimed to evaluate perinatal outcomes following prenatal maternal therapy for fetal supraventricular tachycardia. **Materials and Methods:** This was a 20-year retrospective cohort study. Institutional records were reviewed for antenatal therapy choice and maternal and fetal outcomes. **Results:** Sixty-nine cases met diagnostic criteria for fetal SVT, of which 56 (81%) received maternal antiarrhythmic therapy. Digoxin was the most common, but least effective, first-line therapy in 28 patients, achieving successful rate reversion in 35.7%. Thirty-one patients (55%) required second-line therapy, and this was most successful with digoxin and flecainide poly-

therapy achieving rate reversion in 17 of 18 cases (94.5%) at a median of 3 days (1.5–7). Hydrops was present in 23 (33%) cases at initial presentation, 16 of which achieved rate reversion. There was minimal difference in treatment efficacy comparing single- or multiple-agent treatment in the setting of hydrops (50% vs. 42.8%). Side effects occurred in 14/56 treated patients (25%) but were severe in only 8 (14.3%) women, most commonly with digoxin and flecainide polytherapy (6 of 8 cases). There were 3 (4%) fetal deaths amongst the study cohort. **Conclusions:** Digoxin and flecainide polytherapy were well tolerated and successfully achieved rhythm and rate control in fetuses with prenatally diagnosed supraventricular tachycardia. The presence of hydrops was a poor prognostic feature.

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Introduction

Fetal supraventricular tachycardia (SVT) is a cardiac rhythm anomaly complicating approximately 1:1,000 pregnancies [1]. Although in the majority of cases this is an isolated abnormality, a concomitant structural heart

defect is present in 5–10% of cases [2]. Fetal SVT accounts for up to 90% of all fetal tachyarrhythmias [3] and in most instances arises from retrograde atrial activation across a fast conducting accessory pathway [2, 4]. Postnatally, up to 10% of infants will have Wolff-Parkinson-White syndrome, the majority of which will resolve in the first year of life [2].

Sustained fetal SVT can lead to complications related to poor cardiac output. These include hydrops fetalis in 20–30% of cases – if untreated fetal demise and/or maternal mirror syndrome can ensue [5, 6]. Neonatal outcomes are improved if reversion to sinus rhythm and resolution of hydrops is achieved prior to birth [7].

Management of these rare cases is often difficult and requires prolonged maternal antiarrhythmic treatment to achieve adequate transplacental transfer and therapeutic drug levels in the fetus. As there is no clear consensus regarding the choice of antiarrhythmic agent, duration of treatment, or timing of birth if maternal treatment is unsuccessful in achieving cardioversion, clinical management is often individualized. The aim of this study thus was to review outcomes of all cases of fetal SVT managed at a single Australian tertiary perinatal cardiac center.

Methods

Patient Selection

We conducted a retrospective observational study of all cases of fetal SVT treated at the Queensland Paediatric Cardiac Services and Maternal Fetal Medicine (MFM) department at the Mater Mother's Hospital in Brisbane Australia between 2000 and 2020. Maternal demographic data (parity, gestation), ultrasound findings (presence or absence of hydrops, type of SVT and overall fetal heart rate, umbilical artery, middle cerebral artery, and ductus venosus Doppler), and clinical outcomes (rate reversion, maternal side effects, delivery timing and mode, birth weight, selected fetal outcomes) were extracted from the institution's electronic health records and ultrasound reporting system (Viewpoint® GE). Where necessary, this was supplemented by individual chart review to obtain details of duration and gestation at commencement of treatment, time to achieve sinus rhythm, details of dose adjustment, and need for polytherapy. Ethics and Governance approvals (HREC/14/MHS/37) were granted by the Mater Human Research Ethics Committee and Governance Office, respectively.

All cases were assessed by a fetal cardiologist and an MFM specialist. In addition to a detailed structural survey, fetal echocardiography was also performed. Fetal tachycardia was defined as a fetal heart rate of above 180 bpm and SVT defined as 1:1 AV conduction based on M-mode echocardiography. SVT was occasionally further characterized based upon the ventriculo-atrial (VA) interval [8]. Atrial flutter was diagnosed when the fetal heart rate was >250 bpm with 2:1 AV conduction. Fetal hydrops was defined as the presence of fluid in two or more fetal compartments.

If the diagnosis of fetal SVT was confirmed, women were counseled about management options and maternal antiarrhythmic therapy then commenced. Pretreatment maternal renal and liver function was checked and electrocardiogram and echocardiography performed in all cases. Antiarrhythmic agents used included digoxin, flecainide, and sotalol either as single-agent therapy or in combination. All women were admitted for in-patient monitoring when antiarrhythmic was commenced with subsequent outpatient management once the fetal heart rate had normalized. Maternal side effects were recorded as mild (nausea, dizziness, and fatigue) or severe (abnormal liver function tests, chest pain, abnormal electrocardiogram, or side effects severe enough to precipitate delivery). After commencement of maternal therapy, the fetal condition was closely monitored with regular ultrasound scans 1–2 times a week until delivery. Management of cases varied slightly according to the individual treating pediatric cardiologist.

Results

Over the study period, there were 69 cases that met the diagnostic criteria for fetal SVT. Of these, 56 (81%) received maternal antiarrhythmic therapy (Table 1). The median gestational age at diagnosis was 29+2 weeks (26+0–33+4) and 36+1 weeks (34+0–38+4) at birth. Hydrops was present in 23 (33.3%) cases. Only one fetus had a structurally abnormal heart with multiple rhabdomyomas. Most cases of SVT were unclassified as to subtype (51/69) (73.9%), with only 7 cases (10%) of atrial flutter within the cohort.

Overall, first-line therapy was unsuccessful in 31 of 56 (55.4%) cases (Fig. 1). Of these, 4 women delivered because of advanced gestation and/or maternal side effects and 27 women went on to second-line therapy with different agents following a median first-line treatment duration of 5 days (3–9). Overall success rates of second-line therapy in these 27 patients were high with 23 cases (85%) ultimately achieving rate reversion. The most successful second-line therapy was digoxin and flecainide polytherapy which achieved rate reversion in 17 of 18 cases (94.5%) following a median treatment duration of 3 days (1.5–7).

Digoxin was the most common first-line therapy and used in 28 women (50%). Flecainide was utilized as first-line therapy in 7 (12.5%) and sotalol in 6 (10.7%) women, respectively (Table 2). Successful conversion to sinus rhythm occurred in 10 cases (35.7%) in the digoxin group following a median treatment of 4.5 days (3–9) of maternal treatment. However, when compared to digoxin, both flecainide and sotalol achieved higher rates of cardioversion when used as first-line monotherapy in 5/7 (71.4%) and 3/6 (50%) women although this comprised only 23%

Table 1. Cohort characteristics

	Total	Percentage of cohort, %
Demographics	69	
No transplacental therapy	13	18.8
Delivered at diagnosis	10	
Declined treatment	1	
Clinical decision not to treat	2	
Antenatally treated SVT	56	81
Hydrops	23	33.3
Nulliparous	26	37.6
Multiparous	41	59.4
Gestation at diagnosis, weeks+days	29+2 (26+0–33+4)	
Gestation at delivery, weeks+days	36+1 (34+0–38+4)	
Birth weight, g	2,940 (2,668.5–3,422)	
Diagnosis		
Atrial flutter	7	10
SVT	62	89.8
No structural cardiac anomaly	68	98.5
Mode of delivery (<i>n</i> = 58)		
Caesarean section	38	65.5
Elective	26	68
Emergency	11	28.9
Unknown	1	
Vaginal delivery	20	35.1
Delivery indication (<i>n</i> = 55)		
Immediate delivery, no therapy	10	18
Obstetric indication	16	29
Maternal indication (side effects)	4	7.3
Worsening fetal condition	6	10.9
Rate reverted SVT at term	19	34.5
Outcome		
Delivered without therapy	13	18.8
Rate reverted SVT at delivery	46	66.7
Persistent SVT despite therapy	7	10.1
IUFD	3	4.3

Data are presented as number and percentage for binary variables or median and inter-quartile range. SVT, supraventricular tachycardia.

of the treated cohort of 56 cases. The median latency to rate reversion was only 3 days (2–4) in the flecainide cohort and 6 days (3.5–10) in the sotalol cohort.

Of the 23 cases that had hydrops, 21 received antenatal treatment with the other 2 women delivered because of their relatively advanced gestation at diagnosis. Polytherapy was used more frequently as first-line treatment when fetal hydrops was present (11/21, 52%). Digoxin and flecainide in combination were used in 7 cases and were successful in correcting the FHR in 3 cases (42.8%) at a median of 5 days (range 4–6) whilst digoxin and sotalol were used together in 4 cases. Of these, cardioversion was achieved in only 1 case. Of the remaining 10 cases of hydrops, monotherapy with either flecainide or digoxin was used with successful reversion of the SVT in 5 cases.

Overall, treatment in the context of fetal hydrops was successful in 42.9% (9/21) of cases.

Side effects occurred in 14 (25%) of the 56 treated patients (Table 3), although in 6 women, these side effects were mild. The remaining 8 patients required either alternative agents or delivery due to significant side effects most commonly occurring with digoxin and flecainide polytherapy. Of women receiving digoxin and flecainide, 2 were delivered for severe nausea, 2 had therapy changed for palpitations with detectable QT prolongation on 12-lead ECG, and 2 had deranged liver function which resolved with alternative agents.

There were 3 (4.3%) fetal deaths amongst the cohort all of which were hydropic at initial presentation. Of these, although rate reversion was achieved in 2 fetuses

Fig. 1. Study criteria and outcomes.

using digoxin and flecainide, respectively, hydrops did not resolve and fetal demise occurred at 10 days and 35 days, respectively, following treatment. In the third case, despite 3 different agents including amiodarone, the SVT remained refractory, and fetal death was diagnosed 10 days following initial therapy. A further 6 fetuses (8.7%) were delivered on the basis of worsening hydrops or abnormal Doppler parameters.

The median gestation at delivery was 36+1 weeks (34+0–38+5). Of the 58 women in the study cohort for whom mode of delivery details were available, 38 (65.5%) were delivered by caesarean section. However, the indication for recommending delivery was only documented in 55 women. Of these 55 women, 10 (18%) were delivered for maternal side effects or worsening fetal condition, and a further 10 (18%) delivered immediately without therapy. In 10 (18%) women, preterm labor or preterm prelabor rupture of membranes precipitated delivery.

Discussion

In this large, single-center study, we demonstrate high success rates for treatment of fetal SVT when digoxin and flecainide were used in combination. Overall, this dual-agent regimen achieved rate reversion in 22 of 27 (81.5%) cases. Our results are comparable to other published series which report success rates of 59–90% using digoxin, flecainide, or sotalol in combination [9–13]. Our results also indicate that in almost 1 in 3 cases without hydrops and 1 in 2 cases with hydrops, initial monotherapy failed thus requiring progression to second-line polytherapy.

Digoxin was the first-line agent in the majority of cases and achieved rate reversion in 35.7% in line with other published series [3, 10, 14]. Digoxin was the preferred initial treatment because of its safety and side effect profile and relatively rapid response time [10, 11]. However, we note that studies reporting high treatment efficacy of digoxin used much higher daily doses of up to 750 µg/day [11], as

Table 2. Outcomes following antiarrhythmic treatment

Agent	First-line therapy			Second-line therapy					Overall treatment efficacy [#]					
	total cohort		treatment efficacy, n (%)	latency to reversion, days		total cohort		treatment efficacy, n (%)	latency to reversion, days		n (%)			
	total	H		total	H	total	H		total	H				
Flecainide	7	4	5 (71.4)	3 (75)	3 (2–4)	2 (3)	2	–	1 (50)	–	13	–	6/9 (66.9)	3/4 (75)
Digoxin	28	6	10 (35.7)	2 (33)	4.5 (3–9)	9 (2)	0	–	–	–	–	–	10/28 (35.7)	2/6 (33)
Sotalol	6	–	3 (50)	–	–	–	–	–	–	–	–	–	3/6 (50)	–
Digoxin + flecainide	9	7	5 (55.6)	3 (42.8)	5 (4–5)	5 (4)	18	5	17 (94.5)	5 (100)	3 (1.5–7)	2 (1–10.5)	22/27 (81.5)	8/12
Digoxin + sotalol	6	4	2 (33.3)	1 (25)	9.5 (8,10)	12	7	4	5 (71)	2 (50)	7 (5–7)	8 (2)	7/13 (53.8)	3/8 (37.5)
Overall	56	21	25 (44.6)	9 (42.8)	7.5 (4–15)	4 (1.5–7.5)	27	9	23 (85.2)	7 (77.8)	5 (3–7)	7 (1–9)	48/56 (85.7)	16/21 (76)

Data are presented as median and interquartile range (or range in the event of small numbers) or number and percentage for binary variables. H, hydropic fetus; total, total cohort including hydropic and nonhydropic at diagnosis. [#]Regardless if used as first- or second-line therapy.

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opposed to only 500 µg/day in our cohort. When hydrops was present, treatment efficacy in achieving rate reversion was higher (5/7 cases, 71.4%) when digoxin and flecainide were used in combination. Our results are consistent with other published outcomes that range from 59 to 78% using this approach [14–18]. However, dosing regimens in the literature vary significantly [2, 7, 9, 10, 15], and interval to fetal rate reversion from diagnosis may be longer with polytherapy. This likely reflects current practice in utilizing polytherapy mainly after failed first-line monotherapy [17].

Our results demonstrate that rate reversion occurred at a median of 7.5 days (4–15) of starting maternal treatment. Second-line treatment was trialled by 7 days of failure of rate reversion in all by 8 of 56 fetuses. The indication for addition of a second agent was lack of fetal response in 90% of cases, with worsening fetal condition observed in only 2 fetuses over this initial treatment time period.

Overall, maternal side effects were relatively uncommon in our cohort, reported in only 25% of women. Serious side effects warranting dose adjustment or delivery were encountered in 14.3% of patients. Although women on flecainide monotherapy did not report any side effects, this was not the case when it was used in combination with other agents. In 6 out of 8 cases of serious maternal side effects, flecainide was implicated. Significant maternal side effects were seen when the dose of flecainide was >300 µg/day. Likewise, sotalol at a dose of >160 mg/day was associated with 50% of side effects attributable to this drug. In general, maternal serum levels of digoxin and flecainide aid more in monitoring for maternal toxicity rather than as a guide to therapeutic fetal levels as these have yet to be quantified [19]. The higher maternal side effect profile of flecainide is often cited as a reason to use alternative first-line agents [14, 15, 18, 20].

In this series, cardioversion was only possible in 42.9% (9/21 cases) of hydropic fetuses following treatment. Fetal hydrops is associated with increased fetal volume of distribution – this is believed to be responsible for the lack of efficacy when digoxin is used in this setting [15, 19, 21] [10, 15, 22]. Consistent with other studies, we were unable to ascertain if polytherapy with digoxin and another agent was superior to digoxin monotherapy alone [23]. Historically, mortality rates amongst hydropic fetuses on treatment have been reported to be as high as 27% [2], though more recent case series report more conservative rates around 5% [9]. We report an overall mortality rate of 4.3% (3/69), though this was 13% (3/23) amongst the cohort with hydrops at diagnosis.

The low rate of subclassification of SVT amongst our cohort makes it difficult to draw conclusions regarding

Table 3. Maternal side effect profile

Agent	Complications		Associated dosage
	mild	serious (or requiring alteration of therapy)	
Overall	6/56 (10.7%)	8/56 (14.3%)	
Digoxin	1	0	D 625 µg BD
Flecainide	0	0	
Sotalol	1	1	(1) Lethargy and nausea S 80 mg TDS
Amiodarone	0	1	(1) Palpitations and chest pain
Digoxin + flecainide	2	6	(2) Nausea (necessitating delivery) (2) QT prolongation (2) Deranged LFTs (D 250 µg BD, F 100 mg BD) (D 250 µg BD, F 100 mg TDS) (D 250 µg BD, F 100 mg BD) (D 250 µg BD, F 100 mg TDS) (D 250 µg TDS, F 100 mg TDS) (D 250 µg OD, F ?)
Digoxin + sotalol	2	0	(D 375 µg BD, S 80 mg BD) (D 250 µg BD, S 100 mg BD)

Three patients delivered due to intolerable side effects. All >34+0 at time of delivery. D, digoxin; F, flecainide; S, sotalol; OD, once daily dosing; BD, twice daily dosing; TDS, 3 times daily dosing.

subtype response to therapy. We postulate that although the underlying mechanism of SVT may influence fetal response [24], this impact may have been underestimated in the past, and so subclassification diagnosis was not often documented. Sotalol as first-line treatment was our preference for long VA SVT. This approach is supported by data showing that both digoxin and flecainide monotherapy for long VA SVT is associated with a longer delay to reversion and poorer response [23, 24]. Accurate identification and subclassification of SVT through characterization of the VA interval at fetal echocardiography may highlight subgroups such as atrial flutter, which are more likely to respond to polytherapy as first-line treatment.

Cases refractory to treatment represent a therapeutic challenge. Only 3 (4.3%) cases in our series demonstrated persistent SVT. Although both oral and intravenous amiodarone is an effective agent for the treatment of fetal SVT, its side effect profile and the need for careful maternal monitoring preclude its use as first-line therapy, and it is normally reserved for refractory cases [25]. However, in 2 of our 3 refractory cases, amiodarone also failed to achieve rate reversion. Although it was not used in our cohort, intra-amniotic digoxin has been used prenatally, with rapid resolution of fetal SVT [26]. This may be an alternative option at very preterm gestations when delivery is not an option.

Once rate and rhythm control was achieved, vaginal birth was offered. There were no cases of recurrent fetal

SVT in labor. Whether therapeutic rate control with transplacental therapy impairs accurate detection of fetal hypoxia in labor manifested by cardiotocographic changes is unknown. In our series, of the 11 emergency caesarean sections, only 4 were performed in labor. Unfortunately, markers of fetal hypoxia such as cord artery pH were not available for all cases. Limitations of our study include its retrospective nature, treatment preferences by individual cardiologists, and lack of some outcome data.

Conclusion

Robust protocols to guide treatment of fetal SVT are lacking. Although several antiarrhythmic options and treatment protocols exist in the literature, refractory cases and nonresolution of hydrops despite rate reversion remain therapeutic challenges. Key to optimizing perinatal outcomes is rapid rate reversion using the lowest maternal dose, thus minimizing maternal side effects and maximizing compliance. Recognition of antenatal factors predisposing to treatment failure is important in deciding the choice of initial treatment. We await the outcomes of the Fetal Atrial Flutter and Supraventricular Tachycardia Therapy Randomised Clinical Trial (FAST RCT) (Clinical Trials Identifier NCT02624765) which will hopefully provide guidance as to the optimum management for these difficult cases.

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Statement of Ethics

Ethics exemption and Governance approvals (HREC/14/MHS/37) were granted by the Mater Human Research Ethics Committee and Governance Office, respectively. Specifically, the ethics exemption includes waiver of patient consent for audit purposes.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Data Availability Statement

All data analyzed in this study are included in this article. Further enquiries can be directed to the corresponding author.