Fetal arrhythmias: prenatal evaluation and intrauterine therapeutics

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Abstract

Introduction: Fetal arrhythmias are a common phenomenon with rather complicated etiologies. Debates remain regarding prenatal diagnosis and treatment of fetal arrhythmias.

Methods: The literature reporting on prenatal diagnosis and treatment of fetal arrhythmias published in the recent two decades were retrieved, collected and analyzed.

Results: Both fetal magnetocardiogram and electrocardiogram provide information of cardiac time intervals, including the QRS and QT durations. M-mode ultrasound detects the AV and VA intervals, fetal heart rate, and AV conduction. By using Doppler ultrasound, simultaneous recording of the atrial and ventricular waves can be obtained. Benign fetal arrhythmias, including premature contractions and sinus tachycardia, do not need any treatment before and after birth. Sustained fetal arrhythmias that predispose to the occurrence of hydrops fetalis, cardiac dysfunction or eventual fetal demise require active treatments. Intrauterine therapy of fetal tachyarrhythmias has been carried out by the transplacental route. If maternal transplacental treatment fails, intraumbilical, intraperitoneal, or direct fetal intramuscular injection of antiarrhythmic agents can be attempted.

Conclusions: The outcomes of intrauterine therapy of fetal tachyarrhythmias depend on the types or etiology of fetal arrhythmias and fetal conditions. Most are curable to a transplacental treatment by the first-line antiarrhythmic agents. Fetal cardiac pacings are effective methods to restore sinus rhythm in drug-resistant or hemodynamically compromised cases. Immediate postnatal pacemaker implantation is warranted in refractory cases.

Keywords: Arrhythmias, Fetus, Treatment

Introduction

Fetal arrhythmias are diagnosed in 1–3% of pregnancies [1], and account for 10–20% of the referrals to fetal cardiology [2]. In a non-randomized prospective study on 100 fetuses at 15–40 weeks of gestation for cardiac referral, 45 fetuses had cardiac arrhythmias, including premature atrial contractions (PACs) (28/45, 62.2%), atrial bigeminal ectopic beats (3/45, 6.7%), premature ventricular contractions (PVCs) (2, 4.4%), supraventricular tachycardia (SVT) (5/45, 11.1%), ventricular tachycardia (1, 2.2%), second-degree atrioventricular (AV) block (1, 2.2%) and complete AV block (5/45, 11.1%) [3]. A 10-year observational study on the pregnant women demonstrated 29 cases of fetal arrhythmias: 12 (41.4%) of which were fetal tachycardias (10 cases with SVT, 2 cases with atrial flutter (AF)), 5 (17.2%) were fetal bradyarrhythmias (all 5 cases with AV block), and 12 (41.4%) were fetal irregular cardiac rhythms (premature atrial beats) [4]. The overall incidence of malignant fetal arrhythmias, such as complete AV block and SVT, are relatively rare, found in 1:5000 pregnancies [5].

Genetic studies have shown that GATA4, NKX2-5, TBX3, and TBX5 genes are responsible for cardiac structural development, whereas mutations of these genes may lead to congenital heart diseases and conduction disorders [6]. The occurrence of paroxysmal AF can be a result of TBX5 gain-of-function mutations and overexpressions of Nppa, Cx40, Kcnj2 and Tbx3 genes [7]. Na1.5 gain-of-function mutation is proved to be associated with an increased risk of multifocal atrial and ventricular ectopies and dilated cardiomyopathy [8].
The fetuses with benign arrhythmias, such as PACs < 11 beats per minute (bpm) and sinus tachycardias, did not need any treatment before or after birth, whereas those with postnatal arrhythmias associated with hemodynamic fluctuations require interventions, as they may lead to preterm delivery in some occasions [9]. Besides, sustained fetal arrhythmias predispose to the occurrence of hydrops fetalis, cardiac dysfunction, or even fetal demise [10]. Therefore, prenatal treatment is warranted for improving the fetal survival rate. The aim of the present study is to discuss the complex and challenging issue concerning the prenatal evaluation and intrauterine therapeutics of fetal arrhythmias.

Diagnosis

M-mode ultrasound can detect the AV and ventricular atrial (VA) intervals, fetal heart rate, AV conduction, and even ejection fraction [11], but detection qualities may be compromised by early detection in first trimester, unfavorable fetal position, hydrops fetalis, fetuses with cardiac contractile dysfunction and obese pregnant women [12]. Crowley et al. [13] reported that they used a two-dimensional scan head with M-mode recordings for the diagnosis of fetal arrhythmias. Fetal heart rate and rhythm were measured by detecting semilunar and AV valve opening and closing points, A waves, plus ventricular wall motion. In 2 fetuses of their patient setting, the arrhythmias were diagnosed using two-dimensional echo alone. The anatomic M-mode provides simultaneous two-dimensional real-time images and therefore can obtain good quality tracings of atria and ventricles than by standard M-mode views.

By using Doppler ultrasound, simultaneous recordings of the atrial and ventricular waves can be obtained. The mechanisms of SVT can be classified as mechanical VA intervals as short VA or long VA [14]. Measurement of the VA interval by Doppler echocardiography helps distinguish short VA interval from long VA interval types of fetal tachycardias, such as AV nodal reentrant tachycardia and permanent junctional reciprocating tachycardia [15].

The Doppler ultrasound records ascending aorta and superior vena cava flow velocity waveforms better than the M-mode. In fetuses with short VA tachycardia, it may display a distinctive Doppler flow velocity pattern with a 1:1 AV conduction and a tall A wave superimposed on the aortic ejection wave. It was regarded as a reentrant tachycardia through a fast-conducting AV accessory pathway. In long VA tachycardia, an A wave of normal amplitude with normal AV time interval could be detected in front of the aortic ejection wave [16]. Doppler waveforms detected from the inferior vena cava and the descending aorta helps in obtaining information of atrial and ventricular systoles simultaneously. However, this results may be compromised when the fetus is in an improper position for simultaneous recordings [17]. By detecting flow imaging frequency spectrum of the pulmonary arteries and pulmonary veins, the pulse Doppler echocardiography can determine the rhythm changes between the spectra and the arrhythmic patterns. This technique can readily identify atrial and ventricular systoles, and measure the PR interval [17].

Fetal electrocardiography (ECG) does not provide beat-to-beat analysis by detecting the signal averaging of electrocardiographic complexes. Thus, it is not helpful in diagnosing fetal rhythm and conduction disorders with irregular heart rates.

Fetal magnetocardiography (MCG) allows real-time detection and classification of arrhythmias [18] with better signal quality than electrocardiography due to more favorable transmission properties of the magnetic signals. It can be helpful in making prenatal diagnoses of a variety of fetal arrhythmias, such as complete AV block, premature contractions, paroxysmal SVT and Wolff-Parkinson-White syndrome and long QT syndrome [19]. However, the use of the magnetic analogue of ECG requires a magnetically shielded room. Both MCG and ECG may provide useful information on cardiac time intervals, such as the QRS and QT durations.

Treatment

Irregular arrhythmias

The majority of fetal arrhythmias are premature contractions. Capuruço et al. [9] reported that PACs were the most common fetal arrhythmias representing 55.5% (100/180), followed by bi- or trigeminy (12/180, 0.7%), sinus tachycardia (18.3%, 33/180), SVT (15.6%, 28/180), and AF 0.4% (7/180). Most of the PACs are benign, and do not have a genetic cause, while a few PACs can be associated with congenital heart defects or as a manifestation of Costello syndrome caused by HRAS mutations [20]. In fetuses with premature contractions, fetal echocardiogram is useful for cardiac structural and functional assessments, and for disclosing the mechanisms of fetal isolated PACs and multiple ectopic beats [21]. PACs are usually benign and often resolve spontaneously, but follow-up is necessary for preventing from developing into ventricular tachycardia [22]. Respondek et al. [23] reported that PACs required antiarrhythmic treatments with digoxin, verapamil, or both in 14% of the cases.

Fetal PVCs were less common than PACs. Most isolated fetal PVCs usually resolve spontaneously. The sustained PVCs may also resolve within 6 weeks, and do not cause severe arrhythmias [24]. Fetal PVCs warrant close monitoring as they may develop into proxsymal ventricular tachycardias (VTs).


**Tachyarrhythmias**

The transplacental administration of antiarrhythmic agents, including digoxin, flecainide, sotalol, and amiodarone, is applied for fetal tachycardia in many centers [25]. Flecainide and sotalol cross the placental barrier easier, especially in hydropic fetuses, and a higher drug concentration can be achieved in the amniotic fluid. The management protocols are shown in Table 1.

The modes of administration, intraumbilical, intramnioniotic, intraperitoneal, intramuscular and intracardiac, have been selected as routes of administration. The intraumbilical and intracardiac injections aim at a quick response to therapy by a direct access to the fetal circulation, but they pose a traumatic risk to the fetus. Intraperitoneal, intramnioniotic, and intramuscular injections allow instant delivery of the drugs while the fetuses carry less traumatic injuries [27]. If maternal transplacental treatment fails, direct administrations, such as intraumbilical, intraperitoneal, or intramuscular injection of antiarrhythmic agents can be considered as alternative approaches. Intraumbilical administration of antiarrhythmic agents can be performed under ultrasound guidance, but with somewhat technical difficulty, especially when the fetus is in an unfavorable location. This direct treatment is indicated in cases of tachyarrhythmia with hydrops fetalis as an adjunctive to the higher dose of maternal transplacental therapy [28].

Fetal tachyarrhythmias are usually SVT (63.4%), AF (28.0%) and VT (8.5%). There are other rare types of fetal arrhythmias, such as ventricular tachycardia, junctional tachycardia, and multifocal atrial tachycardia [14]. Fetal MCG may reveal a strong association between AF and an accessory pathway [29]. SVT mechanism was classified by mechanical VA time intervals as short VA or long VA. It has been reported that short VA interval occurred in 67 fetuses (80%) and long VA in 17 (20%). Treatment success was defined as conversion to sinus rhythm, or rate control, defined as >15% rate reduction [14]. Digoxin, flecainide and sotalol can be the first-line treatments. Amiodarone, propafenone, and combined therapies are reserved for refractory fetal tachycardias [30].

Digoxin has been considered the first-line agent for the treatment of fetal SVT. Digoxin is praised for its safety and efficacy, but maternal higher doses are required to maintain a therapeutic serum level especially in the presence of hydrops fetalis [31]. Digoxin monotherapy showed a lower effective rate than combined digoxin and flecainide/sotalol for the treatment of fetal tachyarrhythmias (27.8% vs. 72.2%). The transplacental administration of combined digoxin and flecainide is an effective regimen for SVT with long VA interval [32]. Flecainide is an effective first-line treatment for fetal SVT with a high successful rate of 88.2%, low side effect and relatively easy utilization [33]. Flecainide is highly effective in achieving sinus rhythm in hydropic and nonhydropic fetuses with SVT, refractory SVT or SVT with signs of heart failure. Oral flecainide (100 mg three times daily) is reserved for those cases unresponsive to sotalol and digoxin [34]. It is more effective than digoxin, especially for hydropic fetal tachycardia, with no adverse fetal outcomes found [14]. Flecainide was preferred in converting SVT to normal sinus rhythm or in slowing AF to well-tolerated ventricular rates [35]. The conversion rate to sinus rhythm of flecainide for short VA SVT was higher than digoxin (96% vs. 69%, P = 0.01). For long VA SVT, the conversion rate to sinus rhythm did not differ significantly between the two drugs (67% vs. 50%, P = 0.13). In nonhydropic fetuses, the successful rate of flecainide was higher than digoxin (96% vs. 79%, P = 0.10). In hydropic cases, a same trend was observed (86% vs. 38%, P = 0.07 for flecainide vs. digoxin), while the successful rate of combined flecainide with amiodarone was 100%. The intrauterine or neonatal mortality rate in hydropic fetuses treated with flecainide was much lower than that treated with digoxin (0% vs. 43%, P = 0.06). Strizek et al. [36] reported that the successful rate was 81.2% (26/32) when treated with flecainide as a first-line therapy. The median time to conversion to sinus rhythm was 3 days (range 1–7 days) with flecainide monotherapy and 11.5 days (range 3–14 days) with a combined therapy. For AF persisting for 5 days, flecainide use achieved a much better heart rate control than soltalol [35]. With combined flecainide and digoxin therapy, conversion to sinus rhythm occurred within 5 days (range, 0–14 days). Most fetuses (75%) converted to sinus rhythm within 7 days of treatment [37].

Sotalol is usually well-tolerated and has little or no negative inotropic effect on the fetal heart. It should be used with small doses cross the placenta [31]. Sotalol is the best treatment for fetal AF in most cases and is a safe and effective therapy for SVT [35]. Rebelo et al. [38] reported that successful drug treatment with sotalol in 5/6 (83.3%) cases with no adverse effects for the mothers. In comparison to flecainide or digoxin, sotalol was less effective to convert SVT to sinus rhythm.

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**Table 1 The treatment protocol of fetal tachyarrhythmias** [26]

| Tachyarrhythmia | Short VA SVT/AF, nonhydropic | Short VA SVT/AF, hydropic | Long VA SVT |
|-----------------|-----------------------------|--------------------------|-------------|
| First-line      | Digoxin                     | Digoxin and sotalol      | Sotalol     |
| Second-line     | Digoxin and sotalol         | Digoxin and flecainide/amiodarone | Flecainide |
| Third-line      | Digoxin and flecainide      |                          |             |

AF atrial flutter, SVT supraventricular tachycardia, VA ventriculoatral conduction
et al. [39] documented response to sotalol (43%) or sotalol/digoxin (57%) as first-line treatment in 21 pregnancies. The time to conversion to sinus rhythm for sotalol varied from 1 to 5 days (median 1 day) for Shah et al. [39], 1–35 days (median 7.5 days) for van der Heijden et al. [40] and a median of 12 days for Jaeggi et al. [41]. Freedom from arrhythmia on maintenance therapy was 93 and 90% at 1 and 3 months, respectively. The overall mortality was 8%, only 4% of which was arrhythmia-related. In the absence of hydrops, fetal AF/SVT was associated with low morbidity and mortality rates.

Amiodarone is a second-line treatment, especially in hydropic fetuses with SVT [27]. In the event of life-threatening fetal arrhythmia, direct fetal therapy with adenosine and amiodarone can be a last resort [34]. In cases of refractory SVT with severe hydrops fetalis, the treatment regimen can be a maternal oral loading dose of 200 mg, followed by fetal intraperitoneal dose of 4–7 mg/kg. Fetal intraperitoneal amiodarone was successful in 75% (6/8) cases. The frequency of intraperitoneal injections depended on the therapeutic response, usually 1–4 doses, but up to 11 doses in an extreme case with a conversion time of 11.5 days after the initial injection. Besides, immediate cardioversion was also observed in a fetus receiving intraumbilical injection of amiodarone. Hydrops fetalis resolved in 62.5% (5/8) fetuses, with a mean resolution time of 28.4 days [42].

In general, digoxin is widely accepted as a first-line antiarrhythmic drug. Sotalol, flecainide and amiodarone are used as second-line drugs when digoxin fails to achieve conversion to sinus rhythm. For fetuses with hydrops and fetal SVT with long VA interval, digoxin is rarely effective. For fetuses with hydrops, the placental transfer of the digoxin is limited. Sotalol and flecainide have good placental transfer ability, and they should be used as first-line treatment for hydropic fetal tachyarrhythmias. Fetal direct intramuscular injection of digoxin with maternal amiodarone use is an effective alternative. The treatment of choices for fetal tachyarrhythmias was listed in Table 2.

Stirnemann et al. [45] applied fetal esophageal pacing with a bipolar pacing esophageal lead (FIAB Esokid 4S, Firenze, Italy) positioned behind the left atrium for the treatment of fetal AF. The lead was connected to an asynchronous esophageal pacemaker. It showed an immediate conversion to sinus rhythm.

### Bradyarrhythmias
Fetal bradycardias may be due to sinus bradycardia, blocked PACs, or high degree AV block [46]. Transient bradycardia is somewhat common in the developing fetus and is usually benign. Complete AV block occurred in 2.6% of fetuses with irregular cardiac rhythms [47]. Capuruço et al. [7] reported that the prevalence of fetal bradyarrhythmias was 3.4% (62/1821). Fetal bradycardias may occur in the presence of fetal hypoxia [48], associated congenital structural disorders [49], maternal connective tissue disorders [50], positivity of maternal SSA/Ro and/or SSB/La autoantibodies [50], or due to an unknown cause [51]. Sinus bradycardias are often caused by fetal hypoxia or immaturity of the cardiac conduction system. The transient fetal bradycardia is benign and often need no fetal treatment. The two most common congenital heart defects associated with AV block are left atrial isomerism and discordant AV connection. Maternal anti-SSA/SSB antibody positivity is another cause of fetal AV block. Long QT syndrome can cause 2:1 AV block or sinus bradycardia. Blocked atrial bigeminy also resembles 2:1 AV block and causes fetal bradycardia.

| Parameter | Digoxin | Flecainide | Sotalol | Amiodarone |
|-----------|---------|------------|---------|------------|
| Indication | Paroxymal SVT, short VA, SVT, nonhydrotic fetuses | SVT with NIHF, refractory SVT, SVT with heart failure unresponsive to sotalol and digoxin | AF, SVT | SVT resistant to digoxin, AF |
| Dose | Loading: 1.5–2 mg over 24–48 h; Maintenance: 0.375–1 mg/day | Loading: 200–300 mg divided b.i.d., or t.i.d.; Maintenance: 450 mg/day if no response | Loading: 160–320 mg divided b.i.d.; Maintenance: increased to 480 mg/day | Loading: 1600–2400 mg/day divided b.i.d.; Maintenance: 200–400 mg/day b.i.d. |
| Route | p.o., or i.v. | p.o. | p.o. | p.o., or i.v. |
| Fetal/maternal serum level (%) | 40–90 | 10–50 | | |
| Advantage | Safe and effective | Not accumulate in fetus, not cause intrauterine growth retardation | Little or no negative inotropic effect | |
| Adverse effect | Digoxin monotherapy showed a lower effective rate than combined; Hydropic fetuses refractory to digoxin | Intrauterine death | Negative inotropic effect, intrauterine death | Arrhythmogenic effect, fetal thyroid functional impairment, maternal thrombocytopenia and skin rash |

*AF* atrial flutter, *NIHF* nonimmune hydrops fetalis, *SVT* supraventricular tachycardia, *VA* ventricioatrial conduction
Both M-mode and Doppler echocardiography can help diagnose sinus bradycardia. The prolonged episodes of sinus bradycardia can be caused by fetal distress as a result of fetal hypoxia and acidosis, long QT syndrome, and congenital sinus node dysfunction [34]. Fetal bradycardia with either congenital heart defects or fetal hydrops significantly worsens their prognoses. Moreover, heart function and congenital heart defects exaggerate the severity of congestive heart failure [15].

Fetal complete AV block with structural heart disease often shows a worse prognosis, such as fetal demise or pacemaker implant requirement. All those with complete AV block by maternal autoantibodies positivity survived, but 42.8% needed a pacemaker. The high risks of perinatal demise was often associated with fetal hydrops, structural defects, poor ventricular function and HR < 55 bpm. Regular screening by fetal echocardiography and transplacental treatments for fetal AV block, and they are effective methods to restore sinus rhythm in drug-resistant or hemodynamically compromised cases. Immediate postnatal pacemaker implantation is warranted in refractory cases.

**Conclusions**

Benign fetal arrhythmias, such as premature contractions and sinus tachycardia, do not need any perinatal treatments. Sustained fetal arrhythmias that predispose to the occurrence of hydrops fetalis, cardiac dysfunction, or even fetal demise require early treatments. The effect of intrauterine therapy of fetal tachyarrhythmias depends on the types or etiology of fetal arrhythmia and fetal conditions (hydrops fetalis, cardiac function, and maternal autoantibody positivity, etc.). to the conversion rate was high with the use of the first-line antiarrhythmic agents via the translacental route. Fetal cardiac pacings are effective methods to restore sinus rhythm in drug-resistant or hemodynamically compromised cases. Immediate postnatal pacemaker implantation is warranted in refractory cases.

**Acknowledgements**

No

**Authors’ contributions**

YSM: Substantial contribution to the conception and design of the work; and the acquisition, analysis, and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval
of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved. XZY: Substantial contribution to the conception and design of the work; and the acquisition, analysis, and interpretation of data for the work; drafting the work and revising it critically for important intellectual content; final approval of the version to be published; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved. Both authors read and approved the final manuscript.

Funding
No.

Availability of data and materials
Based on literature review.

Ethics approval and consent to participate
The institutional Review Board approves this study.

Consent for publication
The institutional Review Board and coauthor consent for publication.

Competing interests
The authors declare that they have no competing interest.

Received: 30 October 2019 Accepted: 3 February 2020
Published online: 12 February 2020

References
1. Aggarwal S, Caplicki S, Chintala K. Hemodynamic effect of fetal supraventricular tachycardia on the unaffected twin. Prenat Diagn. 2009;29:292–3.
2. Sajiela R, Sachdeva S, Saggu DK, Koneti NR. Ventricular tachycardia in a fetus: benign course of a malignant arrhythmia. J Obstet Gynaecol India. 2019;69:385–6.
3. Tutschek B, Schmidt KG. Pulsed-wave tissue Doppler echocardiography for the analysis of fetal cardiac arrhythmias. Ultrasound Obstet Gynecol. 2011;38:406–12.
4. Gozar L, Marginean C, Toganel R, Muntean I. The role of echocardiography in fetal tachyarrhythmia diagnosis. A burden for the pediatric cardiologist and a review of the literature. Med Ultrason. 2017;19:232–5.
5. Strasburger JF. Fetal arrhythmias. Prog Pediatr Cardiol. 2000;11:1–7.
6. Ishikawa T, Tsuji Y, Makita N. Inherited bradyarrhythmia: a diverse genetic background. J Arrhythm. 2016;32:552–8.
7. Postma AV, van de Meerakker JB, Mathijssen IB, Barnett P, Christoffels VM, Ilgun Y, et al. A gain-of-function TBX5 mutation is associated with atypical Holt-Oram syndrome and paraxial amal dysplasia. Circ Res. 2008;102:1433–42.
8. Caloie K, Broedenberg AK, Christerssen AH, Pedersen LN, Olesen MS, de Los Angeles Tejada M, et al. Multifocal atrial and ventricular premature contractions with an increased risk of dilated cardiomyopathy caused by a Nav1.5 gain-of-function mutation (G213D). Int J Cardiol. 2018;257:160–7.
9. Capuroço CA, Mota CC, Rezende GD, Santos R. P06.03: fetal tachyarrhythmia: diagnosis, treatment and outcome. Ultrasound Obstet Gynecol. 2016;48(Suppl. 1):167–269.
10. Yashk A, van der Does LME, Lanters EAH, de Groot NMS. Pharmacological therapy of tachyarrhythmias during pregnancy. Arrhythmia Electrophysi Rev. 2016;5(4):1–41.
11. Crisan CD, Ligezan I, Lazar E, Moscu AV. Fetal heart arrhythmies and doppler ultrasound. TMJ. 2003;53:286–9.
12. Bravo-Valenzuela NJ, Rocha LA, Machado Nardoza LM, Júnior EA. Fetal cardiac arrhythmias: current evidence. Ann Pediatr Cardiol. 2018;11:148–63.
13. Crowley DC, Dick M, Rayburn WF, Rosenthal A. Two-dimensional and M-mode echocardiographic evaluation of fetal arrhythmia. Clin Cardiol. 1985;8:1–10.
14. Sridharan S, Sullivan I, Tomel V, Wolfenden J, Skovrérnek J, Yates R, et al. Flecainide versus digoxin for fetal supraventricular tachycardia: comparison of two drug treatment protocols. Heart Rhythm. 2016;13:1913–9.
15. Maeno Y, Hirose A, Kanbe T, Hori D. Fetal arrhythmia: prenatal diagnosis and perinatal management. J Obstet Gynecol Res. 2009;35:623–9.
16. Fouron J. Assessment of fetal arrhythmia by simultaneous Doppler recording of flow patterns in the ascending aorta and superior vena cava. Ultrasound Med Biol. 2003;29:585.
40. van der Heijden LB, Oudijk MA, Manten GT, ter Heide H, Pistorius L, Freund MW. Sotalol as first-line treatment for fetal tachycardia and neonatal follow-up. Ultrasound Obstet Gynecol. 2013;42:285–93.
41. Jaeggi ET, Canvalho JS, De Groot E, Api O, Clur SA, Rammeloo L, et al. Comparison of transplacental treatment of fetal supraventricular tachyarrhythmias with digoxin, flecainide, and sotalol: results of a nonrandomized multicenter study. Circulation. 2011;124:1747–54.
42. Kang SL, Howe D, Coleman M, Roman K, Gnapanragasam J. Foetal supraventricular tachycardia with hydrops fetalis: a role for direct intraperitoneal amiodarone. Cardiol Young. 2015;25:447–53.
43. Alsaeed T, Basker S, Fares M, Alahdab F, Czosek RJ, Murad MH, et al. First-line antiarrhythmic transplacental treatment for fetal tachyarrhythmia: a systematic review and meta-analysis. J Am Heart Assoc. 2017;6:e007164. https://doi.org/10.1161/JAHA.117.007164.
44. Hamela-Olkowska A, Szymkiewicz-Dangel J. Fetal tachyarrhythmia—current state of knowledge. Ginekol Pol. 2010;81:844–50.
45. Stirnemann J, Maltret A, Haydar A, Stos B, Bonnet D, Ville Y. Successful in utero transesophageal pacing for severe drug-resistant tachyarrhythmia. Am J Obstet Gynecol. 2018;219:521–5.
46. Jaeggi ET, Friedberg MK. Diagnosis and management of fetal bradyarrhythmias. Pacing Clin Electrophysiol. 2008;31(Suppl 1):S50–3.
47. Hajdu J, Pete B, Harmath A, Varadi V, Papp Z. Fetal arrhythmias: a clinical review. Donald Sch J Ultrasound Obstet Gynecol. 2009;3:25–37.
48. Christoffels VM, Moorman AF. Development of the cardiac conduction system: why are some regions of the heart more arrhythmogenic than others? Circ Arrhythm Electrophysiol. 2009;2:195–207.
49. Machado MV, Tynan MJ, Curry PV, Allan LD. Fetal complete heart block. Br Heart J. 1988;60:512–5.
50. Ayed K, Gorgi Y, Sfar I, Khrouf M. Congenital heart block associated with maternal anti SSA/SSB antibodies: a report of four cases. Pathol Biol. 2004;52:138–47.
51. Wladimiroff JW, McGhie JS, Hovestreydt-Snijder RP, Tasseron EW. M-mode and pulsed Doppler ultrasound assessment of severe fetal bradycardia. A case report. Br J Obstet Gynaecol. 1981;88:1246–38.
52. Miyoshi T, Maeno Y, Sago H, Inamura N, Yasukouchi S, Kawataki M, et al. Fetal bradyarrhythmia associated with congenital heart defects - nationwide survey in Japan. Circ J. 2015;79:854–61.
53. Carpenter RJ Jr, Strasburger JF, Carson A Jr, Smith RT, Deter RL, Engelhardt HT Jr. Fetal ventricular pacing for hydrops secondary to complete atrioventricular block. J Am Coll Cardiol. 1986;8:1434–6.
54. Walkinshaw SA, Welch CR, McCormack J, Walsh K. In utero pacing for fetal congenital heart block. Fetal Diagn Ther. 1994;9:183–5.
55. Chang HT, Li H. Short- and long-term clinical prognoses of various types of fetal arrhythmia. J Pract Obstet Gynecol. 2012;28:950–3.

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