# Successful Treatment of Fetal Atrial Flutter with Sotalol in a Non-hydrops Fetalis

## Nonhidropik Fetal Atrial Flatterli Fetusda Sotalol ile Tedavi

Serkan Kumbasar[1], Süleyman Salman[2], Ayşe Ender Yumru[3], Pelin Dervişoğlu[4], Erman Sever[1], Engin Aydın[5]

[1]Clinic of Obstetrics and Gynecology, Sakarya Training and Research Hospital, Sakarya, Turkey
[2]Clinic of Obstetrics and Gynecology, Gaziosmanpaşa Taksim Training and Research Hospital, İstanbul, Turkey
[3]Clinic of Obstetrics and Gynecology, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey
[4]Clinic of Pediatric Cardiology, Sakarya Training and Research Hospital, Sakarya, Turkey
[5]Clinic of Pediatric, Sakarya Training and Research Hospital, Sakarya, Turkey

**ABSTRACT**

We presented a patient in whom atrial flutter was detected during the third trimester and who was first treated with digoxin but could not tolerate it; success was then achieved on treating the patient with sotalol. A 26-years-old primigravida patient was referred to our clinic with a prediagnosis of fetal tachycardia at 32nd weeks of pregnancy. Atrial rate was detected as 533 beats/minute and ventricular rate was found as 266 beats/minute during fetal echocardiography (ECG); a diagnosis of fetal atrial flutter was made. Patient was first treated with digoxin; digoxin treatment was interrupted because of nausea, vomiting, hypotension, epigastric pain, and changes in ECG, which were associated with digoxin. Treatment was continued with sotalol in the patient who could not tolerate digoxin. It was observed that fetal heart rate decreased and returned to sinus rhythm following sotalol treatment. Pregnancy was continued until term in a healthy manner. A baby boy with a weight of 2800 g and having an Apgar score of 9 at first min and a score of 10 at fifth min was delivered by vaginal delivery. No structural abnormality was detected in the newborn during ECG. Fetal ECG is a reliable method for the diagnosis and follow-up of fetal tachyarrhythmias. Digoxin is the first-line agent in the treatment of fetal arrhythmia, but second-line agents are required in patients who cannot tolerate digoxin at therapeutic levels and present digoxin-related adverse effects. Sotalol is a good second-line antiarrhythmic agent that can be used safely. *(JAREM 2016; 6: 49-52)*

**Keywords:** Fetal atrial flutter, echocardiography, digoxin, sotalol

**ÖZ**

Üçüncü trimesterde atrial flatter tespit edilen, önce digoksin ile tedavi edilen, sonra digoksini tolere edemeyan hastada sotalol ile başarı ile tedavi ettiğimiz bir hastayı sunduk. Yirmi altı yaşında primigravid olan hasta, gebeliğinin 32. haftasında fetal taşikardi ön tanısıyla kliniğimize gönderildi. Yapılan fetal ekokardiografide (EKG) atrial hız 533 vuru/dak ve ventriküler hız 266 vuru/dak tespit edildi ve fetal atrial flatter tanısı konuldu. İlk olarak digoksin ile tedavi edilen hastada, digoksine bağlı kusma, mide bulantısı, hipotansiyon, epigastrik ağrı ve EKG'de değişiklikler olması üzerine digoksin tedavisi kesildi. Digoksini tolere edemeyen hastada sotalol ile tedaviye devam edildi. Sotalol tedavisinden sonra fetal kalp hızının azaldığı ve sinüs ritmine döndüğü görüldü. Gebelik terme kadar sağlıklı bir şekilde devam ettirildi ve vajinal doğumla 1.dakika Apgar skoru 9, 5. dakika Apgar skoru 10 olan bir adet 2800 gram erkek bebek doğurtuldu. Yenidoğanın ekokardiografisinde yapısal bir anomali tespit edilmedi. Fetal ekokardiografi fetal taşiaritmilerin tanısında ve takibinde güvenilir bir yöntemdir. Digoksin fetal aritmilerin tedavisinde ilk seçenek ajandır ancak terapötik düzeylerde digoksini tolere edemeyen ve digoksine baglı yan etkileri çıkan hastalarda ikinci seçenek ajanlara ihtiyaç duyulmaktadır. Sotalol güvenle kullanılabilecek iyi bir ikinci seçenek antiaritmik ajandır. *(JAREM 2016; 6: 49-52)*

**Anahtar Kelimeler:** Fetal atrial flatter, ekokardiografi, digoksin, sotalol

## INTRODUCTION

Atrial flutter (AF) is a tachyarrhythmia that is generally derived from an extra focus that holds the conduction system between atria. Fetal atrial flutter is seen less often than re-entrant SVTs but is observed at later weeks of pregnancy, and its control is more difficult (1). Structural cardiac abnormalities are more commonly observed than re-entrant tachycardia. Fetal atrial flutter patients are commonly accompanied by severe cardiac defects such as septal defect, hypoplastic left heart syndrome, cardiomyopathy, and Ebstein abnormality (2). Underlying cardiac pathology, atrial rate, and degree of atrioventricular block affect the tolerance power of the fetus to this condition (3). Atrial rate is approximately up to 300-600 beats/minute (min), and mostly there is a 1/2 or 1/3 atrioventricular block (4). The degree of the block determines the ventricular rate. The degree of ventricular rate affects fetal cardiac failure and, thus, the formation of hydrops. The probability of survival was reported as 91% in atrial flutter patients (5). Fetal death was reported in patients in whom ventricular rate was higher than 480 beats/min. In the presence of an atrioventricular block, the outcomes of the patients with a ventricular rate of 220–

**Address for Correspondence / Yazışma Adresi:** Dr. Süleyman Salman, E-mail: ssalman8640@yahoo.com

**Received Date / Geliş Tarihi:** 31.03.2015 **Accepted Date / Kabul Tarihi:** 14.04.2015

*DOI: 10.5152/jarem.2015.723*

240 beats/min were shown to be better (1). However, the failure risk of hemodynamics is continued (1). Examination of Doppler flow waves on M-mode imaging and echocardiography (ECG) are the most commonly used diagnostic methods. Fetal ECG also enables the diagnosis of an underlying congenital heart disease (6, 7). In general, proposed theory in tachyarrhythmia is the treatment of continuous tachycardia without the presence of hydrops. Treatment is similar to SVT treatment. There are no prospective studies showing the superiority of any antiarrhythmic agent over others in the treatment of fetal tachycardia. Digoxin has been commonly and safely used as the first-line drug for a long term. Flecainide, sotalol, and amiodaron are commonly used second-line antiarrhythmics (8).

## CASE PRESENTATION

A 26-years-old primigravida patient was referred to our clinic from an epicenter with a prediagnosis of fetal tachycardia at 32nd weeks of her pregnancy based on her last menstruation date. It was learnt from her history that her dual-screening fetal abnormality scan and 50-g oral glucose tolerance test were normal and no problem was found during pregnancy follow-ups. There were no features, such as previous accidents, operation, drug, and cigarette/alcohol use, in the clinical data and family history of the patient. Blood pressure of the patient was measured as 120/80 mmHg, and it was detected that vital and systemic signs were normal.

On ultrasonography, a single live and tachycardic fetus was present that is compliant with a 32nd week pregnancy. There was no sign of fetal hydrops. On performing fetal ECG (M mode), it was determined that there was an atrial rate of 533 pulse/min, ventricular rate of 266 pulse/min, and probably 2:1 atrioventricular block (Video 1. See corresponding video/movie images at www.jarem.org). The diagnosis of fetal atrial flutter was made because of the observation of regular 2:1 AV transmission. No structural abnormality was detected in the heart (Figure 1, 2).

Intravenous (IV) maternal digoxin was loaded at a dose of 0.50 mg in 24 h at 8-h intervals (1500 µg). On the second day, maintenance treatment was started with 0.5-mg oral digoxin twice a day. She was followed up by performing ECG during treatment. On the second day of treatment, patient presented some complaints such as hypotension, bradycardia, epigastric pain, nausea, and vomiting. Type 1 AV block was found in the patient on ECG. When toxicity signs were found in our case, digoxin level in the blood was 1.25 ng/mL, and it was normal. Because the patient could not tolerate digoxin and fetal heart rate did not return to sinus rhythm, a second alternative agent was required. Digoxin treatment was interrupted. After QTc interval of the mother was evaluated as normal on ECG, with the recommendation of pediatric cardiology, treatment was continued with oral sotalol (160 mg/day, 2 doses). Return to sinus rhythm with 1:1 transmission was observed within the first 24 h following treatment. Heart rate was determined as 132 beats/min at fetal sinus rhythm. Congestive heart failure was not detected on performing serial echocardiography during treatment.

Following 6 weeks after the onset of treatment, uterine contractions started on the 38th week and three days after pregnancy. The patient delivered a baby boy weighing 2800 g and having 1th and 5th Apgar scores of 7 and 9, respectively, at the eighth

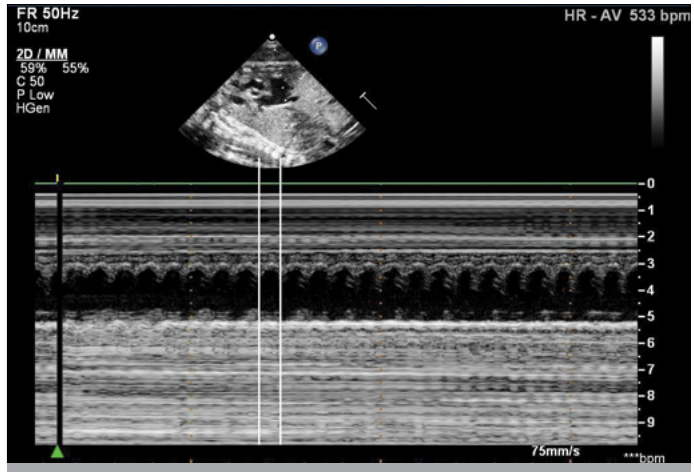


**Figure 1.** Fetal atrial flutter before treatment with atrial rates of 533 bpm and ventricular rates of 266 bpm (M-mode Doppler of the fetal heart)

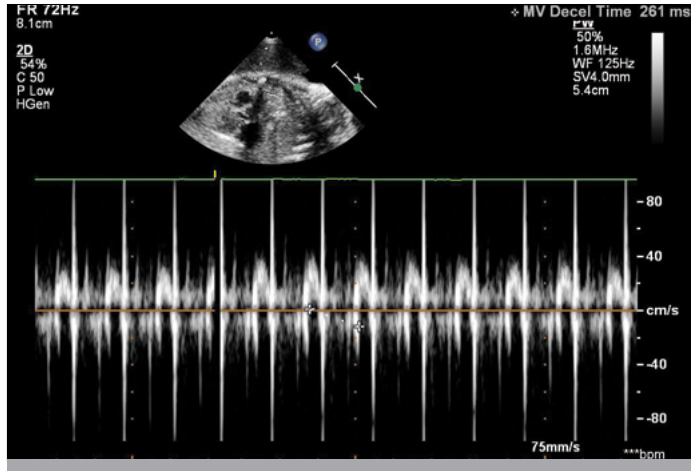


**Figure 2.** Fetal heart rate (MV): 261 on fetal Doppler echocardiography

hour following spontaneous labor through vaginal route. Physical examination, complete blood count, biochemical tests, and thyroid function tests of the newborn were found to be normal. Electrocardiogram showed normal sinus rhythm following delivery; echocardiographic normal cardiac anatomy was observed. Again, normal sinus rhythm was observed during serial echocardiography that was performed for arrhythmia during the neonatal period, and antiarrhythmic treatment was not required.

## DISCUSSION

Fetal tachyarrhythmia can occur in up to 0.4%–0.6% of all pregnancies and may increase fetal morbidity and mortality because of nonimmune hydrops fetalis. Fetal atrial flutter is the second common tachyarrhythmia and is responsible for up to 25% of fetal tachyarrhythmias. Fetal atrial flutter electrophysiological mechanism is an intra-atrial macro re-entry mechanism similar to that in adult-type atrial flutter (9). Fetal atrial heart rate is between 300 and 600 beats/min; a cardiac dysrhythmia that is generally characterized by atrioventricular transmission with 2:1 block is present. Mortality rate is up to 8% in fetal atrial flutter and approximately up to 30% in hydropic fetus (10). In our case, heart (ventricle) rate was 266 beats/min and atrial rate was 533 beats/min, andit was within the heart rate interval that is described for

fetal atrial flutter. In M-mode and PW Doppler echocardiograms that were taken for showing atrium and ventricle contractions simultaneously, atrioventricular transmission was detected as 2:1. Diagnosis of fetal atrial flutter was made for the patient.

Antiarrhythmic drugs that can pass through the placenta are recommended for patients with fetal atrial flutter. First choice of antiarrhythmic treatment is oral or IV administration of digoxin to the mother. It is recommended to start digoxin treatment in three high (1–1.5 mg/day) doses as oral or IV loading and continue with two doses of 0.5 mg/day on the next day (2, 11).

Digoxin exerts its effect by extending the refractory period of the atrioventricular node. Its therapeutic effect depends on its negative chronotropic and positive inotrophic effect. Digoxin response is not good in fetuses with poor ventricular function. Fetal blood digoxin level is lower than maternal blood digoxin level during maternal digoxin treatment; it is based on the scarcity of the placental passage. Treatment should be started with a maternal high dose of digoxin to achieve sufficient fetal blood digoxin level. However, this may cause toxicity signs in the mother such as gastrointestinal system, SSS, cardiac arrhythmia [early pulse (beat), A-V block] (2, 12). When toxicity signs occurred in our case, blood digoxin level was 1.25 ng/mL, and it was at a normal level. Krapp et al. (10) have achieved 55% success with digoxin as monotherapy during the treatment of nonhydropic fetal atrial flutter patients. In the retrospective analysis of 127 fetal tachyarrhythmia patients that was performed by Simpson and Sharland (13), SVT was found to be present in 105 patients and AF in 22 patients. Fifty-two patients were hydropic and 75 were nonhydropic. Although 62% of the nonhydropic fetuses returned to the normal sinus rhythm with digoxin monotherapy, this rate remained at 20% in hydropic fetus. Oudijk et al. (14) recommended the use of guidelines that they developed as a result of their clinical experiences and named it the Utrecht protocol. Antiarrhythmic treatment of atrial flutter is involved in the first protocol of Utrecht, nonhydropic SVT in the second protocol, and hydropic SVT in the third protocol. According to the first protocol, two doses of sotalol treatment including 80 mg/day on the first day is administered for 3 days in fetal atrial flutter patients regardless of the patients being hydropic or nonhydropic. Then, if there is no return to sinus rhythm or no decrease in ventricular rate, sotalol is administered three times a day for 3 days, with a maximum dose of 160 mg. If there is no return to sinus rhythm again, 0.25 mg digoxin is added to the existing treatment including three times a day. Drug is administered in multiple doses for 3 days. If there is no return again, digoxin dose is increased up to 0.5 mg (8). In our clinic, loading dose is initiated as high dose (1–1.5 mg/day) IV digoxin and continued with a low dose different from the Utrecht protocol during the follow-up of fetal atrial flutter patients. If sinus rhythm is not observed on the third day, sotalol is added to treatment as a second antiarrhyhtmic drug.

Sotalol is a type 3, non-selective, beta blocker-type antiarrhythmic drug that is better compared to digoxin, which passes through the placenta (15). In addition, it is reported that sotalol can be used safely as the first choice in hydropic patients (16). However, it may sometimes cause fatigue, loss of appetite, headache, palpitation, breast pain, vomiting, bradycardia, proarrhythmic effect, and sudden deaths of the fetus in the mother. Oudijk et al. (15) have detected intrauterine deaths in 3 out of 4 hydropic fetuses with supraventricular tachycardia after digoxin and sotalol treatment. They proposed that sotalol has initiated proarrhythmic events in these fetuses. They emphasized that this aspect of sotalol should be considered while it is used in hydropic fetuses. Studies have shown that an immature heart has a higher potential to extend QTc interval compared than a mature heart. This leads to severe arrhythmia risk and death in the fetus (16). Arrhythmia history should be questioned in the mother before sotalol use because of proarrhythmic effect and treatment should be started after the evaluation of QTc interval in ECG. Because of the possibility of close monitoring of the mother's heart rate during treatment, bed treatment is generally recommended. In our case, the fetus that was diagnosed with fetal atrial flutter by fetal ECG was successfully treated. Digoxin is the first choice in fetal AF treatment, but it was found that sotalol is a second and safe treatment option in patients who do not respond to sotalol.

## CONCLUSION

Before starting intrauterine antiarrhythmic treatment the following steps should be performed: an exact diagnosis of transmission abnormality should be made, the presence of a structural cardiac abnormality should be investigated, choice of delivery type or intrauterine treatment should be determined according to gestational age or fetal lung maturation among pregnancies close to term, benefits and harms of intrauterine treatment should be well determined, mother and fetus should be monitored during treatment, and consent form should be obtained from the family for the release of all these information. A close cooperation should be established between pediatric cardiologist and obstetrician for an optimal result. Because of these reasons, this type of treatment is possible in tertiary centers that involve all necessary equipments and in which all abovementioned precautions can be taken. Fetal antiarrhythmic treatment that is one of the first and the most satisfactory areas of fetal treatment will provide optimum results only in this manner.

**Video 1.** M-mode Doppler of the fetal heart at the level of the atrioventricular (AV) node. The atrial rate is 533 bpm.

**Informed Consent:** Informed consent was not obtained due to the retrospective nature of the study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept - S.K., S.S., A.E.Y.; Design - S.K., S.S.; Supervision - A.E.Y., P.D., E.S.; Resource - E.A., E.S., S.S.; Materials - S.K., S.S.; Data Collection and/or Processing - P.D., E.S., E.A.; Analysis and/or Interpretation - A.E.Y., S.S.; Literature Review - E.A., E.S.; Writer - S.K., P.D.; Critical Review - A.E.Y., S.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Hasta Onamı:** Çalışmanın retrospektif tasarımından dolayı hasta onamı alınmamıştır.

**Hakem değerlendirmesi:** Dış bağımsız.

**Yazar Katkıları:** Fikir - S.K., S.S., A.E.Y.; Tasarım - S.K., S.S.; Denetleme - A.E.Y., P.D., E.S.; Kaynaklar - E.A., E.S., S.S.; Malzemeler - S.K., S.S.;

Veri toplanması ve/veya işlemesi - P.D., E.S., E.A.; Analiz ve/veya yorum - A.E.Y., S.S.; Literatür taraması - E.A., E.S.; Yazıyı yazan - S.K., P.D.; Eleştirel İnceleme - A.E.Y., S.S.

**Çıkar Çatışması:** Yazarlar çıkar çatışması bildirmemişlerdir.

**Finansal Destek:** Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

## REFERENCES

1. Shenker L. Fetal cardiac arrhytmias. Obstet Gynecol Surv 1979; 34: 561-72. [CrossRef]
2. Strasburger JF, Duffy E, Gidding SS. Abnormal Doppler flow patterns in atrial tachycardia in infants. Am J Cardiol 1997; 80: 27-30. [CrossRef]
3. Copel JA, Friedman AH, Kleinman CS. Manegement of fetal cardiac arrhythmias. Obstet Gynecol Clin North Am 1997; 24: 201-11. [CrossRef]
4 Cotton JL. Identification of fetal atrial flutter by Doppler tissue imaging. Circulation 2001; 104: 1206-7. [CrossRef]
5. Vintzileos AM, Campbell WA, Soberman SM, Nochimson DJ. Fetal atrial flutter and X-linked dominant vitamin D-resistant rickets. Obstet Gynecol 1985; 65: 39-44.
6. Carvalho JS, O'Sullivan C, Shinebourne EA, Henein MY. Right and leftventricular long-axis function in the fetus using angular M-Mode. Ultrasound Obstet Gynecol 2001; 18: 619-22. [CrossRef]
7. De Groote KEC, Iasci A, Carvalho JS. Offline free angular M-mode a useful diagnostic tool in fetal arrhytmias. Ultrasound Obstet Gynecol 2005; 26: 327. [CrossRef]
8. Ebenroth ES, Cordes TM, Darragh RK. Second-line treatment of fetal supraventricular tachycardia using flecainide acetate. Pediatr Cardiol 2001; 22: 483-7. [CrossRef]
9. Jaeggi ET, Nii M. Fetal brady-and tachyarrhythmias: new and accepted diagnostic and treatment methods. Semin Fetal Neonatal Med 2005; 10: 504-14. [CrossRef]
10. Krapp M, Kohl T, Simpson JM, Sharland GK, Katalinic A, Gembruch U. Review of diagnosis, treatment, and outcome of fetal atrial flutter compared with supraventricular tachycardia. Heart 2003; 89: 913-7. [CrossRef]
11. Cuneo BF, Strasburger JF. Management strategy for fetal tachycardia. Obstet Gynecol 2000; 96: 575-81. [CrossRef]
12 Rana YS, Sodhi B, Kochar SP, Arora D. Successful Digoxin Therapy of Fetal Supraventricular Tachycardia. South Asian Federation of Obstetrics and Gynecology 2009; 1: 44-6. [CrossRef]
13. Simpson JM, Sharland GK. Fetal tachycardias: management and outcome of 127 consecutive cases. Heart 1998; 79: 576-81. [CrossRef]
14. Oudijk MA, Visser GH, Meijboom EJ. Fetal tachyarrhythmia - Part II: treatment. Indian Pacing Electrophysiol J 2004; 4: 185-94.
15. Oudjik MA, Ruskamp JM, Ververs FF, Ambachtsheer EB, Stoutenbeek P, Visser GH, et al. Treatment of fetal tachycardia with sotalol: transplacental pharmacokinetics and pharmacodynamics. J Am Coll Cardiol 2003; 42: 765-70. [CrossRef]
16. 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. [CrossRef]