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DIGOXIN AND AMIODARON
IN FETAL SUSTAINED SUPRAVENTRICULAR TACHYCARDIA AND NONIMMUNE HYDROPS

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DIGOXIN I AMIODARON
KOD TRAJNE FETALNE SUPRAVENTRIKULARNE TAHIKARDIJE I NEIMUNOLOŠKOG FETALNOG HIDROPSA

Case report

Key words: fetus, tachycardia supraventricular, fetal hydrops, digoxin, amiodarone

SUMMARY. Supraventricular tachycardia is the most common and clinically significant form of sustained fetal tachyarhythmia in pregnancy; depending on duration and high rate variability heart failure and nonimmune hydrops may develop which are associated with a high incidence of perinatal mortality. Doppler/echo diagnosis is usually accidental during second and third trimester of pregnancy. Therapeutic goals are cardioconversion to sinus rhythm and recovery of heart failure. We present a case of fetal supraventricular tachycardia diagnosed at 29 weeks of gestation with nonimmune hydrops. Treatment with digoxin and amiodarone was successful. The heart rate restored to sinus rhythm and nonimmune hydrops resolved within three weeks of treatment. Therapy with two drugs that act synergistically may be more efficient than monotherapy in blocking likely atrio-ventricular reentry mechanism by accessory pathway in sustained supraventricular tachycardia, thus allowing resolution of hydrops with favorable management outcome.

Introduction

Supraventricular tachycardia is the most common and clinically significant form of sustained fetal tachyarhythmia in pregnancy. Depending on duration and high rate variability, heart failure and nonimmune hydrops may develop, that are associated with a high incidence of perinatal mortality. Therapeutic goals are cardioconversion to sinus rhythm and recovery of heart failure, most frequently by digoxin and sotalol.

Case report

A 28 year old primigravida at 29 weeks of gestation (with ultrasound analysis the pregnancy was 2 weeks younger) was referred to our antenatal clinic because of fetal tachycardia detected during her routine antenatal scan. She was transferred from another clinical hospital where she was treated with sotalol on which she developed allergic reaction. Her antenatal period was uneventful till 26 weeks when Doppler/M-echocardiography showed fetal supraventricular tachycardia (SVT) with minimal pericardial effusion. There was no history of fever or thyrotoxicosis. In family history, her mother has angina pectoris and arterial hypertension. The patient was admitted to our hospital for administration of antiarrhythmic therapy. At admission patient’s height was 168 cms and weight 73(+9) kg. Blood pressure was 110/60 mmHg. ECG: sinus rhythm with 76 bpm. Fetal echocardiography showed normal heart position in left hemithorax with higher cardiothoracic index of 0.42 (normal 0.25–0.35), enlarged heart silhouette underlying both dilated atria with normal ventricles and valvular morphology, normal atrioventricular concordance and relations to surrounding internal organs. Pulmonary veins and vv.cavae were of normal anatomy and inflow. Patent foramen ovale with r-l shunt and ductus Botalli with communications between pulmonary artery and aorta corresponded with the mildly decreased same pressures in both pulmonal artery and aorta of 0.4m/s (normal 0.6–07m/s). Doppler/M-mode echocardiography demonstrated paroxysms of SVT in the range of 237–260 beats per minute intermittently falling down to
There are three different types of fetal arrhythmias that can be seen in pregnancy such as *fetal tachycardia* with baseline fetal heart rate over 160/min (SVT, atrial flutter or fibrillation, ventricular tachycardia), *fetal bradycardia* with baseline heart rate less than 110/min., and the most common, *premature beats* as atrial and ventricular extrasystoles. An initiating premature beat caused by abnormal automaticity can precipitate an episode of SVT sustained by AV reentry mechanism and accessory pathway with AV conduction 1:1 up to 220 to 260 bpm (accounts for 93% of total SVT with 1:1 AV conduction).5,4 It is the most commonly encountered fetal cardiac arrhythmia in pregnancy that may be associated with adverse perinatal outcome if untreated.6 Fetal SVT can be presented like non sustained (tachycardia with intermittent sinus rhythm) and sustained (prolonged uninterrupted tachycardia of >12h), which is hemodynamically more dangerous for fetal life.4 In this case, sustained SVT with 1:1 atrioventricular conduction was diagnosed prenatally by the presence of 1:1 atrioventricular contraction sequence during tachycardia, abrupt onset and terminations with minimal heart rate variability. Our patient was without favorite risk factors for development of arrhythmia like smoking, caffeine and illicit drugs. Fetal Doppler/M-echocardiography showed structurally normal heart with only mildly enlarged cardiac silhouette and both atra.

In addition, there are some newer methods used today for the diagnosis of SVT such as magnetocardiogram (MCG) and Doppler myocardial deformation analysis.5,7

The prognosis and treatment of this kind of arrhythmia depend on the presence or absence of fetal hemodynamic compromise, gestational age of fetus at which the tachycardia occurs, the ventricular rate, the percentage of the time that the tachycardia is present and the site of origin of the tachycardia.5,8 Spontaneous resolution of SVT has been reported in some cases to occur in utero or later, during neonatal period.9,10 In fetus with a normal anatomical survey, the management depends upon the gestational age and the presence or absence of hydrops. In our case we demonstrated nonimmune hydrops fetalis secondary to sustained SVT that appeared 2 weeks after its initiation to develop heart failure from multiple episodes of tachycardia and recurring at relatively »slow heart rates.5,11

The most important goal of treatment is the prevention or resolution of hemodynamic compromise. Today, numerous antiarrhythmic drugs have been prescribed for the treatment of fetal tachycardia as digoxin, sotalol, amiodarone and flecainide. We began the treatment transplacentally with digoxin which is the drug of first choice for the treatment of SVT and two weeks later in the sense of developing hydrops phenomenon, we included in the treatment additionally oral amiodarone, preserving myocardial contractility, because the treatment and prognosis of SVT depends not only of suppression rate of SVT but recovery from fetal congestive
heart failure and hydrops as well.12 Digoxin is cardiac glycoside and for a long time prominent drug in the therapy of congestive heart failure. It has positive inotropic and negative chronotropic properties that increase cardiac output and decrease heart rate. With these characteristics, digoxin prolongs the refractoriness of the AV node and terminates the circular movements within re-entrant circuit so that aberrant wave of excitation reaches depolarized tissue.3 Digoxin is effective and nontoxic in relatively narrow serum range (0.8 – 2.0 ng/mL), so the optimum therapy for pregnant women or fetus requires an accurate measurement of serum digoxin levels.13 During pregnancy increased digoxin dosage may be necessary because of enhanced renal clearance and expanded blood volume. Reported fetal : maternal (F:M) plasma concentration ratios vary from 0.4 to 0.9.14,15 However, in case of fetal hydrops, this ratio is reduced because the placental transfer of the digoxin is limited. In addition, conversion to sinus rhythm with digoxin is achieved in 50% of nonhydropic fetuses and only in 15–25% in hydropic fetuses.3,16,17 Hence, medication with good placental transfer, such as amiodarone, should be used from the beginning of fetal treatment for hydrops. Digoxin has a few maternal side effects which are related to overdosing like nausea, vomiting and headache.7 There also can be found maternal cardiac adverse effects such as ventricular extrasystoles or heart block that was seen in our case.

Because of low conversion rate with digoxin, second line drugs are frequently required to achieve sinus rhythm as it was in our case with inclusion of amiodarone in therapy.

Amiodarone prolongs the repolarization of the myocardium. A large study by Strasburger et al.16 was published in which amiodarone had a 93% successful rate of conversion as second line therapy in fetal SVT tachycardia complicated with hydrops. Treatment with amiodarone has been associated with transient biochemical neonate hypothyroidism, maternal photosensitive skin rash and thrombocytopenia. In addition, amiodarone is a suitable second line treatment in hydropic SVT and because of insignificant possibility of proarrhythmic events in distinction of flecainide and sotalol. Amiodarone administration has been found to increase the steady-state digoxin concentration, and maintenance doses of digoxin should be decreased by ≥50%.19

There is also a question whether to treat prenatally or postnatally. The decision mainly depends on gestational age and in early gestational weeks prenatal treatment is the reasonable management. However, if hydrops does not resolve in 2 weeks, postnatally treatment is recommended.2 Transplacental therapy is proper mode of therapy in nonhydropic fetuses and first choice in hydropic fetuses. But, when conversion to sinus rhythm is not achieved, direct fetal therapy should be recommended.

After successful fetal rhythm conversion, dosage is maintained till delivery. If the heart rate is controlled, vaginal delivery is recommended and newborns are treated for at least 6–12 months.9 In the case of cesarean section, the maturity of fetal lungs must be verified to avoid neonatal adverse affects. One third or more neonates postnatally will be free of further SVT probably due to involution of the abnormal pathway.

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U ČASOPISU »GYNAECOLOGIA ET PERINATOLOGIA« OBJAVLJENE PREPORUKE (SMJERNICE) HRVATSKOG DRUŠTVA ZA PERINATALNU MEDICINU HLZ-a

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2) Primjena prostaglandina u novorođenčadi sa srčanom greškom (str. 182/2008).
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5) Antenatalni probir i dijagnostika kromosomopatija (str. 125/2010).
7) Trudnoća/porod nakon ranijega carskog reza (str. 123/2010).
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