

Response to Letter Regarding Article, “Comparison of Transplacental Treatment of Fetal Supraventricular Tachyarrhythmias With Digoxin, Flecainide, and Sotalol: Results of a Nonrandomized Multicenter Study”

We thank Drs Uzun, Sinha, and Beattie for taking interest in our study. We fully agree that sustained fetal supraventricular tachycardia and atrial flutter (AF) is a life-threatening situation, and maternal drug therapy is therefore offered in the majority of these cases.

In 1980, the first report appeared of a hydropic fetus with incessant supraventricular tachycardia that was successfully treated with transplacental digoxin therapy.¹ Since then numerous retrospective studies in fetal supraventricular arrhythmia (SVA) have looked at different maternal drug therapies showing variable results.²

Our study indicates that digoxin and flecainide controls fetal SVA more effectively than sotalol, although we were unable to find differences in survival among the 3 drug cohorts. Despite relatively low conversion rates, the overall arrhythmia-related mortality was only 5%.³

The authors recommend the combination of digoxin and flecainide as first-line therapy for fetal supraventricular tachycardia and AF, even in the absence of hydrops. They base this on their excellent results in 29 SVA cases that were treated in this way with fast conversion rates and only 1 treatment failure.⁴ Their positive findings are in line with the favorable results of digoxin and flecainide as single or combination therapies as reported in our study.

The authors also point at the risks of using digoxin and flecainide as single agents for fetal SVA. They use the well-known argument that digoxin can facilitate rapid antegrade conduction over the accessory pathway during atrial fibrillation or AF. We disagree with this interpretation, because digoxin has been used safely in many fetuses for many decades, and the risk of atrial fibrillation in Wolf-Parkinson-White syndrome is extremely rare in the fetus or newborn.² Furthermore, at birth, ventricular preexcitation is present in only a minority of fetal supraventricular tachycardia cases, and it is an infrequent finding in fetal AF.⁵

Regarding the use of flecainide as monotherapy for fetal AF, we agree on the potential risk of rapid 1:1 atrioventricular conduction due to slowing of the AF rate, which may be prevented by adding digoxin. Although it is rare, 1:1 atrioventricular conduction can occur in fetal AF, as was shown in 2 of our cases before treatment. Thus far, this complication has never been reported during maternal flecainide treatment, which may be explained by the usually high atrial rates in fetal AF.

We share the opinion of Dr Uzun and colleagues that flecainide and digoxin in combination may offer theoretical advantages regarding rhythm control and improvement of hemodynamics in the hydropic fetus.² Having said this, there is no evidence from randomized trials to support the superiority of this 2-drug combination over single agents or other combinations such as digoxin and sotalol. This emphasizes the need for a randomized trial, including arms with combination treatment in hydropic fetuses. The feasibility of such a trial is currently being investigated, and hopefully we can move

forward involving as many fetal medicine centers as possible to test the different therapies in terms of efficacy and safety to develop evidence-based guidelines for the optimal management of fetal SVA.

Disclosures

None.

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