CEOG Clinical and Experimental Obstetrics & Gynecology

Letter to the Editor

Maternal beta$_2$-sympathomimetic administration for fetal atrioventricular block: some additions and concerns

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Dear Editor,

Sainz *et al.* [1] showed that in a fetal isolated complete atrioventricular block (AVB), maternal administration of beta$_2$-sympathomimetic (terbutaline) increased the fetal heart rate (56→68-70 bpm) and ameliorated fetal hydrops. Starting sympathomimetics at 28 weeks, with cesarean performed at 35 weeks, pregnancy was prolonged by seven weeks after sympathomimetic administration. I have an addition and a concern.

My experience shows similarities to Sainz *et al.*'s case. Long-term tocolysis with ritodrine hydrochloride (beta$_2$-sympathomimetic) has long been employed in Japan, and, thus, Japanese obstetricians are well accustomed to ritodrine use. Ritodrine was administered for three cases with isolated complete AVB: heart rate increased from 57→72 [2], 49→57 [3], and 53-57→60-65 bpm [4], respectively. Pregnancy continued after ritodrine administration for ten [2], two [3], and four [4] weeks, respectively. In one case, hydrops ameliorated after ritodrine administration [3], similar to Sainz *et al.*'s case, and in another, AVB resolved, with normal AV conduction eventually resuming [4]. The heart rate increased by 8 bpm (median) (before *vs*. just after ritodrine administration), similar to Sainz *et al.*'s case. Our three patients survived without sequelae. Hutter *et al.* [5] also showed that beta$_2$-sympathomimetics increased the heart rate by 5-10 bpm. Sympathomimetics increased the fetal heart rate and pregnancy was continued: this was reconfirmed.

However, whether maternal sympathomimetic administration promotes a better neonatal outcome has yet to be determined. After publishing our experience, an observational multi-center-based study on a relatively large number was published [6]. To isolated fetal complete AVB (with or without maternal autoantibodies), a sympathomimetic (ritodrine) was and was not administered in 33 and 23 cases, respectively. Comparison between the two showed that although ritodrine administration increased the fetal heart rate, it did not significantly increase the fetal/neonatal survival rate.

Hutter *et al.* [5] stated in their comprehensive review, "transplacental treatment with steroids and beta-stimulants may prevent or reduce myocardial inflammation and increase ventricular rate and likely has significantly contributed to the improved outcome of fetuses with major cardiac neonatal lupus erythematosus (AVB)". Sainz *et al.*'s statement [1] is in line with this, "in case of complete AVB due to autoimmunity with poor prognosis should be treated with positive inotropic drugs". I also considered this in previous reports [3, 4]. However, this statement of Sainz *et al.* should be softened. The "55 bpm rule" is widely known [1, 5]; however, whether < 55 bpm jeopardizes fetal wellbeing has yet to be determined [6]. Furthermore, in Sainz *et al.*'s case, close relatives of the baby's father had long QT syndrome, and, thus, this fetus may also have had a long QTc interval. Beta-sympathomimetics may trigger life-threatening ventricular tachycardia: their use should be avoided in a fetus with a possible long QTc interval [6].

Simply, <55 bpm may not determine the sympathomimetic requirement. Since sympathomimetic administration is not without serious adverse events to both mothers and fetuses [5, 6], a future study should be conducted to identify who may or may not benefit from sympathomimetic administration.

References

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Revised manuscript accepted for publication June 19, 2017

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLV, n. 1, 2018
doi: 10.12891/ceog4221.2018

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Reply by Sainz *et al.*

We are of the same opinion as Dr. Matsubara. Simply <55 bpm may not determine the sympathomimetic treatment in cases of complete AVB. We also think that an observational multi-center-based study should be conducted where the maternal sympathomimetic administration is evaluated in cases of complete AVB and again if it improves the neonatal outcome.

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