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Maternal effects of transplacental flecainide for treatment of fetal tachyarrhythmia

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Background:
Transplacental flecainide is an established treatment of fetal tachyarrhythmias. Its use has been cautioned due to the potential for maternal pro-arrhythmic effects. Previous work suggests that prolongation of the QRS duration (QRSd) >50%, PR interval by >30% and QTc by >15% is an indication of toxic flecainide levels. In pregnant mothers relatively high doses are administered (100mg t.i.d) necessitating monitoring.

Methods:
Retrospective review of fetal tachyarrhythmias treated with flecainide from January 1997 to December 2008. Side effects, flecainide levels and ECG data were collected. Automated PR interval and QRSd were manually confirmed. Rate corrected QT interval (QTc) was calculated.

Results:
31 cases were identified with persistent SVT (20), intermittent SVT (7) and atrial flutter (4). Median gestation at initiation 32weeks (range: 21-38).
Median trough flecainide level was 410mcg/l (250-840) within 5days of initiation of treatment (laboratory therapeutic range 200-700mcg/l). An ECG was performed at the same clinic visit as blood levels. ECG measurements and percentage change from baseline are expressed as median(range) in *table 1*. In 9 cases PR interval increased >200ms and in 10 cases QTc increased >450ms reflecting prolongation of QRSd.

Table 1: ECG measurements and percentage change from baseline with flecainide

	PR interval (msec)	% change in PR interval	QRS duration (msec)	% change in QRS duration	Mean QTc (msec)	% change in mean QTc
Pre-treatment	136(100-164)		80(74-104)		415(374-459)	
Early (2-7days) with therapeutic flecainide level	160 (122-200) P < 0.0001	17 (-3-50)	92 (80-116) P = 0.0003	10% (-2 to 30%)	429 (385-505) P= 0.03	4% (-3 to 19%)
At peak flecainide levels	163 (116-218) P < 0.0001	24% (0-50)	96 (72-112) P = 0.0003	13% (-4 to 30%)	429 (338-505) P = 0.03	4% (-18 to 27%)

A 30% increase in PR interval from baseline gave a positive predictive value (PPV) for supra-therapeutic flecainide level of 45% and a negative predictive value (NPV) of 91%. QTc increase >15%, PPV=44%, NPV=85%. QRSd did not increase >50%.

There was no significant correlation between flecainide levels and PR or QRSd (r^2=0.118, 0.105, respectively).

7(23%) mothers had side effects including: nausea and vomiting (n=2), visual disturbance (n=1), palpitations (n=1), malaise (n=2), dizziness (n=3), shortness of breath (n=1), anxiety (n=1) and headaches (n=1). Flecainide levels were supratherapeutic in 2/7 symptomatic patients necessitating dose reduction. Prolongation of the QTc coupled with side effects led to cessation of therapy in 1 patient and reduced dose in 3. There was no maternal mortality or long-term morbidity.

Conclusion:
There is significant prolongation of the PR interval, QRSd and QTc with flecainide therapy. However, there does not appear to be any correlation between maternal flecainide levels and ECG intervals. The predictive value of ECG changes to predict supratherapeutic levels of flecainide appears suboptimal.