ABSTRACT

Heart rate changes mediate the embryotoxic effect of antiarrhythmic drugs in the chick embryo

A significant increase in cardiovascular medication use during pregnancy has occurred in recent years but only limited evidence on its safety profile is available. We hypothesized that drug-induced bradycardia is the leading mechanism of developmental toxicity. We tested metoprolol, carvedilol, or ivabradine for embryotoxicity and their acute effect on chick embryonic model. We used video microscopy and ultrasound biomicroscopy. Significant dose-dependent mortality was achieved in embryos injected with carvedilol and ivabradine. In ED4 embryos, metoprolol, carvedilol and ivabradine reduced the heart rate by 33%, 27%, and 55%, respectively, compared to controls (6%). In ED8 embryos this effect was more pronounced with a heart rate reduction by 71%, 54%, 53%, respectively (controls 36%). Cardiac output decreased in all tested groups but only proved significant in the metoprolol group in ED8 embryos. The number of β-adrenergic receptors showed a downward tendency during embryonic development but a negative chronotropic effect of tested drugs was increasingly pronounced with embryonic maturity. This effect was associated with reduced cardiac output in chick embryos, probably leading to premature death. Metoprolol in usual doses appears to be relatively safe in pregnancy whereas carvedilol and ivabradine have a potentially adverse effect on the foetus.

Adenylyl cyclase signalling in the developing chick heart: The deranging effect of antiarrhythmic drugs

We analysed the number of key components of myocardial adenylyl cyclase in the developing chick embryo and assessed the impact of metoprolol and carvedilol on this system. Application of these drugs at embryonic day (ED) 8 significantly downregulated (40 %) expression of adenylyl cyclase 5 level, the amount of Gsα protein and the activity of adenylyl cyclase stimulated by forskolin. Interestingly, when administered at ED4, these drugs did not produce such as profound changes except for markedly increased expression of Giα protein. These data indicate that β-blocking agents can strongly derange adenylyl cyclase signalling during the early chick embryonic heart development.

Five years two center retrospective analysis of patients with toxic digoxin serum concentration

Digoxin is an old cardiovascular drug used for treatment of advanced chronic heart failure. We aimed to determine main characteristics of patients with toxic digoxin serum concentration with respect to drug interactions and mortality. Databases of two teaching hospitals were retrospectively reviewed from 2001 till 2005 and 222 (0.2% of all admissions) patients with serum digoxin level ≥3.0 nmol/ml were identified. The average age was 78 years, 41% males, 14% had creatinine clearance ≥60ml/min, and 64% of patients were prescribed at least one medication with known digoxin interaction. Hospital mortality was 8%. Statistically significant predictors of mortality were low creatinine clearance (p=0.01) and intravenous administration of digoxin (p=0.02). Borderline association was between mortality and low ejection fraction of the left ventricle (p=0.05) and with low body weight (p=0.08). Concomitant use of ACEI/ARB was protective (p=0.01). Toxic serum digoxin concentration is uncommon finding in modern medicine with relatively high mortality. Typical patient is an elderly with low body weight, renal insufficiency and polypragmasia. Concomitant therapy with ACEI/ARBs and beta-blocker appears to have a protective effect.

Ibutilide-Induced Cardioversion of Atrial Fibrillation During Pregnancy

We present two cases of successful cardioversion of atrial fibrillation using intravenous ibutilide during pregnancy. One patient had atrial fibrillation, complicating the Wolff-Parkinson-White syndrome and the other had a history of nonobstructive hypertrophic cardiomyopathy. No adverse maternal or fetal effects were observed during or after pregnancy in either case.