

Influence of gestational Diabetes *mellitus* on the enantioselective transplacental distribution of metoprolol in hypertensive parturients

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Introduction: Metoprolol, a drug used to treat hypertension during pregnancy, is available as a racemic mixture of its enantiomers S-(-) and R-(+)-metoprolol, although S-(-)-metoprolol is considered the eutomer responsible for β_1 adrenergic receptor blockade. **Objective:** This study evaluates the influence of gestational Diabetes *mellitus* on placental distribution of the stereoisomers of metoprolol and its metabolites α -hydroxymetoprolol and O-desmethylnmetoprolol in parturients after administration of a single oral dose of metoprolol tartrate. **Methods:** The hypertensive parturients (n=35) were distributed in the control group (n=24) or in the gestational Diabetes *mellitus* group (n =11). The hypertensive parturients were treated with a single oral dose of 100 mg racemic metoprolol tartrate 1-11 h before delivery. Maternal blood, umbilical cord blood and amniotic fluid samples were simultaneously collected at delivery. Metoprolol enantiomers and its metabolites were quantified by LC-MS/MS or by fluorescence detection. **Results:** The transplacental distribution (umbilical cord/maternal plasma) was approximately 1 for metoprolol and α -hydroxymetoprolol isomers and approximately 0.8 for metoprolol acid metabolite enantiomers. The concentrations of both metoprolol enantiomers (amniotic fluid/maternal plasma = 3.0 for R-(+)-metoprolol and 3.2 for the S-(-)-metoprolol) and α -hydroxymetoprolol isomers (liquid amniotic fluid/maternal plasma = 5.1 for 1'S,2R; 4.0 for 1'S,2S; 1.6 for 1'R,2R and 2.3 for 1'R,2S) are higher in amniotic fluid than in maternal plasma. However, metoprolol acid metabolite enantiomers reached lower concentrations in amniotic fluid than in maternal plasma (amniotic fluid/maternal plasma = 0.29 and 0.37 respectively for the R-(+)- and S-(-)- enantiomers). **Conclusion:** Gestational Diabetes *mellitus* reduces in approximately 20% the transplacental distribution of the isomers 1'S,2S; 1'R,2R and 1'R,2S- α -hidroximetoprolol but does not alter the transplacental distribution of both metoprolol O-desmethylnmetoprolol enantiomers.

Keywords: metoprolol; enantiomers; placental distribution; gestational Diabetes *mellitus*; parturient; hypertension.

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