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Metabolism and transplacental distribution of metoprolol and its metabolites isomers in parturients with well-controlled gestational diabetes mellitus

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Metoprolol is a drug indicated in the treatment of hypertension during pregnancy. This study aimed to investigate the influence of gestational diabetes mellitus (GDM) on the kinetic disposition and transplacental and amniotic fluid distribution of the isomers of metoprolol, α -hydroxymetoprolol and O-desmethylmetoproloic acid in hypertensive parturients. The study was conducted on hypertensive parturients with well-controlled GDM (n=11) and non-diabetic hypertensive parturients (n=24) with a gestational age of 35 to 42 weeks, all receiving a single 100 mg oral dose of racemic metoprolol tartrate. Serial maternal blood samples (0-24 h) and umbilical blood and amniotic fluid samples were collected for the quantitation of metoprolol and its metabolites isomers using LC-MS/MS or fluorescence detection. The kinetic disposition of metoprolol and its metabolites isomers using LC-MS/MS or fluorescence detection. The kinetic disposition of metoprolol and its metabolites isomers using LC-MS/MS or fluorescence detection. The kinetic disposition of metoprolol and its metabolites was stereoselective in diabetic and control groups. Well-controlled GDM prolonged t_{max} for both isomers of metoprolol (1.5 vs 2.5 h - R-(+)-MET; 1.5 vs 2.75 h - S-(-)-MET), of O-desmethylmetoproloic acid (2.0 vs 3.5 h - R-(+)-OAMD; 2.0 vs 3.0 h - S-(-)-OAMD), and of α -hydroxymetoprolol (2.0 vs 3.0 h for isomers 1'S,2R-; 1'R,2R- and 1'R,2S-OHM; 2.0 vs. 3.5 h or isomer 1'S,2S-OHM) and reduced the transplacental distribution of isomers 1'S,2S; 1'R,2R; and 1'R,2S-OHM by approximately 20%. The kinetic disposition of metoprolol and its metabolites isomers and reduced by about 20% the transplacental distribution of the 1'S,2S, 1'R,2R, and 1'R,2S-OHM isomers. Thus, well-controlled GDM did not change the activity of CYP2D6 and CYP3A involved in metoprolol metabolism.

Biography

Natalícia de Jesus Antunes has completed her Master degree at age 27 years from School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo. She is PhD student at the School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo. She did a PhD internship at the Division of Pharmaceology, Leiden Academic Centre for Drug Research, Leiden University. She has worked with PK/PD modelling and pharmacokinetics studies of antihypertensive drugs during the pregnancy.

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