ORIGINAL ARTICLE

Pregnancy and newborn outcome of mothers with inflammatory bowel diseases exposed to anti-TNF-\(\alpha\) therapy during pregnancy: three-center study

MARTIN BORTLIK\(^{1,2}\), NADEZDA MACHKOVA\(^1\), DANA DURICOVA\(^1,3\), KARIN MALICKOVA\(^4\), LUDEK HRDLICKA\(^1\), MARTIN LukAS\(^1,2\), PAVEL KOHOUT\(^5\), OLGA SHONOVA\(^6\) & MILAN LUKAS\(^1,4\)

\(^1\)IBD Clinical and Research Centre, ISCARE, Charles University, Prague, Czech Republic, \(^2\)Department of Internal Medicine, Military Hospital, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, \(^3\)Institute of Pharmacology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, \(^4\)Institute of Medical Biochemistry and Laboratory Diagnostics, 1st Faculty of Medicine, Charles University and General University Hospital, Prague, Czech Republic, \(^5\)Department of Internal Medicine, Thomayer Hospital, Prague, Czech Republic, and \(^6\)Department of Gastroenterology, Hospital Česke Budejovice, Česke Budejovice, Czech Republic

Abstract
Objective. Substantial number of women with inflammatory bowel disease (IBD) conceives while on anti-TNF-\(\alpha\) therapy. The aim was to assess the safety and efficacy of anti-TNF-\(\alpha\) treatment during pregnancy and to analyze relationship of neonatal and maternal anti-TNF-\(\alpha\) levels at delivery with gestational age at the last exposure. Material and methods. Women with IBD exposed to anti-TNF-\(\alpha\) therapy during pregnancy were included. Data on anti-TNF-\(\alpha\) treatment, disease activity, concomitant medication, pregnancy and newborn outcome were recorded. Anti-TNF-\(\alpha\) levels from cord blood were assessed by ELISA. Results. Forty-one pregnancies (27 Crohn's disease; 14 ulcerative colitis) were exposed to infliximab (IFX; 32) and adalimumab (ADA; 9). Ten (24%) women had active disease at conception and 31 (76%) were in remission with 3 patients experiencing relapse during pregnancy. Anti-TNF-\(\alpha\) therapy started prior to and after conception in 32 and 9 women, respectively. There were 34 (83%) live births (median birth weight 31 45 g) of which 28 were at-term and 6 preterm deliveries. Five (12%) pregnancies ended in spontaneous and two in therapeutic abortion. No congenital malformations except for one case of hip dysplasia were observed. Similarly, no serious perinatal complication occurred. IFX cord levels measured in 11 children positively correlated with gestational week at the last drug administration and maternal levels at delivery, while no such correlation was found in case of ADA. Conclusions. The results confirm that anti-TNFs are effective and safe during pregnancy. A positive correlation between IFX cord levels and gestational week of last exposure as well as maternal serum levels was observed.

Key Words: adalimumab, inflammatory bowel disease, infliximab, outcome, pregnancy

Introduction
Substantial part of patients with inflammatory bowel disease (IBD), including females of childbearing age, currently receive therapy with anti-TNF-\(\alpha\) antibodies. In a recent study from a tertiary center, almost 20% of women with IBD and active conception plans were treated with anti-TNF-\(\alpha\) therapy, that is infliximab (IFX) or adalimumab (ADA) \([1]\). Both IFX and ADA belong to the IgG1 class of antibodies and are capable to cross the placental barrier particularly during the late second and third trimester. They can be detected in the cord blood at delivery, usually in levels exceeding those in maternal serum \([2,4]\). Moreover, both