

Impact of Anti-Tumor Necrosis Factor Alpha Antibodies Administered to Pregnant Women With Inflammatory Bowel Disease on Long-term Outcome of Exposed Children

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Background: Prenatal exposure to anti-tumor necrosis factor α (TNF- α) antibodies seems to be safe for fetal development. Data on long-term outcome of exposed children are missing. Our aim was to assess long-term postnatal development of children exposed to anti-TNF- α during pregnancy.

Methods: Consecutive children aged ≥ 12 months exposed to anti-TNFs prenatally for maternal inflammatory bowel disease in 3 centers in the Czech Republic were enrolled. Data on psychomotor development, infections, antibiotics, vaccination, and allergy were retrospectively obtained from mothers, treating pediatricians, and children's vaccination cards. Furthermore, standardized laboratory tests on humoral and cellular immunity were performed.

Results: Twenty-five children exposed to biologicals were included (median age, 34 mo; range, 14–70 mo). All children had normal growth, and all but 1 had normal psychomotor development. Majority (80%) experienced at least 1 infection (mainly respiratory), and 60% of infants received antibiotics, 32% of those within the first year of life. Vaccination was undertaken according to vaccination protocol to 23 infants (92%). Fifteen children also had tuberculosis vaccination without serious complication. Immunological investigation was performed with 17 children (68%). Cellular immunity was normal in all infants, and 7 children had mild decrease in IgA and/or IgG immunoglobulins without clinical significance. All children had a detectable serologic response to vaccination.

Conclusions: Exposure to anti-TNF- α antibodies seems to be safe for growth and psychomotor development of children, although clinical significance of relatively high frequency of infections and antibiotic use among infants remains questionable because of the lack of a control group. Continuous follow-up of exposed children is absolutely warranted.

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Key Words: anti-TNF- α therapy, children, inflammatory bowel disease, prenatal exposure, immune system

Inflammatory bowel disease (IBD) frequently manifests in patients of childbearing age.¹ Because disease activity, either at the time of conception or during pregnancy, increases the risk

of unfavourable pregnancy outcomes, keeping pregnant IBD patients in remission is the primary goal of medical therapy.¹

A growing body of evidence supports that anti-TNF alpha (anti-TNF- α) antibodies infliximab (IFX) and adalimumab (ADA) are safe if given to pregnant IBD patients.^{2–4} A recent systematic review identified 375 pregnancy exposures to IFX or ADA in IBD patients.³ In general, the results confirmed favorable outcomes of pregnancies with anti-TNF- α exposure with rates of spontaneous abortions, stillbirths, and congenital abnormalities not exceeding those in the general population. Moreover, the live birth rate in the anti-TNF- α exposed group was even higher than that of the general population in the United States.³ In our own series of 41 pregnancies of IBD patients, we have not observed any harmful effect of IFX or ADA therapy in terms of pregnancy outcomes and newborn outcomes up to the first 30 days postpartum.²

Both IFX and ADA belong to the IgG1 class of antibodies and are capable of crossing the placental barrier particularly during the second half of pregnancy. They can be detected in the cord blood at delivery, usually in levels exceeding those in maternal serum.^{2,4–7} Moreover, both agents can be present in

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