

Pregnancy Outcome in Women Exposed to Anti-TNF-alpha Medications: The OTIS Rheumatoid Arthritis in Pregnancy Study. Christina D. Chambers, Diana L. Johnson, Kenneth Lyons Jones, The OTIS Collaborative Research Group. University of California, San Diego, San Diego, CA

Purpose: Anti-tumor necrosis factor-alpha (anti-TNF-alpha) medications, which are used to treat a variety of autoimmune disorders, have not been well studied with regard to safety for a developing fetus. A recent survey of members of the American College of Rheumatology suggests that this lack of data results in poor consensus regarding the use of these medications in pregnancy.

Methods: Between 1999 and 2004, the OTIS Rheumatoid Arthritis in Pregnancy Project prospectively followed 32 pregnant women with first trimester exposure to either etanercept (n = 29) or infliximab (n = 4), all of whom were treated for rheumatoid arthritis and none of whom used methotrexate. We compared pregnancy outcome in the anti-TNF-alpha group to 77 women with rheumatoid arthritis who did not use any anti-TNF-alpha medications (RA Controls), and 50 women without RA (Non-Diseased Controls), all of whom were prospectively followed in an identical manner.

Results: Three women (1.9%) were lost to follow-up and two (1.3%) terminated their pregnancies, one with etanercept exposure in a pregnancy not known to be abnormal, and one in the RA Control group following prenatal diagnosis of a chromosomal anomaly. In the remaining 155 pregnancies, spontaneous abortion occurred in 3/28 (10.7%) of the etanercept-exposed women, 1/4 (25%) of the infliximab-exposed women, and 5/74 (6.8%) and 2/49 (4.1%) of the RA Control and Non-Diseased Control groups respectively ($p = 0.36$). The only major structural defect that was reported in the anti-TNF-alpha group was a chromosomal anomaly, Trisomy 18, which occurred in an etanercept-exposed pregnancy that ended in spontaneous abortion. Including liveborn infants, spontaneous abortions and terminations, the overall rate of malformations in the anti-TNF-alpha group (1/33 or 3.0%) was similar to the proportion of major malformations (4.0% and 4.1%) in the two control groups respectively. Preterm delivery was significantly more common in the anti-TNF-alpha group and in the RA Control group relative to Non-Diseased Controls: etanercept 7/25 (28.0%); infliximab 2/3 (66.7%); RA Controls 16/68 (23.5%); Non-Diseased Controls 2/47 (4.3%) ($P < 0.01$). Mean birth weight in full term infants was also significantly lower in the anti-TNF-alpha group (3155 gm \pm 517) and the RA Control group (3285 gm \pm 401) relative to Non-Diseased Controls (3585 gm \pm 421; $P < 0.001$). Findings regarding both preterm delivery and growth remained statistically significant after adjustment for potential confounders in multivariate analysis.

Conclusions: These preliminary data suggest that the rate of major structural defects in the anti-TNF-alpha group is consistent with population rates, and that the increased risks for preterm delivery and poor growth in the offspring of women with rheumatoid arthritis are likely to be attributable to the underlying maternal disease and/or the concomitant use of systemic steroids.

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