Babies exposed to TNFi or tofacitinib in utero experience very few serious infections

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A new study found that very few serious infections were seen in children born to mothers with chronic inflammatory diseases who used non-TNFi biologics or tofacitinib during pregnancy compared to children not exposed to these drugs and children exposed to TNFi biologics in utero. These findings are being presented this week at the 2019 ACR/ARP Annual Meeting (Abstract #1901).

Treatments for some rheumatic diseases may include tumor necrosis factor inhibitors (TNFi) or tofacitinib. TNFi is a group of medications used worldwide to treat inflammatory conditions that reduces inflammation and can stop disease progression by targeting an inflammation-causing substance called tumor necrosis factor. Tofacitinib is an oral, small molecule drug used to treat adults with moderately to severely active rheumatoid arthritis (RA) in which methotrexate did not work well.

During pregnancy, circulating immunoglobulin G (IgG) antibodies from the mother are actively transported across the placenta. Some biologic drugs have the potential to cross the placenta too, and often reach higher levels in the fetus than in the mother. This possibility raises concerns that exposed offspring could develop immunosuppression (a partial or complete suppression of the immune response of an individual). This large cohort study compared risk of serious infections in children born to mothers with chronic inflammatory diseases who took non-TNFi biologics or tofacitinib during pregnancy with unexposed children and children exposed to TNFi biologics in utero.

"Our overarching goal is to provide pregnancy safety data on new biologic and small molecule drugs used to treat women with inflammatory arthritis. These conditions predominantly affect women, particularly during their childbearing years. In pregnant women with inflammatory arthritis, flares are common and associated with adverse pregnancy outcomes. Disease control with effective drugs is often warranted," says Evelyne Vinet, MD, Ph.D., Associate Professor of Rheumatology and Clinical Epidemiology at McGill University in Montreal, Canada, and the study's lead author. "Yet, data in pregnant women and their offspring is lacking, as pregnant patients are excluded from clinical trials. Our findings will help guide counseling and management of pregnant women with inflammatory arthritis that require non-TNFi biologics and tofacitinib during pregnancy."

The researchers identified women with one or more hospitalizations for delivery after a diagnosis of RA, ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA) or inflammatory bowel diseases (IBD). They also randomly selected a group of unaffected mothers, matched 4:1 for age, year of delivery and state of residence, using the MarketScan database from 2011 to 2016. Only women continuously enrolled in MarketScan for 12 months or longer prior to their deliveries and with available child linkage information were included in the study.

The researchers defined tofacitinib, TNFi and non-TNFi biologic exposure based on one or more filled prescription and/or infusion procedure codes during pregnancy and/or the preconception period. Non-TNFi drugs include abatacept, rituximab, tocilizumab, ustekinumab and vedolizumab. They defined serious infections in the offspring based on one or more hospitalizations with infection as the primary diagnosis within the first year of life. They also characterized all the exposure groups in the study according to maternal demographics, disease type, comorbidities, pregnancy complications and use of drugs, such as corticosteroids, DMARDs or biologics.

Participants included 16,490 offspring of mothers with RA (4,142), AS (381), PsO or PsA (5,743) and IBD (6,731), as well as 164,553 children born to unaffected matched mothers. Among the offspring of mothers who had inflammatory diseases, 105 were exposed to tofacitinib or non-TNFi biologics, including four to tofacitinib, 33 to abatacept, four to rituximab, 12 to tocilizumab, 42 to ustekinumab and 10 to vedolizumab. In addition, 1,611 offspring were exposed to TNFi biologics during pregnancy.

The researchers found two cases of serious infections in children exposed to tofacitinib or non-TNFi biologics: one to tofacitinib and one to abatacept. They found that the percent of serious infections in offspring of inflammatory disease mothers with no TNFi exposure was 2.1, while for those with TNFi in utero exposure, it was 2.3. They also found 1.6 percent of children born to unaffected mothers had serious infections.

Additional research is needed to determine the specific effects of individual non-TNFi biologics during pregnancy, as well as small molecule drugs for inflammatory diseases, the researchers concluded.

"Our project innovates by using the largest cohort of pregnant women with chronic inflammatory diseases ever assembled to address drug safety in pregnant women, who are regularly excluded from clinical trials," says Dr. Vinet. "We provide the first data on infectious risk in offspring exposed to non-TNFi biologics and tofacitinib. This is a first step, as we need more data to confirm safety, particularly regarding other pregnancy outcomes. It is imperative that we further study this issue to provide firm evidence to guide treatment decisions prior to conception and throughout pregnancy."

More information: Study: Serious Infections in Offspring Exposed in Utero to Non-TNFi Biologics and Tofacitinib