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INVITED EDITORIAL

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Editorial: thiopurines but not anti-TNF monotherapy are linked to worse pregnancy outcomes in a large population-based study

Studies have shown that pregnant IBD patients are more likely to stop therapy due to concerns surrounding medication safety.[1] We know from multiple studies that the best pregnancy outcomes are associated with adequate inflammation control.[2,3] Recent data from the PIANO registry were reassuring about the safety of both thiopurine and biologic exposure during pregnancy.[4] This prospective evaluation of 1490 IBD pregnancies found no increase in congenital malformations, spontaneous abortions, pre-term birth, low birth weight or infections within in the first year in those exposed to thiopurine or biologic therapy during pregnancy.[5] It is important for female patients to continue medications during pregnancy to maintain remission and prevent clinical relapse, which can have impact on pregnancy outcomes.

In this study Meyer et al. looked at pregnancy outcomes from 2010 to 2018 in the French national health database with exposure to thiopurines (n = 3554), anti-TNF monotherapy (n = 3525) and combination therapy (n = 839) and compared the cohorts to IBD pregnancies that were unexposed (n = 19,811). Pregnancy outcomes assessed were vital status at birth, birth term and weight for gestational age. They found that pregnancy thiopurine exposure resulted in an increased risk for stillbirth (aOR = 2.04), pre-term birth (aOR 1.76) and decreased frequency of small for gestational age (SGA) (aOR = 0.79) when compared to unexposed pregnancies. There was no difference in outcomes in those patients with anti-TNF monotherapy exposure compared to unexposed, but compared with thiopurines, anti-TNF pregnancies were less likely to have pre-term birth but more likely to have SGA. In those exposed to combination therapy, they found an increased rate of pre-term birth (aOR 1.55) and larger for gestational age (aOR 1.61), likely due to the risk associated with thiopurine exposure. Due to the nature of this study, they were not able to assess for infant outcomes including congenital anomalies or rates of infection in the first year.

This was a well-done, large-scale, French population-based study that found increased association with thiopurine monotherapy and combination therapy for pre-term birth, and thiopurine monotherapy for stillbirth and SGA. Although these outcomes had been seen in smaller thiopurine exposure studies,[6,7] the risk was not present in the smaller (n = 242) prospective PIANO registry data.[4] A major limitation of this study was that they were not able to control for disease activity, which could impact the outcomes seen, especially in the thiopurine monotherapy cohort. One could argue that the thiopurine monotherapy population can be undertreated and more likely to have active disease.

Overall, this study adds to our current understanding and highlights that anti-TNF monotherapy exposure during pregnancy is safe and not associated with worse pregnancy outcomes. Providers caring for IBD patients during pregnancy should stress the importance of continuation of medical therapy and overall disease control and highlight this and prior studies showing safety of biologic therapy. However, as we continue to advance our therapeutic options in IBD with additional mechanisms of action, we will need to continue to explore the safety of these therapies in pregnancy with both prospective and large healthcare database studies.

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LINKED CONTENT

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