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Anti-TNF Exposure in Utero, What About My Twins?

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To the Editor: We read with great interest the study by Chaparro et al. in regard to outcomes of infants exposed to anti-TNF in utero [1]. In their study, they found no increased risk for serious infections in those infants exposed to anti-TNF agents in utero compared with non-exposed. However, they did find a higher proportion of complications in terms of cesarean sections, need for ICU admission and low birth weight.

This is important work that adds to our body of knowledge with a large cohort followed for more than just a few weeks. In their analysis the authors found that it was pre-term birth, and not the use of anti-TNF therapy that was associated with an increased risk of adverse birth outcomes. These results should be comforting to our patients, who are concerned about the risks of continued biologic exposure during pregnancy.

But as with other large studies on pregnancy to date this study was limited to only singleton pregnancies. As the number of women undergoing assisted reproductive technology (ART) increases, we clinicians get the obvious question: what will happen to my twins? There are known increased risks for both maternal and neonatal outcomes in multiple gestation pregnancies, but hard to counsel anxious patients without data. We do have some recent population-based data as to the outcomes of twins in the healthy population [2]; future multicenter experience with multiple gestation pregnancies will be just as important to study as the singleton pregnancies.

CONFLICT OF INTEREST

Guarantor of the article: Sunanda Kane, MD, MSPH.

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Pregnancy and Inflammatory Bowel Disease: A Long Way to Go

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To the editor: We thank Drs. Kane and Becker for their interest on the TEDDY study [1, 2]. Our study aimed to know the long-term safety of anti-TNF agents in children born to mothers with inflammatory bowel disease (IBD). The safety of these drugs during pregnancy has been demonstrated; however, little is known about their impact on children outcomes. For that reason, we hope that TEDDY study could bring some data to mothers and clinicians to make evidence-based decisions.

However, we think that the TEDDY study is only the first step in a long way to go. IBD affects patients in their reproductive years. To maintain disease in remission is crucial for pregnancy outcome. In the previous years, new biologics have been approved for the treatment of IBD: vedolizumab for Crohn's disease and ulcerative colitis, and ustekinumab for Crohn's disease. Recently, a JAK inhibitor—tofacitinib—has been approved for ulcerative colitis. In the near future, new drugs are expected to increase the therapeutic armamentarium of IBD. All these

drugs will be increasingly used in clinical practice and, therefore, patients will wish to become pregnant while receiving those treatments.

In consequence, it is an urgent need to get information about the safety of those new treatments during pregnancy and in children development. In addition, special situations such as multiple gestations should also be considered, as their outcome in IBD is largely unknown. To that aim, prospective multicenter registries are warranted and eagerly awaited.

CONFLICT OF INTEREST

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The Best Surveillance Intervals for Detection of Intestinal Metaplasia and Dysplasia after Successful Endoscopic Eradication Therapy of Barrett's Esophagus

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To the Editor We read the article “Higher rate of Barrett's detection in the first year after successful endoscopic therapy: meta-analysis” with great interest [1]. Sawas et al. [1] found that detection rate of intestinal metaplasia (IM) and dysplasia after successful endoscopic eradication therapy (EET) of Barrett's esophagus (BE) was significantly higher within the first year of surveillance compared to the surveillance years that followed. EET as the first-line treatment for BE with dysplasia is highly effective if dysplasia or early cancer is found [2]. However, as the authors mentioned that current surveillance intervals after complete remission of IM (CRIM) were based on expert opinion, which made the detection rate of IM, and dysplasia after successful EET of BE quite unstable. Therefore, the author's findings have great reference value for judging the surveillance

intervals after achieving CRIM with endoscopic therapy. We conducted a cumulative meta-analysis according to the data provided by the authors to further support the authors' conclusions.

The cumulative meta-analysis is used to determine the point where further similar studies are unlikely to change the confirmed conclusions [3]. In our cumulative meta-analysis, studies were added one at a time according to the order of published year, and the aggregate effect estimate was recalculated after addition of each study. Our cumulative meta-analysis showed that IM detection rate in the first year was not significantly higher compared to all the subsequent years after until adding a 2017 study by Cotton et al. [4] (RR = 1.52, 95% confidence interval (CI): 1.11–2.08, Fig. 1a), and thereafter, the results remained stable. Figure 1b showed a forest plot for the cumulative meta-analysis of dysplasia detection rate after achieving CRIM between the first year and the subsequent years. A statistically significant difference was first achieved by adding a 2014 study by Conio et al. [5] (RR = 2.44, 95% CI: 1.02–5.83). Thereafter, seven more studies published between the years 2014 and 2017 made the difference not statistically significant (RR = 1.52, 95% CI: 0.96–2.41), while an essential change occurred when the study by Cotton et al. [4] published in 2017 was added (RR = 1.84, 95% CI: 1.22–2.79), and thereafter, this result that dysplasia detection rate was significantly higher in the first year compared to the subsequent years has remained stable after adding three studies published in 2017 and 2018 (RR = 1.90, 95% CI: 1.31–2.76). Regardless of which study was added, the difference in high-grade dysplasia (HGD)/esophageal adenocarcinoma (EAC) detection rate between the first year and all the subsequent years remained not statistically significant (data not shown).

The results of cumulative meta-analysis can help researchers justify additional studies or realize the need to reorient their research [6]. Our cumulative meta-analysis confirmed again that IM and dysplasia detection rate after achieving CRIM in the first year was significantly higher compared to all the subsequent years after. Relevant studies might not be needed for supporting