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Summary

THIOPURINE SHUNTING IN INFLAMMATORY BOWEL DISEASE PREGNANCIES INCREASES THE RISK OF INTRAHEPATIC CHOLESTASIS OF PREGNANCY AND CAN BE MANAGED WITH SPLIT-DOSING: A PICCOLO-X STUDY

Lani Prideaux

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IBD

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Prospective cohort study of 131 thiopurine-exposed and 147 biologic monotherapy pregnancies in IBD finds thiopurine exposure associated with 6.7% risk of intrahepatic cholestasis of pregnancy versus 0% in controls, driven by metabolic shunting in late pregnancy and antenatal dose increases.

KEY POINTS

- Thiopurine exposure was associated with significantly increased risk of intrahepatic cholestasis of pregnancy (6.7% versus 0% in biologic monotherapy pregnancies, p<0.01), with risk factors including shunting in third trimester (RR 8.9) and at delivery (RR 11.4), antenatal dose increase (RR 5.3), and prior ICP history (RR 21.1).
- In thiopurine-exposed pregnancies with no dose changes, the MMP/TGN ratio increased from preconception to third trimester (p<0.01), with 24-26% of participants demonstrating metabolic shunting (MMP/TGN >11) in each trimester.
- Split dosing of thiopurines in second trimester for shunting management reduced median MMP/TGN ratio from 18 in second trimester to 7 in third trimester (p<0.01) and to 3 at delivery (p=0.04).
- No increased risk of preterm delivery (RR 0.40) or low birth weight (RR 0.61) was observed in thiopurine-exposed versus biologic monotherapy pregnancies, and disease activity measured by faecal calprotectin remained stable throughout pregnancy in both groups.
- This material is relevant for gastroenterologists and obstetricians managing pregnant patients with IBD on thiopurine therapy who require guidance on metabolite monitoring and dose optimization strategies to minimize ICP risk.

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