

Inflammatory bowel disease in pregnancy:

management strategy based on best evidence and European guidelines

Clinical Question

What can the primary care practitioner offer men and women with inflammatory bowel disease who are contemplating starting a family?

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Inflammatory bowel disease (IBD) affects approximately 620 000 people in the UK. IBD (including both Crohn's disease and ulcerative colitis) is a chronic condition commonly presenting in the teens and twenties.¹ Thus it may affect individuals who are anxious about the impact of their medications or their disease on fertility, pregnancy, neonatal outcomes, and breastfeeding. For most patients, their GPs, specialist IBD nurses, or midwives are likely to be the first port of call to address such concerns.

Several studies report that patients with IBD believe that their medications are contraindicated in pregnancy or at the very least cause some degree of harm to their unborn child despite evidence to the contrary.²

This article is aimed at primary care practitioners and is a concise summary of various specialist reviews and guidelines on the optimal management of IBD in pregnancy.

PRECONCEPTION AND CONCEPTION

Several studies have shown that women with IBD are just as likely to become pregnant as those without IBD,³ with two exceptions: women with active Crohn's disease who may have reduced fertility and women who have had pelvic surgery. The effect of pelvic surgery is most marked in those who have an ileo-anal pouch (50% infertility). Women awaiting possibly definitive surgery (and reversal of stoma) should consider having this delayed until after they have completed their family. All those who have had pelvic surgery should be referred for assisted conception early if they have difficulty becoming pregnant.²

Drugs that need to be discontinued include the immunosuppressant mycophenolate mofetil (MMF), which interferes with purine metabolism in a similar way to azathioprine, and the folic acid antagonist methotrexate (MTX). These are associated with an increased risk of congenital abnormalities

and should be stopped 3 months before conception. Women on MMF can be switched to azathioprine before pregnancy. In men, unless the patient has active disease or is nutritionally deficient, fertility should be comparable with their non-IBD counterparts. Sulfasalazine has an adverse effect on sperm count but this resolves once the drug is discontinued. There is very little evidence that MTX or MMF in men cause fetal abnormalities. A recent study⁴ showed that there was no increased risk of adverse pregnancy outcome from paternal low-dose MTX (≤ 30 mg/week), making the previously suggested 3-month MTX-free period before conception no longer necessary.

ADVICE ON NUTRITION AND MONITORING

General advice such as smoking and alcohol cessation, weight management, healthy eating, and lifestyle modification remain valid, and pregnancy provides an opportune moment to intervene successfully. Smoking cessation is of particular importance in Crohn's disease because smoking exacerbates disease activity; flares can also be good times to try to modify patient lifestyle. With regards to folic acid and checking for iron deficiency anaemia, special attention is warranted given the increased risk of malabsorption as well as the effects on folate metabolism of some drugs, such as sulfasalazine. Some patients with IBD need to be on higher doses of folic acid than the standard dose (5 mg/day versus 400 µg/day). Indeed, the 2010 European Crohn's and Colitis Organisation (ECCO) guidelines state that all IBD patients should be prescribed 1 mg folic acid daily in anticipation of pregnancy.³

Patients on long-term or repeated glucocorticoid therapy should be monitored for osteopenia and assessed for fracture risk according to National Institute for Health and Care Excellence guidelines.^{5,6} Calcium and vitamin D supplements are appropriate but these will not correct vitamin D deficiency. This necessitates high oral

Table 1. Common drugs used in inflammatory bowel disease⁷

| Drug | Advice in pregnancy | Advice in breastfeeding |
|---|---|--|
| Prednisolone | Supplement calcium, give 'stress dose' at delivery in patients with chronic exposure. Risk of gestational diabetes | Safe up to 40 mg/day. At higher doses monitor baby for adrenal suppression |
| Budesonide | Limited data with only one case series in IBD but appears safe | No data, but theoretically safe |
| Dexamethasone Betamethasone | Use alternative steroid agent as high placental transfer | Use alternative steroid agent |
| 5-ASA (aminosalicylate) except olsalazine | Use considered safe where necessary. Avoid doses greater than 3 g/day due to risk of fetal nephrotoxicity | Appears safe, but monitor infant for diarrhoea |
| Olsalazine | Use alternative 5-ASA | Use alternative 5-ASA |
| Sulfasalazine | Give high-dose folic acid supplementation (5 mg/day) | Benefits likely to outweigh risks in those on established treatment |
| Azathioprine/ mercaptopurine (MP) | Extensive experience suggest use is safe. Azathioprine preferable to MP as fetus cannot convert to MP and is therefore less exposed to the active metabolites. Be aware of risk of myelosuppression in neonate | Benefits likely to outweigh risks in those on established treatment |
| Ciclosporin A | Extensive experience in transplant patients. Likely to be safe on treatment | Benefits likely to outweigh risks in those established on treatment |
| Methotrexate | Avoid | Avoid |
| Methotrexate mofetil | Avoid | Avoid |
| Infliximab and adalimumab | Likely to be safe. Use where benefits are deemed to outweigh risks. Try to avoid use in the third semester. Avoid live vaccines in the newborn in first 6 months if mother received biologic therapy during pregnancy | Benefits likely to outweigh risks in those established on treatment |

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doses of cholecalciferol, which are safe in pregnancy. In addition, these patients should be screened for gestational diabetes mellitus. All patients on IBD medication or with active disease should be promptly referred to the appropriate specialist.³

MEDICATIONS IN PREGNANCY AND BREASTFEEDING

Treatment regimens mostly remain unaffected by pregnancy except for MTX and MMF, which are contraindicated and should ideally be stopped 3 months before conception. Table 1 summarises the best available evidence.

Despite women's reticence to continue medications during pregnancy² it is imperative for physicians to highlight the fact that the benefits of remission far outweigh the risks to the fetus from medication. Should patients experience a flare during pregnancy, prompt referral to their gastroenterologist is indicated because flare is associated with preterm delivery and fetal loss.

All manufacturers advise that patients should avoid using IBD medications during breastfeeding. However, from the

limited evidence available, the conclusion by specialists is that medications such as mesalazines, sulfasalazine, corticosteroids, azathioprine, and biologics are all safe in breastfeeding. Given that best practice often contradicts manufacturers' advice, the GP should have a candid discussion with patients about this situation and tailor advice to the individual and on a case-by-case basis guided by the specialist.

While some studies show that certain medications may be associated with preterm delivery, they remain controversial and evidence is inadequate. The current guidance to clinicians is that:

*'... in the majority of patients, maintaining remission with medical treatment outweighs the potential risks of adverse drug effects.'*³

DELIVERY

Most women with IBD can have a vaginal delivery. Women with active perianal Crohn's disease are recommended to have a caesarean section to limit the risk of complications from a third-degree tear. There is limited evidence with regard to management of those who have had an ileo-anal pouch and advice should be taken from the colorectal team.

CONCLUSION

Patients with IBD can have pregnancies comparable with the wider population and with normal outcomes. The consensus is that disease remission is the best prognostic indicator of optimal outcome for both mother and baby. All patients with IBD should be encouraged to continue their medications during pregnancy and while breastfeeding, having discussed with the GP the current evidence of risks and benefits. The GP can lead and coordinate such advice with the patient.

Provenance

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Competing interests

Catherine Nelson Piercy has received lecturing and advisory board fees from Warner Chilcott. Peter Irving has received honoraria for acting in an advisory capacity or speaking for Abbvie, MSD, Shire, Warner Chilcott, Ferring, Takeda, Genentech, Tillotts, Vifor Pharma and Pharmacosmos.

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