Pregnancy and inflammatory bowel disease

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Abstract

Overall, around 25% of women with inflammatory bowel disease will conceive during their disease. Most of the women with inflammatory bowel disease will have a normal pregnancy and healthy children. However, specific problems may arise related to these pregancies. This paper reviews what is known on fertility, risk of disease transmission, effect of the disease on the pregnancy and the reverse, delivery, medical follow up and treatment as well as breastfeeding in the setting of inflammatory bowel disease. (Acta gastroenterol. belg., **2002**, 65, **230-232**).

Key words : Crohn's disease, ulcerative colitis, pregnancy.

Introduction

Inflammatory bowel disease (IBD) mostly affects young adults, including many women in a period of their life during which they wish to have babies. Indeed, about 25% of women with the diagnosis IBD conceive after the diagnosis has been made (1). Specific problems may be addressed on pregnancy during IBD. They often correspond to the questions the patients will ask to the gastroenterologist. Some of these questions are about the risk of transmission of the disease to the child, the capacity to conceive, the impact of the disease on the pregnancy and the fetus, the impact of the pregnancy on the disease, the treatments and complementary explorations allowed, the delivery and the possibility of breastfeeding.

What is the risk of transmission to my child ?

This question touch upon the problem of genetics in IBD. We have known for some years that IBD are polygenic, multifactorial disease with genetic heterogeneity. This has been recently confirmed by the discovery of an association between NOD2 mutations and Crohn's diseases (2,3). This association has not been found with ulcerative colitis (UC), clearly showing the heterogeneity between these two entities, but furthermore, only 20-30% of CD patients carry a NOD2 mutation, demonstrating an heterogeneity inside CD. Finally, These mutations are also found in 5-7% of healthy subjects showing that beside this gene, other genes or environmental factors must be involved. Globally, the risk to develop IBD in offspring of parents affected is 5-10% (4) if one parent is affected and May rise to 36% if two parents are affected (5).

What's about my ability to conceive ?

This capacity is normal in UC and maybe slightly diminished in CD (6). The fact is that women with CD have significantly less children than healthy controls. It is difficult however to know whether this relates to a real decrease in fertility or with a lower desire to have children. A true diminution of fertility in CD may be explained by local inflammatory changes in the ovaries, or fallopian tubes, poor nutritional status, reduced libido due to perianal disease.

What would be the effect of the disease on my pregnancy ?

If the conception occurs in inactive disease, the rate of spontaneous abortion is around 10%, which is similar to the one in general population (6). This rate may rise up to 20-60% in case of active disease. Premature birth are 2 to 3 times more frequent in IBD (7). This also is influenced by the activity of the disease but is present even in inactive disease. Birth weight is also significantly lower in IBD and again correlates with the activity of the disease (8). Finally, there is no increase in congenital abnormalities (1).

What would be the impact of a pregnancy on my disease ?

There is no universal rule. Grossly, one third of the diseases stay stable, one third improve and one third become worse (9). Therefore, it is recommended to conceive during remission. In this case the risk of relapse during pregnancy is around 20% (8). As it has been described for several dysimmune diseases, the evolution of IBD during pregnancy may be influenced by the HLA disparity between the fetus and the mother, the disease generally improving when the HLA disparity is greater (10).

Would my medical follow up be particular during pregnancy ?

The visits to the gastroenterologist must be more frequent during pregnancy. The two major aims are to

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avoid and rapidly treat any relapse and to avoid nutritional deficiencies. Folate supplementation is particularly important since its resorption may be impaired in IBD and some treatment (sulfasalazine) may increase this problem. In need of complementary explorations, CRP level remains a good reflect of systemic inflammation, ultrasound and magnetic resonance imaging are safe, abdominal plain film should be used in the same indications as for non pregnant women, CT scanner associated with higher level of irradiation should be avoided and colonoscopic examination should be limited to the distal part of the colon with a caution for the bowel preparation (11).

Would vaginal delivery be possible and safe ?

A higher rate of caesarian section has been described in CD (12). It is specially indicated in case of active or inactive perirectal, rectovaginal, or perianal fistulae ; it may also be preferable in active Crohn colitis (4). Some reports have suggested an increased risk of developing de-novo perianal disease in CD after vaginal delivery (linked to episiotomy) (13), but it has not been confirmed by others (14).

What's about my medical treatment ?

Enough data are available to declare that salazopyrine and 5ASA (at least up to 2gr./d.) are safe during pregnancy (15, 16). Patient under salazopyrine must also take folate supplementation. Classical corticosteroids are also safe and may be used as required (17). To little data is available on new topical steroids (budesonide). Cyclosporine is not teratogenic but may be associated with growth retardation and prematurity (17). Methotrexate and thalidomide are teratogenic and strongly contra-indicated (18). Antibiotics such as metronidazole and ciprofloxacine may be used for short courses but preferably not in the first trimester (17). The most difficult and probably important problem is with azathioprine and its active compound 6-mercaptopurine (6-MP). These drugs are teratogenic at high dose in animals (19). Furthermore, under azathioprine, small amount of 6-MP is detected in fetal blood (20). The largest experience of azathioprine/6-MP in pregnancy comes from transplanted women and does not indicate a significant increase of congenital abnormalities (21,22). Only limited experience of pregnancies under azathioprine/6-MP in IBD has been published. The preliminary data are reassuring however (23). Obviously the risk is low but can not currently be certified as zero. Therefore the decision has to be taken with the informed patient, taking also into account the high risk of relapse of the disease in the months following its cessation. When feasible it is probably safer to try and postpone the pregnancy for a few years because the risk of relapse when stopping azathioprine seems to be lower when patients have been maintained for a longer period of time in remission under azathioprine (more than 4 years) (24). If a pregnancy starts while the patient is treated with azathioprine or 6-MP there is no indication for therapeutic termination or even for stopping treatment. It is probably safer then to carry on with the drug. Only preliminary data is available on infliximab. Fifty nine pregnancies had been recorded in CD or rheumatoid arthritis up to the AGA digestive disease week in may 2001. Data were available on 36 of them (24). These 36 women had received 43 injections : 27 before pregnancy, 11 before and during first trimester and 5 later during pregnancy. There were 27 live births, 5 therapeutic terminations and 5 miscarriages. In the 27 live births, there were 2 complications : one death due to prematurity and low weight and one Fallot tetralogy.

Is breathfeeding allowed ?

There is no contra-indication to breathfeeding in IBD. However many treatments are contra-indicated. Only 5-ASA, sulfasalazine and steroids are allowed (25, 26).

Are their specific problems when the father has got an IBD ?

After IBD surgery, some men may suffer from dysfunction and retrograde ejaculation. Sulfasalazine sometimes lead to reversible reduced spermiogenesis. There is still an open problem about azathioprine and 6-MP. The literature describes a case of Wilms tumor in a 4 years old child whose father had taken 6-MP at conception (27). More recently a series of 13 cases in which the father had taken 6-MP within 3 months of conception has been reported. These were compared to fathers having stopped 6-MP more than 3 months before conception and fathers who had never taken 6-MP. The risk of complication was significantly higher in the first group (treated with 6-MP within 3 months of conception) ; there were two spontaneous abortions and two congenital anomalies.

Conclusion

A majority of women with IBD are able to have normal pregnancies and the repercussion of IBD on these pregnancies are most often without clinical significance. The most important point is to start the pregnancy in remission of the disease and with a good nutritional status. The pregnancy should be planned and the treatment adapted to fulfil this aim.

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