Breastfeeding and Medication

Breastfeeding and Inflammatory Bowel Disease (IBD)

Inflammatory bowel disease is a chronic condition affecting the gastro-intestinal tract. The morbidity produced by the condition can be considerable, particularly in younger patients. It can affect growth, fertility, education, employment and limit much of normal life. Inflammatory bowel disease fluctuates through cycles of remission and relapse controlled by medication and surgery, including temporary or permanent stoma formation. Hospital admissions may be frequent during flares. The most common age for diagnosis is 10–40 years.

The incidence of ulcerative colitis is 10.4 per 100,000 and Crohn's disease 5.6 per 100,000 in western populations. Extrapolating this, about one person in every 400 in the UK has IBD with 50% being diagnosed before the age of 35 years. Twenty five per cent of females with IBD will conceive after their diagnosis. The cause of IBD is not clear with genetic and environmental factors having been identified.

There is no evidence that pregnancy causes progression of the disease and some evidence that it has a favourable effect. However, the activity of the disease at the time of conception strongly influences its course during the pregnancy. Patients with active disease at the time of conception have an increased risk of miscarriage – reportedly up to 35%. Crohn's disease (CD) carries an increased risk of low birth weight and pre-term birth. Women with IBD may benefit from 5 mg folic acid under 12 weeks of pregnancy because they have a higher rate of vitamin deficiency. Women should be advised to attempt to become pregnant when their disease is in remission in order to minimise the risk to the foetus.

Whorwell et al. (1979) studied 57 patients with IBD and matched controls. He found that 29.9% of the patients had been artificially fed compared with 11.8% of controls, a statistically significant difference. He did not find a similar difference in patients with CD but did find significantly different incidences of early gastroenteritis in the first six months of life. He hypothesised that a pathogenic infection occurred that persisted and manifested as CD in later life. Whorwell et al. suggested that either bottle feeding was harmful or that breastfeeding is protective, possibly due to sensitisation to cow's milk proteins in early life, due to increased permeability to macromolecules. Also that artificial feeding may alter bacterial flora at a time when sensitisation to bacterial antigens may occur.

There is a higher chance of developing IBD if there is a first-degree relative with the condition. Patients with IBD have a 5% risk of having a child who develops IBD. If both parents have the condition the risk rises to 35%. However, in only 45% of monozygous twins do both develop IBD and fewer in dizygotic twins. Environmental risk factors identified include smoking, diet, vitamin C consumption and the use of the oral contraceptive for females.

The incidence of diarrhoeal disease in the first six months of life seems to increase the risk of developing both CD and ulcerative colitis (UC) (Koletzko et al. 1989). Similarly, recurrent respiratory infections were significantly more common in UC and CD patients than matched controls, and patients with CD were more likely to have taken antibiotics. Breastfeeding is known to lower the incidence of gastrointestinal disease and respiratory tract infections and may therefore be expected to prevent these influences on the development of IBD.

Corrao et al. (1998) studied 819 cases of IBD diagnosed between 1989 and 1992 (594 with UC and 225 with CD). He found that being a former smoker increased the odds ratio for UC whilst being a current smoker increased the odds ratio for CD by 1.7. For females, using the oral contraceptive increased the risk for CD but had no effect on UC risk. Lack of breastfeeding in infancy accounted for the highest proportion of CD in females in later life (odds ratio UC 1.5, CD 1.9). However, the data collected on breastfeeding was minimal or none with no account taken for duration or exclusivity. Other factors investigated included limited physical activity, dietary factors, previous diseases, e.g., psoriasis, early infections, absence of appendectomy, alcohol intake, contact with animals, but the results of these investigation was conflicting.

Kane and Lemieux (2005) studied 122 women with IBD who had delivered in the previous five years. Only 44% had breastfed their babies. The reasons cited for choosing to formula feed included recommendation by the caring physician, fear of the safety of medication reaching their baby, as well as personal choice. Of the women with CD, only 29% chose to breastfeed, with a median duration of eight months (3–14 months). Of the population in the study who breastfed (54), 43% (23) experienced a postpartum flare, but when adjusted for medication cessation this was not statistically significant. Factors associated with a flare in the postpartum period (defined as an increase in disease activity within eight months of delivery) were hypothesised as discontinuation of medication, resumption of smoking and a possible significant change in hormones.

More women with CD expressed a desire to stay on their medication following delivery, fearing a flare and therefore choosing not to breastfeed. Of the 30% who experienced a flare, 64% had been breastfeeding in the month before development of symptoms but 74% had chosen to stop their medication. The drugs most frequently cited were mesalamine and azathioprine. At the time of the study 60% of women in the general population were initiating breastfeeding.

In a meta analysis of 17 articles Klement et al. (2004) found evidence that supported the hypothesis that breastfeeding is associated with a lower risk of developing both CD and UC, although few studies were of good quality and data on the duration and exclusivity of breastfeeding were lacking or limited in all studies. All but two studies were retrospective, case-controlled studies so therefore subject to recall bias. However, the latent period for the development of IBD makes prospective studies difficult. Launer et al. (1992) have demonstrated the high accuracy of recall of breastfeeding

duration by mothers up to 18 months after delivery but, in many of the studies analysed by Klement et al. (2004), data was collected after many years.

Xu et al. (2017) performed a systematic search and concluded that breastfeeding in infancy protects against CD and UC with the greatest benefit being with 12 months' breastfeeding duration.

Infliximab

In 2002, the NICE (NICE 2002) recommended that this drug be only used for the treatment of severe, active CD when treatment with immunosuppressant drugs and corticosteroids is not tolerated or has failed. It should only be prescribed by consultant gastroenterologists. Infections are common in patients treated with infliximab or other drugs that inhibit tumour necrosis factor (TNF). The incidence of tuberculosis is particularly marked. Blood dyscrasias, including leukopenia, thrombocytopenia, pancytopenia and aplastic anaemia, have been reported rarely with TNF inhibitors; in some cases, the outcome was fatal. Infliximab is a large molecular weight antibody and preliminary results suggest it is too large to pass into breastmilk and it is not orally bio-available. It is distributed primarily in the vascular compartment and has a terminal elimination half-life of 8–9.5 days. After recommended doses, infliximab has been detected in serum for at least eight weeks. It is suggested that use by a mother should not preclude breastfeeding based on this data (Peltier et al. 2001; Forger et al. 2004; Mahadevan and Kane 2005; Vasiliauskas et al. 2006).

The BNF states that the amount in breastmilk is too small to be harmful.

Compatible with breastfeeding due to poor bio-availability and hence low-level absorption by the infant.

References

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Adalimumab (Humira®)

Adalimumab is a recombinant human monoclonal TNF antibody that binds specifically to TNF- α. Elevated levels of TNF are found in the affected tissues of patients with CD and UC. It is used where there is no response to conventional treatment or relapse with infliximab (Wasan and Kane 2011).

Adalimumab has a low oral bio-availability, a half-life of two weeks, a molecular weight of 148,000. It is likely that any small amounts in milk are destroyed in the baby's gut. Two infants of women who took adalimumab 40 mg subcutaneously during lactation were followed until 14.5 and 15 months of age. No adverse reactions were found in the infant that could be attributed to exposure of the drug in breastmilk. Both infants were reported to have met all developmental milestones (Fritzsche 2012). The BNF, however, states that it should be avoided by breastfeeding mothers and that the manufacturer advises it should be avoided for at least five months after the last dose. Earlier information recommended that infliximab should not be used in a breastfeeding mother until six months after the last dose.

Compatible with breastfeeding due to poor bio-availability and hence low-level absorption by the infant. Mother should be aware of limitations of research.

References

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