Motherisk Update

Celiac disease during pregnancy

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ABSTRACT

QUESTION One of my patients was diagnosed with celiac disease and maintains a strict gluten-free diet. Is her fetus at risk of neural tube defects because she does not get folic acid from bread and other flour-based foods?

ANSWER A woman with celiac disease must supplement her diet with multivitamins, including folic acid. Most prenatal vitamins contain 0.8 to 0.9 mg of folic acid, double the amount recommended by Health Canada for prevention of neural tube defects. Without supplementation (eg, undiagnosed pregnancy), women with celiac disease might not take in enough folate to maintain protective levels.

RÉSUMÉ

QUESTION Une de mes patientes a reçu un diagnostic de maladie cœliaque et elle suit un régime alimentaire strict sans gluten. Son fœtus est-il à risque d'anomalie du tube médullaire parce qu'elle ne bénéficie pas de l'acide folique contenu dans le pain et les autres aliments à base de farine?

RÉPONSE Le régime alimentaire d'une femme atteinte d'une maladie cœliaque doit comporter un supplément de multivitamines, notamment d'acide folique. La plupart des vitamines prénatales contiennent de 0,8 à 0,9 mg d'acide folique, soit le double de la dose recommandée par Santé Canada pour prévenir les anomalies du tube médullaire. À défaut de supplément (par exemple, une grossesse non diagnostiquée), les femmes atteintes d'une maladie cœliaque pourraient ne pas prendre suffisamment d'acide folique pour maintenir les taux voulus pour la protection contre ce risque.

Celiac disease is a lifelong inflammatory condition of the gastrointestinal tract, specifically the small intestine.[1] Exposure to gluten triggers an immune response that causes inflammatory damage to the cells of the intestinal mucosa. This results in loss of the intestinal epithelium and a malabsorption syndrome.

Prevalence during pregnancy

The prevalence of undiagnosed celiac disease among pregnant women is unknown.[2] The rate of celiac disease is higher in women than in men, but we do not know why.[1] An Italian study screened 845 pregnant women and identified 12 with celiac disease, for a prevalence of 1/70.[2] The authors called for routine testing for celiac disease during antenatal care because it is at least as common as many other diseases for which pregnant women are routinely screened.

Rates of diagnosed celiac disease in Minnesota have recently increased from 2.1 per 100 000 people from 1950 to 1989 to 3.3 per 100 000 in the 1990s. The authors speculated that this was due to an increased detection rate and possibly a true increase in incidence.[3] One British study found that one in 60 mothers of children with neural tube defects had celiac disease. This study used the serum endomysial antibody (EMA) test, which has high sensitivity and specificity for celiac disease.[4]

Clinical effects

Celiac disease causes malabsorption of folic acid and other nutrients and has been linked to unfavourable outcomes of pregnancy.[1,5] In a case-control

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study of 94 women with untreated celiac disease and 31 women with treated celiac disease, women with untreated celiac disease had a relative risk (RR) of 8.9 for abortion and of 5.8 for low birth weight babies compared with their treated counterparts.[5] The untreated women's duration of breastfeeding was 2.5 times shorter than the treated women's.[5] Another case-control study of 68 patient-control pairs found that celiac patients were older at menarche and younger at menopause, had a lower mean number of children, and had many more conceptions ending in miscarriage.[6]

A recent systematic review has found that patients with untreated celiac disease have higher rates of miscarriage, fetal growth restriction, and lower birth weight babies.[7] In contrast, a large population-based cohort study of 5055 pregnant women in Italy observed no association between celiac disease and unfavourable pregnancy outcome.[8] Using validated screening techniques, 51 previously undiagnosed celiac cases were identified (prevalence: 1/80). Most of the women identified by screening had no major clinical complaints, but there was a non-significant trend toward reduced birth weight and an increased abortion rate among celiac patients. This study had a different design from the previously cited case-control studies. The case-control studies looked mostly at women with severe clinical symptoms. The authors of this study[8] do not deny that undiagnosed and untreated celiac disease can lead to unfavourable outcomes in pregnancy, but state that women identified by general screening are likely asymptomatic and therefore not necessarily at higher risk of negative pregnancy outcomes.

Women with celiac disease might not absorb folic acid efficiently. Although flour is fortified with folic acid, those with celiac disease abstain from eating bread and put their fetuses at risk of having neural tube defects (NTD). Whether women with untreated celiac disease are at higher risk of delivering babies with NTDs is still unclear. A PubMed search using the terms "celiac," "neural tube defect," and "pregnancy" turned up only two studies. A study by Haslam and colleagues[9] showed that five of 216 women with hemoglobin levels lower than 11g/dL were positive for celiac disease compared with none of 350 with hemoglobin levels at or above 11 g/dL.

This study[9] found no association between positive celiac serology and folate deficiency, and none of 30 mothers of children with NTDs were found to have positive celiac serology by EMA test. A study by Dickey et al[4] found that one in 60 mothers of children with NTDs tested positive for celiac disease. The authors suggested that the most important risk factor for NTDs is abnormalities in folic acid metabolism rather than absorption. One in 60 is, however, a slightly higher prevalence than was found in other studies. Both studies[8,9] preceded flour fortification with folic acid, and hence cannot answer this question.

Further study of the effects of celiac disease during pregnancy is warranted. Celiac disease has been associated with reproductive disorders, and it has been recommended that patients with reproductive disorders be tested for celiac disease.[10] Whether general screening for celiac disease in pregnant women is necessary is still a matter of debate and needs further study.

Management

Nutrient absorption improves rapidly and intestinal mucosa heal once gluten has been eliminated from the diet.[1] In most cases, after 6 to 12 months of a gluten-free diet, no increased unfavourable outcome of pregnancy is observed.[1] While implementation of a gluten-free diet is difficult, it is not impossible. Some web resources to assist with gluten-free diets are **www.gluten.net**, **www.csaceliacs.org**, **www.celiac.org**, **www.celiac.com**, and **www.glutenfreeinfo.com**.

In gluten-free diets, a major source of dietary folic acid is lost because commercial cereal, bread, and pasta products must be excluded. In 1998, fortification of flour with folic acid became mandatory. Since then, there has been a decrease in the prevalence of NTDs.[11] Health Canada recommends that pregnant women and women intending to become pregnant take supplements of 0.4 mg/d of folic acid in addition to their dietary intake. Women unable to consume commercial flour, such as women with celiac disease or others on low-carbohydrate diets, might be at increased risk of having children with NTDs and might need to increase their supplementation.

Conclusion

Celiac disease appears to be a relatively common yet a neglected disorder during pregnancy. Undiagnosed and untreated celiac disease can pose health risks to both mother and fetus. Unfavourable pregnancy outcomes associated with celiac disease could be prevented with a gluten-free diet. Managing a gluten-free diet is difficult; proper supplementation must be achieved in women of reproductive age, especially of folic acid because the main dietary source (flour) is eliminated.

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Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Ms Hancock is a member and Dr Koren is Director of the Motherisk Program. Dr Koren is a Senior Scientist at the Canadian Institutes for Health Research. He holds the Ivey Chair in Molecular Toxicology at the University of Western Ontario.

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