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10

Medical Problems in Obstetrics: Inherited Metabolic Disease

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An increasing number of women with rare inherited disorders of metabolism are becoming pregnant. Although, in general, outcomes for women and their children are good, there are a number of issues that need to be considered. Currently, limited specific guidance on the management of these conditions in pregnancy is available. Prepregnancy counselling with information on inheritance, options for reproduction, teratogenicity risk, potential impact on maternal health and long-term health of children should be offered. With appropriate specialist management, the teratogenic risk of conditions such as maternal phenylketonuria (PKU) can be eliminated, and the risk of metabolic decompensation in disorders of energy metabolism or intoxication significantly reduced. Multidisciplinary management, and close liaison between obstetricians and other specialists, is required for those women in whom there is cardiac, renal, respiratory, joint or other organ involvement.

Introduction

Inherited metabolic diseases (IMDs) are individually rare; are clinically widely heterogeneous; can present at any age; and typically, but not always, are associated with abnormal biochemical tests (usually specialist rather than routine biochemistry). Broadly speaking, they can be divided into the following three groups:

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1. Disorders of intoxication – these disorders of intermediary metabolism give rise to an acute or progressive intoxication secondary to the accumulation of toxic compounds proximal to a metabolic block, for example, disorders of amino acid metabolism such as phenylketonuria (PKU, Online Mendelian Inheritance in Man® (OMIM) #261600), the organic acidurias and urea cycle defects such as ornithine transcarbamylase (OTC) deficiency (#311250).
2. Disorders of energy metabolism – these give rise to their symptoms chiefly because of an energy deficiency in tissues such as liver, muscle, brain or heart. Examples include mitochondrial respiratory chain defects, fatty acid oxidation defects and glycogen storage disorders.
3. Disorders of complex molecules – these involve disturbance in the synthesis or catabolism of complex molecules. Symptoms tend to be progressive and not dependent on dietary / energy intake. Examples include the lysosomal storage disorders and the peroxisomal disorders.

Factors including improved medical care, increased awareness of metabolic conditions and newborn screening with early treatment have led to an increased number of patients with IMD surviving to adulthood and wishing to have children of their own [1]. Although many women have successful pregnancies, with an excellent outcome, these patients present various challenges from the reproductive perspective. Apart from PKU, for which there is substantial evidence for management guidelines during pregnancy, information on pregnancy for most of the other inherited metabolic conditions comes from either isolated case reports or small case series, and no single centre is likely to have enough experience with any single condition to provide definitive guidelines for management. Although in general long-term outcome for these (mostly) autosomal recessive conditions following pregnancy is assumed to be good, there are in fact little data on the long-term follow-up of children born to mothers with IMD.

The aim of this review is not to suggest definitive treatment or provide a review of pregnancy in all potential inherited disorders of metabolism but instead to use specific examples to highlight how these disorders may afffect pregnancy and the puerperium, with emphasis on both the maternal and fetal outcome. One of the most common inherited disorders of metabolism is familial hypercholesterolaemia (#143890), but as this condition is usually managed within adult lipid clinics rather than an IMD clinic and there are a number of published reviews on the management of pregnancy, it is not discussed further in this article [2,3]. Table 1, although not exhaustive, lists some of the specific issues that need to be taken into account when a woman with an inherited disorder of metabolism plans a pregnancy. If at all possible, the care of women with an inherited disorder of metabolism in pregnancy should be discussed/managed together with a physician and/or dietitian with expertise in this field. The Society for the Study of Inborn Errors of Metabolism – Adult Metabolic Physicians Group (SSIEM-AMG: http://www.ssiem.org/amp/contact.asp) can provide contact details for specialist centres worldwide. Similarly, the British Inherited Metabolic Disease Group (BIMDG: www.bimdg.org.uk) can provide details of centres within the UK.

The preconception period

When women with an inherited disorder of metabolism reach childbearing age, they should be counselled on the potential impact of pregnancy on their condition, as well as the impact of their condition on pregnancy and the outcome for their children. As with any woman planning a pregnancy, prepregnancy advice includes starting folic acid supplementation; stopping smoking; limiting caffeine and alcohol intake; and optimizing weight, diet and general physical health [4]. Many women with an inherited disorder of amino acid or energy metabolism will be treated with a modified diet, which, depending on the specific condition, may be low in protein, high in carbohydrate, low in fat or high in fat. In this context, the nutritional requirements of pregnancy will therefore need to be carefully managed. The goal is to optimize metabolic control and nutritional status if possible *prior* to pregnancy.

Medications may need to be altered if the patient is prescribed any potentially teratogenic drugs, for example, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers or certain anticonvulsants. The impact of these alterations on maternal health needs to be discussed. A decision to stop other specific medications, for example, sodium benzoate and sodium phenylbutyrate in women