Pregnancy in patients with cystic fibrosis

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Résumé : Un examen des articles sur les femmes enceintes souffrant de fibrose kystique (FK) (voir pages 809 à 813) a révélé que la grossesse était tolérée par la plupart de ces femmes et qu'elle n'affectait pas défavorablement la fonction pulmonaire ou l'état nutritionnel pourvu qu'on leur donne des soins médicaux et obstétricaux optimums. Cependant, chez les patientes gravement atteintes, la grossesse est liée à une incidence accrue de complications maternelles et foetales. Toutes les études examinées comportaient quelque lacune inhérente, ce que la Fondation américaine de la FK est en train d'essayer de corriger par un suivi prospectif des femmes atteintes de FK qui ont été enceintes.

Once a disease limited to children, cystic fibrosis (CF) is now a disease of adults, since about 50% of people with CF are expected to live into the fourth decade and even longer.[1] Although women with CF have reduced fertility as a result of alterations in the physiochemical properties of cervical mucus[2] and the effects of chronic disease, an increasing number are having children. The article by Drs. Nancy E. Kent and Duncan F. Farquharson in this issue (see pages 809 to 813) is therefore timely because it reviews the experience with pregnancy in women with CF since the early 1960s.

Even in healthy women, pregnancy has measurable effects on respiratory mechanics and gas exchange and is associated with increased nutritional requirements and circulating blood volume.[3] These physiologic stresses may obviously pose a threat to patients with CF who have underlying lung disease, who may also have significant hypoxemia, pulmonary hypertension and malnutrition due to pancreatic insufficiency. What information can be gleaned, therefore, from the review by Kent and Farquharson of the risks of pregnancy (for mother and fetus)?

Clearly the overall outcome for pregnancy in patients with CF has significantly improved since the condition was first described, in 1960. The most important determinant of outcome for both the mother and child is the clinical status of the mother immediately before pregnancy and the stability of pulmonary function during the preceding years. For this reason, women with CF who seek advice about embarking on or completing a pregnancy should be carefully evaluated by their physician. This assessment should include a review of the overall medical and nutritional status, lung function tests, blood gas analysis, cardiac evaluation and Shwachman scoring[4] of clinical status. Obviously the final decision to proceed with a pregnancy rests with the patient and her partner; however, rational decisions can be made only with accurate information.

On the basis of the review by Kent and Farquharson and our experience[5,6] it is evident that patients with mild CF and a high Shwachman score (greater than 75), good nutritional status and mild airflow obstruction (e.g., a forced expiratory volume in 1 second greater than 70% of the predicted value) can tolerate pregnancy well. Patients who are not steatorrheic and have residual pancreatic function appear to have a favourable prognosis,[5,6] probably because in general they have milder disease. Patients who are homozygous for ΔF_{508} may have more severe underlying disease[7] and therefore a less favourable outcome than those with other genotypes.[8]

Patients at the other end of the spectrum are those with advanced CF, as indicated by a history of right-heart failure, severe hypoxemia, airway obstruction and malnutrition, in whom pregnancy would result in an unacceptably high risk for both the mother and the fetus.

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Such patients should be discouraged from becoming pregnant and counselled about the possible need for therapeutic abortion should pregnancy occur. Kent and Farquharson appropriately stress that the minimum level of pulmonary function at which pregnancy is inadvisable has not been clearly defined. Pregnancy was previously contraindicated in women with CF who had a forced vital capacity (FVC) of less than 50% of the predicted value,[9] but there are reports of a number of successful pregnancies in women with FVC values slightly below this level.[5,6] For such patients, the pregnancy may be allowed to continue provided the patient has not experienced a rapid decline in lung function or recurrent acute pulmonary exacerbations requiring intravenous antibiotic therapy 6 to 12 months before conception.[5,6] Such patients need to be closely monitored, and therapeutic abortion may be considered if their condition significantly deteriorates.

A pregnant woman with CF should be managed with close collaboration between an obstetrician, an internist, a family physician, a dietitian, a physical therapist and a social worker. Before becoming pregnant the patient should be made aware of the increased risk (2.5%) of having a child with CF or of the absolute certainty that the child will be a carrier of the disease. Genetic counselling and screening[10] should be offered. Screening of prospective fathers for the most common CF mutations is possible and currently identifies approximately 85% of carriers.[11] Women should be made aware of antenatal diagnosis through chorionic villus sampling. In addition, preconception counselling should cover the increased risks of fetal growth retardation, gestational diabetes and preterm labour and delivery. The early detection and management of these conditions requires meticulous antenatal care. The impact of chronic disease and the patient's reduced life expectancy on parenting ability should also be discussed.

During pregnancy, the monitoring of maternal weight gain and uterine fundal height, as well as repeat ultrasonography, are needed to identify fetal growth retardation. Patients should be tested for glucose intolerance at the first visit and at 26 to 30 weeks' gestation. As Kent and Farquharson emphasize, close attention should be paid to nutritional status throughout the pregnancy, supplementation being given if necessary. Pulmonary function should be monitored and systemic antipseudomonal antibiotic therapy instituted if the condition worsens. Antibiotics such as aminoglycosides and quinolines have potential teratogenic effects, although the former have been used in pregnant patients with CF without ill effects on the fetus.[5,6]

Labour may have to be induced at or before term because of suboptimal fetal growth, diabetes or increasing respiratory difficulty late in the third trimester. Epidural anesthesia is recommended, supplementary oxygen may be needed, and the fetus should be closely monitored for fetal distress. Women with CF can breastfeed successfully, and as Kent and Farquharson indicate, their breast milk probably has a normal sodium content once lactation has been established.

In summary, pregnancy can be tolerated by most women with CF and does not adversely affect pulmonary function or nutritional status, provided optimal medical and obstetric care is given. However, in patients with severe disease pregnancy is associated with an increased incidence of maternal and fetal complications, although selected patients with more advanced disease (who are stable in the pregravid period) can have a successful pregnancy.

Unfortunately, all the studies Kent and Farquharson reviewed have inherent deficiencies: small numbers of patients, a retrospective design or lack of appropriate controls. To rectify these problems the US CF Foundation is prospectively following women with CF who have been pregnant.[12] It is hoped that this effort will more clearly define the effect of pregnancy on the natural history of the disease and identify the parameters that have the greatest impact on outcome for both mother and child.

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