Medical genetics: advances in brief

Randomised study of risk of fetal loss related to early amniocentesis versus chorionic villus sampling

Although there has been much interest in the possibility of early amniocentesis as an alternative to chorionic villus sampling (CVS), there are few controlled trials to compare the techniques. Potential advantages of early amniocentesis include a smaller risk of miscarriage and a result more accurately reflecting the fetal karyotype without the possibility of placental confined mosaicism. In this study amniocentesis at 11-13 weeks was compared to CVS at 10-12 weeks. A filter was used when collecting the amniotic fluid to enhance the number of cells in the sample. Allocation to procedure was randomised. Fetal loss was compared between the groups, midtrimester scanning was offered, and all pregnancies were followed to term. The women were similar in the two groups at baseline. There were more culture failures in the CVS group (7/555) than the early amniocentesis group (1/54). The results were obtained almost exclusively from the amniocentesis samples; the authors suggest that these positive outcomes are secondary to the use of a filter. Fetal loss rates were similar between the two groups (5.4 and 4.8%), but a greater number of abnormal pregnancies would have miscarried before early amniocentesis. The trial was stopped before completion because of clustering of cases of talipes equinovarus in the early amniocentesis group (1.7%). There seemed to be increased likelihood of talipes if the procedure was done early and if there was amniotic fluid leakage. Other studies have also found a similar incidence of talipes and the authors explain it as perhaps secondary to a disruption of amniotic fluid pressure affecting physiological development of the lower limb. Sundberg and colleagues still hope that early amniocentesis may be a good method of early prenatal diagnosis but make some suggestions for future trials, such as use of smaller bore needles to reduce risk of leakage and delaying amniocentesis until late in the first trimester.

ANGELA BARNICOAT

Renal cystic disease in tuberous sclerosis: role of the polycystic kidney disease 1 gene

Renal involvement in patients with tuberous sclerosis (TS) is common, and manifestations may include angiomyolipomas, cystic disease, and renal cell carcinoma. The radiological and macroscopic appearance of the kidneys in TS patients resemble those found in autosomal dominant polycystic kidney disease (ADPKD), but the clinical onset is often early. Major genes for TS (TSC2) and ADPKD (PKD1) lie adjacent to each other on chromosome 16 (p13.3) suggesting that PKD1 may be involved in TS patients with renal involvement. In this study, 27 unrelated patients with TS and renal cystic disease were studied clinically, radiologically, and at a molecular level. Twenty-two patients had contiguous deletions of TSC2 and PKD1. (No similar mutations were found in 81 TS patients with TS but normal renal ultrasound scans.) In 17 of the 22 patients with constitutional deletions, cystic disease was severe with early renal insufficiency, but the one patient with a deletion of TSC2 and of only the 3 UTR of PKD1 had few cysts. Four patients were somatic mosaics and the severity of their cystic disease varied considerably. Mosaicism and mild cystic disease were also found in parents of three of the constitutionally deleted patients. Five patients without a contiguous deletion had relatively mild cystic disease; of these, three had gross rearrangements of TSC2 and two had no identifiable mutation. Significant renal cystic disease in TS usually occurs when the PKD1 gene is involved and mosaicism for large deletions of TSC2 and PKD1 occur quite often. In future, knowledge of TS patients' underlying mutation may influence the type of renal surveillance and follow-up recommended. It would also be interesting to review a population of patients with PKD1 to see how many have previously unsuspected involvement of the TSC2 gene.

FRANCES FLINTER