Pilot study of the acceptability of cystic fibrosis carrier testing during routine antenatal consultations in general practice

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SUMMARY

Background. *In 1989, the gene for cystic fibrosis was cloned and it became possible to detect carriers of the gene among the general population, including pregnant women.*

Aim. *The aim of the pilot study was to assess the acceptability of integrating cystic fibrosis carrier testing into antenatal care by general practitioners at the first booking appointment.*

Method. *Between 1 September 1991 and 31 August 1992, inclusive, all patients receiving routine antenatal care in a two-partner training practice in south Manchester were offered carrier testing for cystic fibrosis using a computer protocol for antenatal care developed by the practice. A questionnaire including a Spielberger state-trait anxiety inventory was sent to patients 2 weeks after they received the results of their carrier test, and interviews with the patients in their home were carried out 4 weeks and one year after they received the result.*

Results. *All but one patient (75 out of 76) booking before 14 weeks of pregnancy accepted the offer of cystic fibrosis carrier testing, and 96% (72 out of 75) felt that they had made the right decision and that they had enough time for discussion with their general practitioner before testing.*

Conclusions. *Cystic fibrosis carrier testing can be successfully integrated into the antenatal booking appointment in general practice and is acceptable to patients. This is a model for other genetic screening opportunities resulting from advances in medical genetics.*

Keywords: cystic fibrosis; mutation; antenatal; genetic counselling; screening.

Introduction

CYSTIC fibrosis is a severe disease, affecting one in every 2000 births in the UK, and is the commonest recessively inherited condition among the northern European Caucasian population, with a carrier frequency of one in 23 (one in 20 in the north-west of England). Carrier couples have a one in four risk of having an affected child.

In 1989, the gene for cystic fibrosis was cloned, and this made it possible to detect carriers in the general population. A number of different models for population-based carrier detection are being evaluated at the present time which test for only the commonest of more than 400 mutations. For example, testing for four common mutations (△F508, G551D, G542X and 621+1G>T) in the north-west of England detects 85% of carriers. Generally, carrier detection in pregnancy is performed in the hospital antenatal clinic, which delays until the second trimester the time when termination of affected pregnancies may be offered. Testing at the first hospital antenatal clinic appointment has been shown to delay screening by 4–6 weeks compared with carrier testing in primary care in very early pregnancy (average gestational age 8 weeks).[1] Additional advantages of screening in primary care include the familiar doctor and surgery setting when information and discussion about the test can be successfully integrated into the first antenatal booking appointment. The timing of the test allows for less pressurized consideration of reproduction options in the event of a carrier couple being detected .

Concerns have been raised that antenatal screening may cause anxiety to the patients, and it has been suggested that this can adversely affect infant bonding. Accordingly, patients who accepted cystic fibrosis carrier testing were subjects of an independent evaluation 4 weeks after their result and one year after the result.

Method

The methods used in the study for testing for carriers of the cystic fibrosis gene have been described previously.[2] Briefly, between 1 September 1991 and 31 August 1992, all patients booking before 14 weeks of pregnancy in a two-partner training practice in south Manchester (with a list size of 4400, predominantly Caucasians) were offered cystic fibrosis carrier testing at the booking appointment, and were allocated alternately to maternal (in which the woman was tested first and her partner only if she tested positive) or couple testing (in which the woman obtained a test sample from her partner before her result was known). All women offered testing were informed that this was a research project for which ethical approval had been obtained. They were counselled by their general practitioner and then given an explanatory leaflet. The leaflet included factual information on the disease, mode of inheritance, frequency of the gene in the population and the discussion of further prenatal diagnostic tests available for carrier couples. Those who accepted testing provided mouthwash samples in the surgery for DNA mutation analysis[3] in the DNA laboratory of St Mary's Hospital, Manchester. Those women offered couple testing were given the explanatory leaflet to take home for their partner to read and the kit with which to collect his mouthwash sample, to be returned to the practice the next day. Carrier testing was integrated into routine antenatal care, adding about 10 min to the consultation. The doctor was prompted on computer screen to prepare patients by discussing other antenatal screening procedures (for Down syndrome or neural tube defect) that would be offered at the hospital antenatal clinic. All patients were informed of their individual carrier test result and its risk to the pregnancy. Carriers were

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informed by their general practitioners within 5 days, and patients who tested negative were informed by post 2 weeks after testing. Carriers were asked if close relatives were planning a pregnancy, and these individuals were offered a test. Children of carriers were not offered screening, but information and testing in the future was discussed with the parent.[4]

A self-administered questionnaire and Spielberger state-trait anxiety inventory[5] were sent to participating patients 2 weeks after the test result. The questionnaire addressed the following areas: patients' knowledge of cystic fibrosis, the timing and the person offering the test, and the factors influencing the decision to have this test. This was followed one month later by a semi-structured interview in the patients' home conducted by a genetic associate (DS or NH), who was based in the Department of Medical Genetics at St Mary's Hospital, Manchester, independent of the general practice. The same genetic associate again followed up the patient in her home one year after the test result using a short questionnaire that focused on the woman's retention of knowledge of cystic fibrosis and her attitude to carrier testing, a Spielberger state-trait anxiety inventory and interview. Because the anxiety surrounding all antenatal tests has raised concern about infant bonding,[6] patients were also asked to complete a questionnaire relating to feelings about their pregnancy and the baby at one year after testing.

Results

All but one patient (75/76) booking before 14 weeks of pregnancy accepted the offer of cystic fibrosis carrier testing. The age of the patients at the time of the booking ranged from 16 to 38 years (median age 28 years). Forty-two patients were allocated to the maternal testing group and 34 to the couple testing group. In the maternal group, two carriers of cystic fibrosis were detected; both their partners tested negative. Three male carriers were detected in the couple group, but their partners tested negative. Only one patient reported a family history of cystic fibrosis (two cousins affected). No couple in which both partners were carriers was identified in this pilot study. When one partner was found to be a carrier of cystic fibrosis, the risk of the baby having cystic fibrosis was given as one in 480 (low risk). Eighteen women were not offered cystic fibrosis carrier testing for the following reasons: termination of pregnancy on social grounds (11); miscarriage before the booking appointment (2); and booking too late, i.e. after 14 weeks of pregnancy (5).

One-month follow-up

Sixty-four out of the 75 patients completed the one-month questionnaire and 57 of these were interviewed at home. Because explanatory literature was not provided before the initial counselling session, patients reported at the one-month evaluation that they had not expected to be offered the test for cystic fibrosis carrier status. Nevertheless, 64/75 (86%) felt they had had enough time to discuss the test with their general practitioner and that counselling was adequate. Sixty-seven out of 75 (90%) of patients did not want more time to make up their mind, but two patients would have liked to have seen a clinical geneticist. More than half believed that they knew something about cystic fibrosis, but more than half were unaware that cystic fibrosis is an inherited disease. Forty-eight out of 75 (64%) of patients were able to answer three or more out of five factual questions relating to information on the leaflet given at the time of the test, and 40/75 (54%) of patients still had the leaflet. Fifty-two out of 75 (70%) had shown their leaflet to their partner, family members and friends. Twenty-two out of 75 (30%) of patients reported feeling a little more worried while waiting for the test result (up to 2 weeks) and 49/75 (66%) of patients still had their results letters. Most patients who had received a negative result knew that they had a low risk of giving birth to a child with cystic fibrosis, although only two patients could give their risk figures precisely. Because only the four most common of 400 cystic fibrosis mutations are tested for, detecting 85% of carriers in the north-west population, a residual risk remains associated with a negative result. When both partners test negative for four mutations, the risk to the pregnancy of cystic fibrosis is given as one in 50 000. When only one partner is tested, result negative, the risk to the pregnancy is given as one in 9000. When one partner tests positive and the other negative for four mutations, the risk to the pregnancy is given as one in 480. Residual risk is a difficult concept for patients and doctors not trained in genetics to understand. Most patients accepted that no genetic test is perfect.

Why did patients accept cystic fibrosis carrier testing in pregnancy? Sixty-six out of 75 (88%) patients felt that all tests in pregnancy were important, 13/75 (17%) felt they could not refuse the test, 30/75 (33%) were sure that they did not want to have a child with cystic fibrosis and 6/75 (8%) wanted to know if they were a carrier of the cystic fibrosis gene.

What would patients have decided if both parents had been found to be carriers? Out of the 57 patients interviewed, 43 were asked this question. Nine said they would want prenatal diagnosis and termination if the fetus was found to be affected, four would consider prenatal diagnosis but not termination, and seven said they would not want prenatal diagnosis or termination of pregnancy. Seven women said they would rather wait for the results of prenatal diagnosis before making a decision and four wanted more information; seven said that they had not thought about it and five did not know what they would do. Some women (15) who already had healthy children perceived themselves to be at low risk of producing a child with a handicap.

Overall, 72/75 (96%) of patients felt that they had made the right decision to have a cystic fibrosis carrier test in early pregnancy. One patient regretted having the test.

One-year follow-up

Forty-four out of 64 patients (69%) who completed the questionnaire at one month also completed the questionnaire at one year and 37/44 (84%) were interviewed at home. The reasons for dropping out of the study were as follows: six patients could not be contacted, 12 declined further interview and two were inappropriate to follow-up. Most [42/44 (97%)] were glad to have had the test and did not regret their decision. Some patients expressed positive feelings about how the test was offered and the simplicity of providing a mouthwash sample. Eleven out of 44 (25%) thought it would be better to offer the test before conception and a few (five patients) thought that the test should be offered to couples only. Ten out of 44 (23%) women suggested that the test should be available in all general practitioner surgeries. For 3/44 (7%) patients, their negative test result had been reassuring when their baby was admitted to hospital in the first year of life and the possibility of cystic fibrosis had been raised. The results of the questionnaire on infant bonding did not show that early pregnancy testing for cystic fibrosis affected women's feelings about their pregnancy and the baby. Likewise, the Spielberger state-trait anxiety inventory at one year did not show any raised level of anxiety. Factual recall was good, and 35/44 (80%) of patients had retained information about cystic fibrosis and were able correctly to answer three out of five questions relating to the literature given at the beginning of pregnancy. Twenty out of 44 (46%) of patients reported that their raised awareness of cystic fibrosis after testing had been reinforced by

reading or watching a television programme on cystic fibrosis during the previous year.

Discussion

The high uptake of cystic fibrosis carrier screening in this pilot study probably reflects both the convenience of the GPs' surgery and the confidence felt by patients in a test offered by a doctor who is well known to them and has a responsibility for their continuing care. When interviewed independently at the practice, most patients stated that the counselling they received was sufficient to allow them to decide whether to accept the offer of screening. Similarly, there was no indication that patients felt rushed and most did not want more time to consider the test. This is supported by the patients' retention of knowledge about the test and its implications one year after testing. Furthermore, normal state-trait anxiety inventory scores at one year provide reassurance that testing in very early pregnancy does not create undue anxiety and stress during pregnancy.

Our experience in the pilot study and in a definitive study involving eight general practices with a population of nearly 50 000 (report in preparation) convinces us that general practice is the right setting for initiating genetic screening in pregnancy. Indeed, primary care has a crucial role in the management of all genetic disorders, and is the gatekeeper without which genetic services will be unable to cope with the acceleration of new screening, counselling and diagnostic problems that are being generated by the Human Genome Project.[7] We believe that general practitioners and primary care teams will form increasingly close relationships with genetics centres, no doubt assisted by developments in information technology. This means that general practitioners and other members of the primary health care team will require training if they are to be able to impart genetic information and risk accurately and with empathy. The management of genetic disorders and of the genetic predisposition to common diseases (such as cancer, diabetes, coronary heart disease and hypertension) will bring about changes in the organization of general practice, which is likely to undergo radical transformation in the shift from secondary to primary care.

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