Implementation of an antenatal serum screening programme for Down's syndrome in two districts (Brighton and Eastbourne)

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Abstract

Objectives **– To evaluate the introduction to two health districts of an antenatal serum screening programme for Down's syndrome using the triple test – measurement of α fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin concentrations in second trimester serum samples.**

Methods **– All women delivering at the main maternity units in both districts were eligible for the screening programme. A serum sample was taken between 15 and 22 weeks' gestation, confirmed by ultrasound scan. An estimated risk of 1 in 250 or greater was considered to be a screen positive result and further diagnostic tests were offered. As far as possible the outcome of all screened pregnancies was recorded, and babies with Down's syndrome born to women who declined serum screening were also identified.**

Results **– 6990 singleton pregnancies were screened over a two year period, representing an estimated uptake of 67% (6990/10 443). After a screen positive result 80% of women (168/211; 95% confidence interval 74·2 to 85·1%) opted for amniocentesis. The false positive rate was 2·9% (203/6979; 95% confidence interval 2·5 to 3·3%). The detection rate in the screened population was 73% (8/11). The estimated cost of identifying one Down's syndrome affected pregnancy was about £31 000.**

Conclusions **– Successful introduction of the triple test to health districts where there is no established serum screening programme for neural tube defects is possible. The programme seems to be acceptable to most of those screened. Uptake of the programme is sufficient to make it more effective than a policy for Down's syndrome screening dependent on age only.**

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In 1989 the antenatal Down's screening programme in Eastbourne district was reviewed. The main findings suggested that the screening programme, based on offering amniocentesis to older mothers, had little effect on the number of cases of Down's syndrome detected. At that time it was estimated that 70–79% of the older women in Eastbourne either declined or were not offered amniocentesis.[1] In the neighbouring district of Brighton a medical audit project found that the present age only policy had a detection rate of only 24%. As part of both reviews serum screening using the triple test[2] was considered. It was concluded that introduction of the serum screening programme should increase the detection rate of Down's syndrome affected pregnancies. Furthermore, the resources required would be most effectively used if shared by the two districts.

Both districts were granted funding by the South East Thames Regional Health Authority from the Medical Advances Fund for a two year period. The aim of the project was to evaluate the introduction of the triple test to districts which did not have teaching hospitals, regional protein reference laboratories, or α fetoprotein screening programmes for neural tube defects. The aim was not to repeat evaluation of the test itself.[2]

The first two years of the programme are described here, with particular attention paid to the problems encountered. Further details of the whole project and operational policies have been described elsewhere.[3]

Method

Brighton and Eastbourne are coastal districts of the United Kingdom. Brighton is geographically smaller but has a larger population. It is predominantly an urban district, whereas Eastbourne has a large rural hinterland.

ELIGIBILITY CRITERIA

Most women deliver at the main maternity unit in their district. Only those women planning to deliver at one of these units were eligible for the screening programme, regardless of their district of residence. Antenatal care is centralised in Eastbourne, whereas Brighton uses a community booking system based around doctors' surgeries. Twin pregnancies were excluded from the programme.

SELECTION OF ASSAY KITS

Both α fetoprotein and chorionic gonadotrophin were measured by time delayed fluorescence using Delfia kits (Wallac Oy, Turku, Finland), and maternal serum unconjugated oestriol was measured by radioimmunoassay

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using Amalex M (Kodak Clinical Diagnostics Ltd, Amersham, United Kingdom). Quality control serum samples at second trimester levels were obtained from Kodak Clinical Diagnostics Ltd.

INFORMED CONSENT

All women were given an information leaflet about the triple test, and the programme was discussed at their booking appointment with either a doctor, community midwife, or consultant obstetrician. Women signed the leaflet to indicate whether or not they wished to have the test, and this information was filed.

TIMING OF THE TEST

All women were offered an ultrasound scan to estimate gestational age before the blood sample was taken. Blood samples for screening were taken between 15 and 22 weeks' gestation, the majority between 16 and 18 weeks.

OLDER WOMEN

Women aged 36 years or over on the estimated date of delivery were also offered amniocentesis as they would have been under the previous age only policy. These women were usually seen at the booking appointment by the obstetrician and a management plan discussed and decided upon.

ORGANISATIONAL ISSUES

A steering group was established and before the programme began a screening coordinator was appointed. Regular seminars were held for participating doctors, midwives, and medical staff to explain the programme.

ESTIMATION OF RISK AND INFORMING OF RESULTS

The risk was derived with the 'alpha' software package.[2 4] The cut off for a screen positive result was agreed to be a risk of 1 in 250 or greater. Women with a screen positive result were told in person by their midwife, who also arranged for further discussion with the obstetrician at the next clinic. This system was tailored to suit individual requirements, was extremely flexible, and hinged on good communication between all professionals.

Screen positive results were telephoned to the women's general practitioners. Copies of all results (both screen positive and screen negative) were sent to the general practitioners. Screen negative results were thus available to the women at their next antenatal visit.

IDENTIFYING AFFECTED PREGNANCIES

Down's syndrome affected pregnancies were identified by amniocentesis at the regional cytogenetics laboratory at Guy's Hospital. Babies born with Down's syndrome to mothers who had either declined the triple test or had a screen negative result were also reported by the labour ward to the coordinator. Local paediatricians and medical officers were sent a monthly card aimed at identifying further cases. The system was based on an accepted proforma developed by the British Paediatric Surveillance Unit programme.[5] Copies of congenital malformation notifications from the Office of Population Censuses and Surveys were also scrutinised regularly.

The outcome of all the pregnancies screened in the programme was recorded on the programme database, overseen by the coordinator each week.

This report gives the results of the first two years of the programme including the follow up so that all the screened pregnancies have been completed.

Results

Between January 1991 and December 1992 6990 singleton pregnancies were screened. The outcome of all but 311 (4%) pregnancies is known. In most cases where the outcome is unknown the women left the districts between having the test and completing their pregnancy.

Uptake of the test was estimated in two ways. Firstly, simply as the number of tests performed (6990) as a percentage of the total number of women booking over the same period (10 443), giving an estimated uptake of 67%. Secondly, by reviewing 100 consecutive births in each district and noting the number of women who had had the test.[6] This showed that 131 of 200 women (66%) chose to have the test, 34 (17%) of the remainder declined, and 12 (6%) booked too late for the test.

Table 1 shows the screen positive rate and uptake of amniocentesis in the programme.

Eleven pregnancies were affected with Down's syndrome in the 6990 women screened. Three of these women had false negative results.

Table 2 shows the sensitivity and specificity of the test.

Women over 36 were also eligible for amniocentesis. Sixty seven women who had a screen negative triple test result also had amniocentesis on the grounds of raised maternal age.

Table 1 Screen positive rate and uptake of amniocentesis in the programme.

	Age at delivery		
	< 36	*≥ 36*	*Total*
Total number screened (%)	6413 (91·7)	577 (8·3)	6990 (100)
Screen positive (% of those screened)	118 (1·8)	93 (16·1)	211 (3)
Uptake of amniocentesis (% of those positive)	97 (82)	71 (76)	168 (80)

Table 2 Sensitivity and specificity of the test.

	Down's syndrome present	*Down's syndrome absent*
Screen positive	8	203
Screen negative	3	6776

Sensitivity = 73%.
Specificity = 97·1%.
False positive rate = 2·9%.
The odds of being a true positive, given a screen positive result, is 1 in 27.

None of these 67 women had a Down's syndrome affected pregnancy. Two hundred and fourteen women who had amniocentesis for raised maternal age did not have the triple test. Five pregnancies associated with Down's syndrome were identified in this group. In the same time period a further six babies with Down's syndrome were born to women of all ages who declined the test.

Discussion

UPTAKE RATE

It is difficult to calculate the precise uptake because of the time lag between women opting to have the test and actually having blood taken. The pregnancy might have miscarried or the women changed their minds or moved away during this interval.

The uptake rate of 67% is lower than that estimated elsewhere.[4] The study of 200 consecutive births is reassuring as it showed that most mothers not having the test had made a definite decision, rather than that the programme had missed them.[6]

The uptake of amniocentesis by women of all ages with a screen positive result was 80% (168/211).

DETECTION RATE

The small number of Down's syndrome affected pregnancies means that conclusions about detection rates in this programme must be made with caution. Six babies with Down's syndrome were born to mothers who declined the test. The community detection rate for serum screening is therefore 47% (8/17) compared with the detection rate or sensitivity of the triple test, which is 73% (8/11). Evaluation of projects on small groups over short time periods will always be difficult unless the incidence of the condition is high.

The false positive rate in this programme was 2·9% (203/6979; 95% confidence interval 2·5 to 3·3%). This is lower than the 4·1% reported elsewhere,[4] probably owing to the routine use of ultrasound scanning to estimate gestational age and good laboratory performance.

WORRY AND ANXIETY

The possible worry and anxiety caused by testing is often raised as a criticism of triple test programmes.[7] It is suggested that the test highlights the possibility that anyone may have a baby affected with Down's syndrome, and that as the triple test cannot identify all the 'at risk' group, some women worry about their baby throughout pregnancy.

In this programme attempts were made to minimise anxiety in a variety of ways: every woman received an information leaflet, the test was then discussed by the midwife at the booking appointment, and results were available routinely at the next antenatal appointment. Women with screen positive results were told in person by their midwife, who also arranged for them to discuss the result and future management with a consultant obstetrician in the clinic, usually on the following day. Women were never given their results on a Friday or a Saturday.

All results were copied to the general practitioners, who were also informed immediately by telephone if their patients had a screen positive result.

OLDER WOMEN AND AMNIOCENTESIS

The policy of offering women aged over 36 the option of amniocentesis was established because an individual woman's risk of having a pregnancy with a chromosomal abnormality increases with age.[8] Replacement of the age only policy with the serum screening programme increases the choice for all women. Older women now have the option of a screening test which reduces the risk of a possibly unnecessary amniocentesis.

Because the test does not detect all cases of Down's syndrome, and does not detect other chromosomal abnormalities, older women who are found to have an estimated low risk may go on to have an abnormal baby which could have been detected by amniocentesis. Screening for Down's syndrome, however, is more efficient if used in conjunction with other tests which use the same markers, such as α fetoprotein screening for neural tube defects.

Women over 36 should be encouraged to discuss the choices available to them with their midwife and obstetrician as parents may have different attitudes towards the pregnancy and towards having a baby with Down's syndrome. For example, because of the risk of miscarriage following amniocentesis a 39 year old woman who has had problems conceiving may be uncertain whether or not to have an amniocentesis. A high risk or low risk result may help her to decide. On the other hand, a 40 year old woman who already has a family may choose the certainty of amniocentesis despite its associated risks.

The triple test, like amniocentesis, should be seen as an additional aid to the management of the pregnancies of older mothers and should be discussed at the start of the pregnancy by parents and clinical staff so that the appropriate choice of test is made.

COSTS OF SCREENING

Unlike other programmes this project did not build on an existing programme of α fetoprotein screening.[4,9] In preparation for the project to become part of routine antenatal care the costs of the service were calculated at £30 for each test. This cost includes all biochemical analysis, office costs, ultrasound scanning, and counselling of all women at booking and after screen positive results.

To estimate the cost of the programme the following values were used: cost of one triple test = £30; cost of one amniocentesis and karyotyping = £200; cost of transportation of specimens from Eastbourne to Brighton for two years = £5000. Thus the total estimated

cost of the programme between January 1991 and December 1992 is given by:

Cost of 6990 tests at £30 each	£209 700
Cost of 168 amniocenteses at £200 each	£33 600
Transport costs from Eastbourne	£5 000
Total cost =	£248 300

The number of Down's syndrome pregnancies identified was eight, and thus the cost for detection of each pregnancy associated with Down's syndrome is £31 037. This cost relates only to the identification of a case and does not include the cost of terminating the pregnancy. The cost is comparable with that reported elsewhere.[4 9]

ULTRASOUND

The advantages of estimating gestational age using a dating scan rather than the last menstrual period alone are an increased detection rate and a reduced number of screen positive results. Before the serum screening programme began Eastbourne was performing routine early dating scans in the booking clinic as well as scans for anomaly at 18–20 weeks. Brighton was only carrying out scans for anomaly at 18–20 weeks. As part of the operational policy, arrangements were made with the department of radiology in Brighton to allow additional scans for those women having the triple test. By the end of the project over 99% of the women screened were having a dating scan.

COMMISSIONERS' CHALLENGES

Since the project began Brighton and Eastbourne Health Authorities have merged with Hastings Health Authority to form East Sussex Health Authority. The serum screening programme is now being extended to include Hastings. The main difficulty for East Sussex Health Authority commissioners is to organise an equitable antenatal screening programme for Down's syndrome for all its residents. For the purposes of this project, which was funded by the regional health authority, it was decided to offer the test only to women attending specific units for their antenatal care. Now this project has ended the commissioners must decide whether to screen those residents who have their antenatal care at units in the neighbouring districts.

If a neighbouring district is not already offering the test as part of its routine national health service antenatal care to all women, how practical will it be for the midwifery, obstetric and administrative staff to operate two different protocols? Furthermore, two women in the same antenatal clinic, but living in different health districts, may naturally be surprised to find that they are not being treated identically. Such problems can be overcome but only with careful organisation and planning.

OPT IN/OPT OUT POLICY

At the start of this project the intention was to have an opt out policy – that is, women would be tested unless they refused. After further consideration a signed opt in/opt out policy was preferred, and this has operated since January 1991.

A leaflet was used to provide information, and the test was discussed at the booking appointment. Women then signed the form at the end of the leaflet and indicated whether or not they wished to have the test; this information was filed.

Conclusions

The small number of pregnancies associated with Down's syndrome in the group screened and the number of outcomes remaining unknown (owing in most cases to mothers moving away before completing their pregnancies) mean that definite conclusions about the detection rate cannot be made. The numbers are sufficient, however, to draw conclusions about the programme's false positive rate.

The special features of our programme, which are not always features of similar screening programmes, are firstly, the accurate dating of each pregnancy by ultrasound scan and the consequence of this – a low false positive rate, and secondly, the follow up of all screened pregnancies, regardless of result.

There was no objective assessment of maternal anxiety in the programme. Ideally, all women and their partners should be counselled before the test and with the result. This ideal may be too expensive for the national health service and even if affordable might be too time consuming for the general public. Efforts were made to minimise maternal anxiety, and a personal visit for those with screen positive results was developed.

The programme was successfully established in the two districts and ran smoothly, owing to excellent cooperation and coordination between all the staff. The steering group had representatives from all relevant disciplines in both districts, and this included both commissioners and providers. The appointment of a screening coordinator was essential for the success of the programme.

Regular audit and quality assurance programmes in all the participating departments were carried out by the coordinator throughout the course of the programme.

The programme has continued to evolve and respond to changes in biochemical methods, obstetric and midwifery practice, and to feedback from users of the service. During the two years of the project the information leaflet has been amended and updated twice and includes information and comments from mothers, midwives, and general practitioners.

A national approach to antenatal screening for Down's syndrome has been called for frequently.[4] There is a need for a coordinating body to draw together the results of various small programmes from around the country. As more districts move to introduce a serum

screening programme they will need to consider the issues raised in this project.

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