On first trimester Down syndrome screening

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Women prefer first trimester screening for Down syndrome

Irene M. de Graaf, Tjeerd Tijmstra, Otto P. Bleker and Jan M.M. van Lith

We determined the knowledge of pregnant women about prenatal diagnostic and screening tests, and what tests they would choose if these were offered to them. Also the preference of pregnant women for late (second trimester) or early (first trimester) screening was assessed.

Pregnant women receiving antenatal care in a primary care system (n=62), and pregnant women that were offered a prenatal diagnostic test (n=148) at the Academic Medical Centre in Amsterdam, were included. Women in the first group are at low risk, i.e. younger than 36 years of age, the women in the second group are at higher risk of carrying a fetus with Down syndrome. A questionnaire was developed, that was sent to the woman’s home address, or the woman’s midwife handed it out at the next visit.

In both groups the response rate was more than 75%. There was no statistically significant difference between both groups, except for maternal age, gestational age and gravidity. Most women in both groups would prefer a screening test for Down syndrome to be performed in the first trimester of pregnancy. A combination of ultrasound nuchal translucency and first trimester serum screening was the option of choice. The knowledge about screening possibilities for Down syndrome are less well known to the women in the low risk group as compared to the women in the high risk group. The offer for a prenatal screening test would have been declined by more than 30 per cent of women at low risk for carrying a fetus with Down syndrome.

Our results clearly show that women prefer screening in the first trimester of pregnancy, using both serum and ultrasound tests. Compared to those women at higher risk, in women at low risk for Down syndrome the knowledge about new prenatal screening methods is less, as well as the demand for prenatal screening.
Chapter 10

Introduction

Prenatal diagnosis aims mainly at early detection of Down syndrome, the most common cause of serious mental handicap. In the Netherlands women at or older than 36 years of age at 18 weeks of gestation are offered invasive prenatal diagnostic procedures. However, most children with Down syndrome are born to women younger than 36 years of age.

Prenatal screening for Down syndrome in the second trimester of pregnancy using maternal age in combination with maternal serum markers is a more effective method to identify women at higher risk of carrying a Down syndrome fetus. This screening method, and further diagnostic procedure in the screen-positive group, can detect over 60% of Down syndrome fetuses (Wald et al. 1988; Haddow et al., 1998), at a false-positive rate of 5%.

First trimester screening tests, ultrasound measurement of the nuchal translucency thickness (Snijders et al., 1998) or maternal serum screening (de Graaf et al., 1999), appear to be as effective as second trimester tests, and may have advantages. With earlier screening the anxiety caused by the delay in obtaining results can be reduced (Green, 1994) and a second trimester termination of pregnancy can be avoided. Kornman et al. (1997) have shown, that women who made use of maternal serum screening in the second trimester would also do so in the first trimester. It also appeared that 44% of the women who were entitled to an invasive diagnostic test due to their age, would have allowed the result of first trimester biochemical screening to influence their decision regarding the performance of such tests.

The offer of screening for Down syndrome to pregnant women can create several problems. Many studies have been performed about anxiety induced by offering Down syndrome screening and by false-positive results (Marteau et al., 1993). Also aspects as decision regret (Tijmstra, 1991), the motives of women to accept the offer of prenatal diagnosis or screening (Santalahti et al., 1998; Heckerling et al., 1994), and what factors influence this uptake (Marteau et al., 1989) have been studied.

However, about the opinions and wishes of pregnant women regarding the offer of these tests is not much known. Our study was conducted to assess women’s opinions regarding the introduction of new screening methods. The aim of the study was to evaluate women’s knowledge about prenatal diagnostic and screening tests. We assessed whether pregnant women consider first trimester screening preferable to second trimester screening.
Patients and methods

The study group consisted of two groups of women, who were asked to complete a questionnaire. The questionnaire was anonymous, and could be returned after completion in a pre-paid envelope.

The first group comprised 195 women who visited the outpatient clinic of prenatal diagnosis at the Academic Medical Centre in Amsterdam. All women were scheduled for pre-test counseling at 10-12 weeks of gestation. During this visit the diagnostic procedures and screening possibilities (measurement of the nuchal translucency (NT) or second trimester maternal serum screening) were explained. Ninety women of the study group underwent an amniocentesis and 57 women a chorionic villus sampling. The remaining 48 women chose for a non-invasive procedure, like first trimester ultrasound screening (11), second trimester ultrasound screening (21) or second trimester maternal serum screening (16). In the majority of cases the indication for prenatal diagnosis was advanced maternal age (155). Other indications were family history of genetic disease (9), previously affected child (10), psychosocial (15), a positive maternal serum screening result (4) or enlarged NT (2). After the women had received the result of the test, a questionnaire was sent to their home address.

The second group comprised 80 women receiving routine antenatal care in a primary obstetrical care system. These women were not informed about Down syndrome screening or prenatal diagnosis; ultrasound and other screening methods for fetal anomalies in pregnancy were not routinely offered, unless a woman was 36 years or older. The midwife handed out the questionnaire.

Both groups of women were presented with descriptions of four situations concerning: invasive prenatal diagnosis (amniocentesis and CVS), first and second trimester maternal serum screening, ultrasound screening and combinations of the previously described methods (see appendix). After the description they were asked if the information given was known to them, and whether they thought this test should be offered to all pregnant women. More specific questions about screening or diagnosis, early or late screening, and the advantages of either one of them were included into the questionnaire.

The results in both groups were related to maternal age, gestational age, education, religion, opinion about abortion, gravidity, previous miscarriages and acquaintance with Down syndrome.
Result

Background of the respondents

The background characteristics of both groups of pregnant women participating in the study are listed in table 1. The two groups differed for maternal age (Chi-square test, p<0.05), gestational age (p=0.012) and gravidity (p=0.017).

Table 1. Background characteristics of the respondents in both groups.

<table>
<thead>
<tr>
<th>Response ( %)</th>
<th>High risk group</th>
<th>Low risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response ( %)</td>
<td>148 (76)</td>
<td>62 (78)</td>
</tr>
<tr>
<td>Mean maternal age (range)</td>
<td>37 (26-45)</td>
<td>31 (25-38)</td>
</tr>
<tr>
<td>Mean gestational age (range)</td>
<td>27 (13-39)</td>
<td>30 (13-40)</td>
</tr>
<tr>
<td>Completed high school ( %)</td>
<td>95 (64)</td>
<td>35 (56)</td>
</tr>
<tr>
<td>Religious ( %)</td>
<td>33 (22)</td>
<td>17 (27)</td>
</tr>
<tr>
<td>Not against abortion ( %)</td>
<td>146 (99)</td>
<td>53 (85)</td>
</tr>
<tr>
<td>Primigravid ( %)</td>
<td>38 (26)</td>
<td>26 (42)</td>
</tr>
<tr>
<td>Previous miscarriages ( %)</td>
<td>49 (33)</td>
<td>17 (27)</td>
</tr>
<tr>
<td>Acquaintance with Down syndrome ( %)</td>
<td>58 (39)</td>
<td>21 (34)</td>
</tr>
</tbody>
</table>

Invasive prenatal diagnosis

As expected almost all (99%) women in the high-risk group were aware of the information about invasive prenatal diagnostic procedures (table 2). Only one woman indicated not to be aware of the stated facts (see appendix). This knowledge is also present in the low-risk group (90%).

Table 2. Women's opinion about the offer and use of invasive tests.

<table>
<thead>
<tr>
<th>Knowledge about invasive tests present</th>
<th>High risk group</th>
<th>Low risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (%)</td>
<td>No (%)</td>
<td>Yes (%)</td>
</tr>
<tr>
<td>Knowledge about invasive tests present</td>
<td>147 (99)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>&quot;Amniocentesis or CVS should be offered to all pregnant women, irrespective of their age.&quot;</td>
<td>86 (58)</td>
<td>47 (32)</td>
</tr>
<tr>
<td>&quot;A test, that gives a small risk to cause a miscarriage, is not acceptable.&quot;</td>
<td>18 (12)</td>
<td>118 (80)</td>
</tr>
</tbody>
</table>

There is a high acceptability in both groups for invasive testing. On the question if an invasive procedure should be offered to all pregnant women, irrespective of maternal age, 58% of the high-risk women and 65% of the low-risk women answered positively, a statistically not significant difference (Chi-square).
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The risk that these tests can cause a miscarriage is for 12% and 31% women, respectively not acceptable. In the high risk group 9 of these 18 women underwent an invasive prenatal diagnostic procedure. The women answering positively differed not significantly according to previous miscarriage rate or maternal age with the women answering negatively.

Maternal serum screening

In the Netherlands physicians are not allowed to offer maternal serum screening to pregnant women. Therefore, informing women about maternal serum screening is not part of standard prenatal counseling. However, the information about maternal serum screening was known to 64 per cent of the high-risk women, and to a significantly lower percentage (31%) of the women with a lower risk for Down syndrome (table 3).

Table 3. Women's opinion about maternal serum screening.

<table>
<thead>
<tr>
<th></th>
<th>High-risk group</th>
<th>Low-risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (%) No (%)</td>
<td>Yes (%) No (%)</td>
</tr>
<tr>
<td>Knowledge about maternal serum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>screening present.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;Maternal serum screening should</td>
<td></td>
<td></td>
</tr>
<tr>
<td>be offered to all pregnant women.&quot;</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>95 (64) 53 (36)</td>
<td>19 (31) 43 (69)</td>
</tr>
</tbody>
</table>

Of the questioned women 82%, and 71%, respectively, felt that maternal serum screening should be offered to all pregnant women. We found no significant relation between education and the knowledge about maternal serum screening in the high-risk group.

There is a strong preference for maternal serum screening in the first trimester (table 4).

Table 4. Women’s preference for early or late maternal serum screening.

<table>
<thead>
<tr>
<th></th>
<th>High risk group</th>
<th>Low risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early (%) Late (%)</td>
<td>Early (%) Late (%)</td>
</tr>
<tr>
<td>&quot;If maternal serum screening was</td>
<td></td>
<td></td>
</tr>
<tr>
<td>offered to you, should you chose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>for the early or the late test?&quot;</td>
<td>140 (95) 4 (3)</td>
<td>53 (85) 3 (5)</td>
</tr>
</tbody>
</table>

Of the women in the high risk group 95% would prefer an earlier maternal serum screening test, as compared to 85% in the other group. Of all questioned women, only 7 indicated to prefer maternal serum screening later in pregnancy (4 in the high risk group and 3 in the low risk group). These women showed no differences according to age, gestational age, previous miscarriage rate, gravidity and education with the total group of respondents.
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Ultrasound and ultrasound screening

In a decentralized prenatal care system as in The Netherlands, ultrasound is not routinely offered to all pregnant women. Of the questioned pregnant population 90 and 81% respectively thought that an ultrasound scan, to determine the gestational age or to exclude a multiple pregnancy, should be offered to all pregnant women. Screening for Down syndrome using measurement of the nuchal translucency is studied over the past few years. Obviously, this method is known to a lesser extend than maternal serum screening; 76% of the high risk group and 32% of the low risk group. With the introduction of a new screening method, the need to inform all women is an important issue for care providers. We asked women if they thought that during ultrasound examination measurement of the nuchal translucency should be a standard procedure, or should be done only on request of the patient. Significantly more women (Chi-square; p=0.02) in the high-risk group thought that measuring the NT should be a standard procedure. Measuring the NT should be done only after informed consent was agreed to by 51 and 65%, respectively.

Table 5. Women's opinion about ultrasound NT screening.

<table>
<thead>
<tr>
<th>Knowledge about NT screening present.</th>
<th>High-risk group</th>
<th>Low risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes (%)</td>
<td>No (%)</td>
<td>Yes (%)</td>
</tr>
<tr>
<td>113 (76)</td>
<td>35 (24)</td>
<td>20 (32)</td>
</tr>
<tr>
<td>&quot;Measurement of the NT should be a standard procedure.&quot;</td>
<td>123 (83)</td>
<td>20 (14)</td>
</tr>
<tr>
<td>&quot;Measurement of the NT should be done only on request.&quot;</td>
<td>76 (51)</td>
<td>65 (44)</td>
</tr>
</tbody>
</table>

Combined screening tests

In the last section we asked women what screening tests to estimate the risk of carrying a fetus with Down syndrome, at what gestational age they preferred (see appendix). The options to chose were: no risk-estimating test at all, maternal serum screening in the second trimester, maternal serum screening in the first trimester, ultrasound NT screening in the first trimester or a combination of first trimester serum and ultrasound NT screening. The answers are listed in table 6.

In the low risk group, 11 women (26%) preferred first trimester serum screening, a significantly higher percentage than in the high-risk group. A combination of first trimester maternal serum screening and ultrasound NT screening was the preferred test combination for 83 and 62%, respectively.
Table 6: Preferred screening tests of the respondents.

<table>
<thead>
<tr>
<th>Test</th>
<th>High risk group</th>
<th>Low risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal serum screening in the second trimester.</td>
<td>2 (1%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Maternal serum screening in the first trimester.</td>
<td>8 (6%)</td>
<td>11 (26%)</td>
</tr>
<tr>
<td>Ultrasound NT screening in the first trimester.</td>
<td>13 (9%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Combined serum and ultrasound screening in the first trimester.</td>
<td>116 (83%)</td>
<td>26 (62%)</td>
</tr>
</tbody>
</table>

As main advantages for earlier screening were given earlier re-assurance (60 and 52%), and easier termination in case of an affected fetus, technically (61 and 65%) as well as less emotional (71 and 65%). The majority indicated not to see any advantages in later screening tests. Some women stated that a longer period to think things over might be an advantage; 5 in the high risk group and 4 in the low risk group.

In the low risk group 20 women (32%), and in the high risk group 9 women (6%) would never chose a test that only estimates the risk of carrying a fetus with Down syndrome. This statistically significant difference was not related to maternal age, gestational age or education.

Discussion

This study clearly demonstrates that women prefer screening for Down syndrome in the first trimester of pregnancy. Obviously, a combination of first trimester maternal serum and ultrasound NT screening is preferred. About one third of the general pregnant population will not make use of screening tests for Down syndrome offered to them.

There might be a bias in our study in that in the high-risk group women provided preferences about prenatal testing after they had decided which test to have. Since the questionnaire was returned anonymously, this can not be excluded.

The knowledge about invasive prenatal diagnosis, and the acceptability of invasive testing, is high (90%) in the general obstetric population. In our study 60% of the respondents even stated that CVS or amniocentesis should be offered to the entire pregnant population. This could mean that if we were to make these tests more widely available, e.g. to younger women, a significant increase in the number of tests carried out each year might occur. However, it is not sure that this will happen; in The Netherlands in 1966 in the 36-year-old and older age group only 45 per cent of the offered invasive tests was accepted (WPD, 1999). This cannot be seen as a consequence of lack of information (Mantingh, 1988). Routine offering of prenatal testing to a low-risk population in the USA resulted in a significant rate of rejection of invasive procedures (Druzin et al., 1993). Of the 591 women aged 35 years or younger, who
were given the offer of an invasive diagnostic procedure, only 133 (23%) accepted this offer.

In our study, knowledge about prenatal screening tests for Down syndrome, as second trimester maternal serum screening and first trimester ultrasound NT screening, is present to a much lesser extent (30%). This can be explained by the fact that in the Netherlands maternal serum screening or ultrasound are not routinely offered to pregnant women. Elsewhere, one of the prime objectives of a screening program is considered to provide information to all prospective parents. To allow them to make informed decisions (Royal College of Obstetricians and Gynaecologists, 1993). An amazing finding in our study is that almost half of the respondents, when questioned about ultrasound NT screening, state that measurement of the NT should be done routinely, and not only on request of the patient. Moreover, 55% of the respondents clearly stated that measuring the NT thickness should only be done if the patients requests for it.

The acceptability of screening tests in our study is high. Between 75 and 85% of the respondents thought that maternal serum screening or ultrasound NT screening should be offered to the entire pregnant population. This great demand for information about and possibility for prenatal screening tests for Down syndrome shows a marked difference with the policy of the Dutch Government concerning prenatal screening for Down syndrome.

When introducing a new screening method, care providers should be aware that some women are willing to participate in almost anything offered to them, and that the responsibility is with those who advice the use of the new technology. Roelofsen et al. (1993) found that women participate in serum screening because it seemed an obvious thing to do. These findings could not be confirmed in our study. In the group of women with a low risk for Down syndrome, 30% would not accept the offer of a screening test for Down syndrome.

In conclusion, in the general Dutch pregnant population the knowledge and acceptability of invasive prenatal diagnostic tests is high. Knowledge about screening tests is present to a much lesser extend, although there is a great demand for ultrasound and maternal serum screening. Pregnant women prefer screening for Down syndrome by a combined serum / NT- test to be performed in the first trimester. This could mean, that after a negative screening result in the first trimester, women will choose to wait with an invasive test till 15 weeks of gestation. Fewer CVS and more amniocentesis will be done, which means more reliable results and a lower miscarriage rate. Counseling remains of great importance; also in our study women found the risk that they actually had acceptable and yet decide to undergo an invasive procedure. Obviously pregnant
Women's choices

women know very well what they want; 30% would not accept screening. Health policy makers should understand our results well. The majority of all pregnant women wants to be informed about and to be offered first trimester screening tests for Down syndrome, and will accept those tests. Nowadays those tests should be made available to them.

References


WPD, Jaarverslag werkgroep prenatale diagnostiek, 1996: 36.

Appendix

1. Prenatal diagnosis

Pregnant women at or older than 36 years of age are at higher risk for a Down syndrome fetus. For instance, the risk for a Down syndrome fetus at the age of 38 years is 1 in 100, at the age of 28 years this risk is approximately 1 in 750. In the Netherlands, women at or older than 36 years of age are offered diagnostic tests for Down syndrome. These diagnostic tests are chorionic villus sampling or amniocentesis. These tests carry a miscarriage risk due to the procedure (a risk of 1 in 100 or 1%). If an affected fetus is found, the pregnancy can be terminated. Women younger than 36 years of age are not offered prenatal diagnostic tests.

1.1. Were you aware of this information?

2. Maternal serum screening

With maternal serum screening it can be determined if the risk of carrying a Down syndrome fetus is high or low. This maternal serum screenings test can be performed from 15 weeks of gestation onwards. If the result of the test is positive, which means a risk greater than 1 in 250, an amniocentesis can be performed. The result of the amniocentesis will be available at 18 weeks of gestation. If an affected fetus is found, the pregnancy can be terminated (by induction of labour).

2.1. Were you aware of this information?

2.2. Maternal serum screening should be offered to all pregnant women, irrespective of their age.

Recent studies have shown that maternal serum screening can be performed earlier in pregnancy, from 8 weeks of gestation onwards. If a higher risk for Down syndrome is found, chorionic villus sampling is still an option. The result from chorionic villus sampling will be available at 12 weeks of gestation. In case an affected fetus is found, the pregnancy can be terminated with suction.

2.3. If maternal serum screening was offered to you, should you chose for the early or late tests?

3. Ultrasound

Many pregnant women are offered ultrasound examination early in pregnancy. At ultrasound examination the gestational age can be determined. It is also possible to see if it is a singleton or multiple pregnancy. Ultrasound examination is save for mother and fetus.

3.1. Ultrasound examination should be offered to all pregnant women.

During ultrasound examination the nuchal translucency thickness can be measured, and the risk of carrying a Down syndrome fetus can be calculated. Measuring the nuchal translucency thickness can be performed between 11 and 13 weeks of gestation. If an enlarged nuchal translucency thickness is seen, the chance that the fetus has Down syndrome is increased. Chorionic villus sampling or amniocentesis can be performed to give a conclusive result. If an affected fetus is found, the pregnancy can be terminated.

3.2. Were you aware of this information?

3.3. Measurement of the NT should be a standard procedure during ultrasound examination.

3.4. Measurement of the NT should be done only on request of the patient.

4. Combined screening tests

4.1. What test should you chose to calculate your risk of carrying a fetus with Down syndrome?

a. I should never chose a test that only gives a risk estimation.
b. Maternal serum screening at 15 weeks of gestation.
c. Maternal serum screening at 8-13 weeks of gestation.
d. Ultrasound NT screening at 11-13 weeks of gestation.
e. A combination of ultrasound and maternal serum screening at 8-13 weeks of gestation.