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Guidelines for Genetic Amniocentesis

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1 INTRODUCTION

Amniocentesis is the commonest invasive prenatal diagnostic procedure performed in Hong Kong. There were a total of 3,846 amniocenteses performed in all Hospital Authority (HA) hospitals in 1997, compared with 308 chorionic villus sampling (CVS) and 83 fetal blood sampling during the same period (Hospital Authority Prenatal Diagnosis and Counseling Working Group). There is no information with regard to the number of procedures performed by private obstetricians.

2 COMMON INDICATIONS FOR GENETIC AMNIOCENTESIS

- 2.1 For detection of chromosomal abnormalities:
 - 2.1.1 Advanced maternal age – The commonly used cut-off is 35 years or above at expected date of confinement
 - 2.1.2 Previous babies with chromosomal abnormalities, e.g. trisomy 21, trisomy 18 and trisomy 13
 - 2.1.3 Couples known to be carriers of chromosomal translocation or inversion
 - 2.1.4 Positive biochemical screening test
 - 2.1.5 At risk of chromosomal abnormalities because of the presence of ultrasound markers or fetal anomalies

- 2.2 For detection of non-chromosomal genetic diseases:

Couples known to be at risk of having fetuses with major genetic diseases, e.g. thalassaemias, haemophilias, inborn errors of metabolism, diagnosable by molecular or biochemical study of amniotic fluid cells.

3 PROCEDURE

3.1 Timing

Genetic amniocentesis is usually performed at 15-20 weeks of gestation. Early amniocentesis before 14 weeks of gestation should preferably not be performed since it has been shown to be associated with a higher incidence of spontaneous abortion and neonatal talipes (4.4% and 1.8%) compared with CVS (2.3% and 0.2%)¹.

3.2 Ultrasound Assistance

3.2.1 Types

Amniocentesis is usually performed under some form of ultrasound assistance, either by “ultrasound guidance” or by “direct ultrasound control”. In “ultrasound guidance”, the operator determines the site of needle insertion using ultrasound, while the process of needle insertion is not under direct ultrasound visualization. This is seldom practised nowadays. In contrast, continuous visualization of the

needle during the whole process of insertion is required in “direct ultrasound control”. The practice of amniocentesis without any form of ultrasound assistance should be abandoned.

3.2.2 Advantages of ultrasound assistance

The use of ultrasound significantly reduces the number of failed procedures (dry tap) and blood-stained samples, and enables the avoidance of the placenta and fetal parts². “Direct ultrasound control” is preferred and should be the standard practice because when compared with “ultrasound guidance”, there are fewer dry taps, blood-stained samples and multiple needle insertions³⁻⁴.

3.3 Placental Passage

The placenta should preferably be avoided during amniocentesis. Passage through the placenta may be acceptable if it provides the only easy access to a pool of amniotic fluid, as increased miscarriage following amniocentesis with placental passage has not been observed⁵⁻⁶.

4 COMPLICATIONS

4.1 Fetal Loss

Fetal loss is the most important complication after amniocentesis. Spontaneous fetal loss must be taken into account for the estimation of amniocentesis-related complications. The largest randomized trial involving 4,606 women showed that amniocentesis was associated with a 1% excess of fetal loss (1.7% after amniocentesis vs. 0.7% without amniocentesis)⁷. A 20 gauge needle was used in the majority of cases in that study⁸. Roper et al reported a fetal loss of 1.2% within 8 weeks after

amniocenteses performed beyond 15 weeks’ gestation⁹. There was no control group for comparison. Since a smaller needle, usually 22 gauge, is used in most centers, the risk of procedure-related fetal loss may be lower than 1%.

Because there is a wide range in the reported incidence of procedure-related fetal loss after amniocentesis, local figures of individual centres should be used if available. However, a reliable estimation of this risk would require hundreds of procedures. In units where such a caseload is not met, the standard figure from the medical literature could be used for counselling.

4.2 Fetal Trauma

Fetal trauma attributed to amniocentesis had been described in case reports but is rare. It is likely that the use of direct ultrasound control will minimize the occurrence of this complication.

5 ALTERNATIVE INVASIVE SAMPLING METHODS

5.1 Currently, alternative invasive sampling methods for fetal karyotyping include chorionic villus sampling (CVS) and fetal blood sampling (FBS). Both CVS and FBS require more skill than amniocentesis and both are performed under direct ultrasound control.

5.2 CVS is usually performed between 10 and 13 weeks of gestation and therefore provides an earlier diagnosis. However, the benefits of earlier diagnosis with CVS must be set against the greater risk of pregnancy loss (odds ratio 1.33 when compared with amniocentesis)¹⁰.

5.3 The advantage of fetal blood sampling is the ability to obtain a full cytogenetic study within 3-5 days and therefore is particularly useful if a high-risk woman presents beyond 21 or 22 weeks of gestation. However, FBS is associated with a fetal loss rate of 1.4% even in experienced hands among low risk pregnancies (i.e. all pregnancies where pathological conditions have been excluded)¹¹. Therefore FBS should only

be considered when there is a clear clinical benefit.

extensive experience in prenatal diagnosis.

6 LABORATORY STUDIES

The vast majority of genetic amniocenteses are performed to exclude numerical chromosomal abnormalities in high-risk women. At present, cytogenetic study of cultured amniotic fluid cells, which usually takes 12-20 days, remains the standard method for a full evaluation of fetal karyotype. Rapid results may be available by using other techniques such as fluorescence in situ hybridization (FISH) or quantitative fluorescence polymerase chain reaction (PCR). However, results generated by these newer methods should be interpreted with an understanding of their limitations, which include but are not limited to, diagnosis of only a limited number of chromosomal abnormalities and the inability to study mosaicism.

7 COUNSELLING

7.1 Principle

All women should be counselled carefully before amniocentesis. The indication (Section 2), details of the procedure (Section 3) and complications (Section 4) should be explained clearly. The results generated from the study of the amniotic fluid sample (cytogenetic study, FISH, PCR etc), and the limitations of the results, should be communicated clearly to the women (Section 6). If alternative invasive sampling (Section 5) is offered, the relative advantages and disadvantages must be explained clearly in terms that the woman will understand.

7.2 Multiple Pregnancy

The counselling of genetic amniocentesis is more complicated in women with multiple pregnancy. Additional issues include the need for multiple sampling, the possibility of sampling error, and management options in case one of the fetuses is abnormal. Such counselling should preferably be provided by those with

8 RECOMMENDATIONS

- 8.1 Genetic amniocentesis should only be offered to women who are at high-risk of carrying a fetus with chromosomal or genetic disease. Genetic amniocentesis should not be routinely offered to all pregnant women, or for fetal sexing without a medical indication.
- 8.2 The indications, risks and alternative options should be adequately explained to all women, preferably with their partners. All women should be given adequate time to decide whether to proceed with amniocentesis or not.
- 8.3 The results generated from analysis of the amniotic fluid sample should be communicated to the women clearly, together with the limitations, as soon as possible.
- 8.4 Amniocentesis should only be performed by competent operators, or trainees under direct supervision by competent operators. An operator is usually deemed competent after performing at least 50 satisfactory amniocenteses under supervision¹².
- 8.5 Training in amniocentesis should preferably include ultrasound training to detect fetal structural abnormalities, patient counseling and management of pregnancies with abnormal test results¹².
- 8.6 Amniocentesis should be performed under direct ultrasound control, preferably with a needle that is below 20-gauge. The practice of amniocentesis without any form of ultrasound assistance should be abandoned. Amniocentesis should preferably be performed between 15 and 20 weeks of gestation
- 8.7 If fetal karyotyping before 14 weeks of gestation is necessary, chorionic villus sampling is a safer alternative than early amniocentesis.

- 8.8 The Rhesus status must be known and Rhesus-negative women should receive anti-D immunoglobulin after amniocentesis.
- 8.9 Complication rates and outcome of pregnancies after amniocentesis should be audited.
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This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.