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Prenatal Diagnosis Procedures and Techniques to Obtain a Diagnostic Fetal Specimen or Tissue: Maternal and Fetal Risks and Benefits

This Clinical Practice Guideline has been prepared by the Genetics Committee and approved by the Executive and Board of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: To provide maternity care providers and their patients with current evidence-based guidelines for maternal risk/benefit counselling for a prenatally identified at-risk pregnancy that requires ultrasound-guided prenatal diagnostic procedures and/or techniques for a genetic diagnosis and for subsequent pregnancy management decisions on questions such as level of obstetrical care provider, antenatal surveillance, location of care and delivery, and continuation or termination of pregnancy. This guideline is limited to maternal risk/benefit counselling and pregnancy management decisions for women who require, or are considering, an invasive ultrasound-guided procedure or technique for prenatal diagnosis.

Patient population: Pregnant women identified as having an increased risk of a fetal genetic abnormality secondary to the process of established prenatal screening protocols (maternal serum ± imaging, high-risk cell-free DNA results, abnormal diagnostic fetal imaging, or a positive family history of an inherited condition). These women may require or request counselling about pregnancy risks and benefits of an invasive ultrasound-guided procedure to determine the etiology, diagnosis, and/or pathology for the possible fetal anomaly or anomalies.

Evidence: Published literature was retrieved through searches of Medline, PubMed, and the Cochrane Library in and prior to June 2014 using an appropriate controlled vocabulary (prenatal diagnosis, amniocentesis, chorionic villi sampling, cordocentesis) and key words (prenatal screening, prenatal genetic counselling, post-procedural pregnancy loss rate). Results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies written in English and published from January 1985 to June 2014. Searches were updated on a regular basis and incorporated in the guideline to June 2014. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical speciality societies.

Key words: Prenatal diagnosis, prenatal genetic counselling, prenatal procedure risk, prenatal procedure benefit, amniocentesis, chorionic villi sampling, cordocentesis

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Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[60]

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.[60]

Values: The quality of evidence in this document was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

Health benefits, side effects, and risks: Patient informed consent, knowledge translation, genetic prenatal risk assessment, anxiety relief, anxiety creation, advocacy, understanding or limitation for fetal testing, pregnancy management choice, pregnancy complication or loss, timely and improved care for birth of a neonate with recognized morbidity.

Recommendations

1. The health care provider should counsel the at-risk pregnant woman on the different levels of genetic fetal testing in order for her to have a clear understanding and expectation of the level of testing and type of results that are offered. (III-B)
2. As part of the informed consent process, the health care provider should review with the at-risk pregnant woman the risks and benefits of in utero genetic diagnostic techniques associated with fetal genetic testing options. (III-A)
3. During risk/benefit counselling, the health care provider should advise that the best estimate of the pregnancy loss rate related to:
   a. amniocentesis is 0.5% to 1.0% (range 0.17 to 1.53%) (I)
   b. chorionic villus sampling is 0.5% to 1.0% (I) and
   c. cordocentesis or percutaneous umbilical blood sampling is 1.3% for fetuses with no anomalies and 1.3% to 25% for fetuses with single or multiple anomalies or intrauterine growth restriction. (II-2A)

INTRODUCTION

The traditional gold standard prenatal diagnostic results for the fetus are obtained through genetic analysis of pregnancy-related tissues from CVS, AC, or cordocentesis. Currently, maternal serum cfDNA is used for genetic screening, which is followed by traditional prenatal diagnostic techniques when a screen is positive. However, in the future, maternal serum cfDNA may itself come to be used for fetal diagnosis. The risks and benefits for the mother and fetus differ with invasive (traditional) and non-invasive (new) approaches.[1–9]

While the scope of prenatal genetic diagnosis is usually based on the identification of fetal karyotype abnormalities, other analyses of specific genetic mutations are also possible using amniocytes, chorionic villus, or fetal blood. Maternal serum cfDNA molecular technology has potential diagnostic capability, but at the present time is generally restricted to fetal sexing, fetal Rh typing, and screening for trisomies 21, 18, and 13. Other fetal genetic mutations have been identified from maternal serum cfDNA, but only on the basis of a case-by-case genetic differential diagnosis or when a specific family mutation has been identified.

Prenatal diagnostic counselling begins with collecting the patient's family history, ethnic background, past genetic, obstetrical, medical, and surgical history, and the indication for diagnostic fetal testing, and learning about the personal values and needs of the woman and her family. Parental karyotyping may be required for family or personal history of recurrent pregnancy loss or when there is a recognized family history for translocation carrier risks. Molecular genetic testing or referral for genetic assessment may be required when one of the parents presents characteristics suspicious of an undiagnosed genetic syndrome. Maternal and paternal