OPINION

HOW CAN WE REDUCE THE RISK OF MOTHER-TO-CHILD TRANSMISSION OF HIV DURING INVASIVE OBSTETRIC PROCEDURES?

C N Mnyani[1], *BA, MB ChB, FCOG*
E Nicolaou[2,3], *MD, FCOG, Dip Fet Med*
E Bera[4], *MB BCh, FCOG*
V Black[5], *BSc, MB BCh*
JC Hull[3], *MB BCh, MRCOG, FCOG, DTM&H*
J A McIntyre[1,6], *MB ChB, FRCOG*
[1]*Anova Health Institute, Johannesburg*
[2]*Maternal Fetal Medicine Centre, Morningside MediClinic, University of the Witwatersrand, Johannesburg*
[3]*Department of Obstetrics and Gynaecology, Chris Hani Baragwanath Academic Hospital, Johannesburg*
[4]*Department of Obstetrics and Gynaecology, Rahima Moosa Mother and Child Hospital, University of the Witwatersrand, Johannesburg*
[5]*Wits Reproductive Health and HIV Institute, University of the Witwatersrand, Johannesburg*
[6]*Centre for Infectious Diseases Epidemiology and Research, School of Public Health and Family Medicine, University of Cape Town*

Antenatal invasive obstetric procedures may be diagnostic or therapeutic, and are performed at different stages of pregnancy for various indications. The most common indication for an invasive procedure during pregnancy is for fetal karyotyping when a chromosomal abnormality or a genetic defect is suspected, either from the couple's history or from ultrasound assessment of the fetus. Other less common but equally important indications may be diagnostic (fetoscopy, fetal tissue sampling, estimation of fetal haemoglobin) or therapeutic (aspiration of various fetal cavities, fetal blood transfusion and embryo reductions). In a high HIV prevalence setting like South Africa, a significant proportion of pregnant women in need of invasive procedures will be HIV-infected.

There are no published data on the number of invasive procedures done in South Africa, but unpublished data from national laboratories suggest that the services are under-utilised.[1] In 2008, 6 out of 7 national laboratories received 529 amniocentesis specimens done for advanced maternal age – this in a background of 1 049 300 live births.[1,2]

In a high HIV prevalence setting like South Africa, where the estimated prevalence in antenatal clinic attendees was 29.4% in 2009, a significant proportion of pregnant women in need of invasive procedures will be HIV-infected.[3] HIV clinicians need to be aware of the risk of mother-to-child transmission of HIV (MTCT) associated with invasive procedures, and should also be aware of strategies available to minimise the risk. This information needs to be given to clients during the counselling session before the procedure, and HIV clinicians may also be asked to advise obstetric colleagues on optimal management in cases where a HIV-infected woman requires a prenatal invasive procedure.

TIMING OF INVASIVE PROCEDURES IN PREGNANCY

Below is a list of commonly performed antenatal invasive obstetric procedures and the gestational age at which each procedure can, or should, be performed.

- Amniocentesis: from 16 weeks
- Chorionic villus sampling: from 11 to 14 weeks
- Cordocentesis: from 20 weeks
- Fetoscopy: usually in the 2nd and 3rd trimesters
- Fetal tissue sampling (biopsies of organs, muscle, etc.): usually in the 2nd and 3rd trimesters
- Aspiration of various fetal cavities, shunt insertion: any gestational age – usually from 16 weeks
- Embryo reductions: from 11 weeks.

Several complications may occur with invasive procedures, and as part of pre-procedure counselling the woman/couple should be made aware of the risk of procedure-related complications. These include injury to maternal bowel, fetal injury, failure to obtain a sample, chorio-amnionitis, and most significantly fetal loss.[4] The Royal College of Obstetricians and Gynaecologists guideline on amniocentesis and chorionic villus sampling advises that patients should be informed of an additional 1% risk of fetal loss following an amniocentesis, and a slightly higher risk following chorionic villus sampling.[5] A 2003 Cochrane Review advises that, for second-trimester testing, amniocentesis is the safer procedure – safer than early amniocentesis or transcervical chorionic villus sampling.[6] For testing before 15 weeks of pregnancy, transabdominal chorionic villus sampling is the safer procedure.[6] There is no literature to suggest that the risk of procedure-related complications is higher in HIV-infected women.

RISK OF MTCT WITH ANTENATAL INVASIVE PROCEDURES

There is limited literature on invasive obstetric procedures in the context of maternal HIV infection. Few studies have been published on the topic, most with a small number of patients. Important risk factors for MTCT such as maternal HIV viral load and $CD4^+$ cell count are not always controlled for, and it may be difficult to infer causality in the reported cases of transmission after an invasive procedure. Without any maternal antiretroviral therapy initiated before an invasive procedure the risk of MTCT with invasive obstetric procedures is high, with rates of over 30% reported in some studies.[7] In one study evaluating the effect of various factors on the risk on MTCT, third-trimester amniocentesis without any antiretroviral cover was associated with a fourfold increase in the risk of MTCT.[8]

With the use of combination antiretroviral therapy before antenatal invasive procedures, the risk of MTCT is reported to be similar to that of a HIV-infected pregnant woman who has not had an invasive procedure.[9-11] In studies reporting no MTCT with combination antiretroviral therapy, a significant number of women were initiated on therapy before conception, and the majority were virally suppressed at the time of the procedure.[9] Despite the decrease in HIV transmission with antiretroviral cover, procedures that require more technical skills – such as chorionic villus sampling and cordocentesis – should still be avoided in the HIV-infected woman, as the risk of transmission to the fetus may be considerably increased.

Guidelines on the techniques of performing invasive procedures should be adhered to, and where possible the transplacental route should be avoided owing to the higher risk of transmission.[12]

RECOMMENDATIONS ON ANTIRETROVIRAL PROPHYLAXIS PRIOR TO INVASIVE PROCEDURES

There is now general consensus that any HIV-infected pregnant woman who needs to undergo an invasive obstetric procedure should have combination antiretroviral therapy initiated before the procedure, regardless of maternal $CD4^+$ cell count.[12,13] Ideally, antiretroviral therapy should be initiated at least 4 - 6 weeks prior to the procedure to achieve a significant level of maternal HIV viral suppression.[14] If the gestational age precludes waiting for the period of 4 - 6 weeks, the clinician can still go ahead with the procedure as continuation of combination antiretroviral therapy after the procedure should provide post-exposure prophylaxis. There is, however, no evidence on the role of post-procedure combination antiretroviral therapy as post-exposure prophylaxis, but an analogy between needling procedures and needle-stick injuries has been made.

There are no data available to suggest a viral load at which HIV transmission is unlikely to occur with an antenatal invasive procedure, and data from general MTCT studies cannot be extrapolated to cases with invasive procedures. However, both the Royal College of Obstetricians and Gynaecologists and the British HIV Association recommend an undetectable maternal viral load at the time of the invasive procedure.[12,13] If resources allow and there is sufficient time to wait before the invasive procedure, the maternal viral load should be determined as part of pre-procedure counselling.

In a high HIV prevalence setting like South Africa, it is advisable that a repeat HIV test be offered immediately before the invasive procedure if a woman has initially tested HIV-negative early in pregnancy.

Although there are no well-established approaches for managing HIV-infected women undergoing invasive procedures, international guidelines and literature published on the topic do offer guidance for the clinician. Local guidelines that are in line with international best practices, but also account for the nature of HIV/AIDS and obstetric practice in South Africa, are required to guide local clinicians.

REFERENCES

1. Urban MF, Stewart C, Ruppelt T, et al. Effectiveness of prenatal screening for Down syndrome on the basis of maternal age in Cape Town. S Afr Med J 2011;101:45-48.
2. Statistics South Africa. Mid-year Population Estimates, 2009. Pretoria: Statistics South Africa, 2009.
3. Department of Health. National Antenatal Sentinel HIV and Syphilis Prevalence Survey in South Africa, 2009. Pretoria: Department of Health, 2010.
4. RCOG Consent Advice No. 6. Amniocentesis, May 2006. Royal College of Obstetricians and Gynaecologists, London. http://www.rcog.org.uk/womens-health/clinical-guidance/amniocentesis-consent-advice (accessed 3 August 2011).
5. RCOG Green-top Guideline No. 8. Amniocentesis and chorionic villus sampling, June 2010. Royal College of Obstetricians and Gynaecologists, London. http://www.rcog.org.uk/womens-health/clinical-guidance/amniocentesis-and-chorionic-villus-sampling-green-top-8 (accessed 3 August 2011).
6. Alfirevic Z, Mujezinovic F, Sundberg K. Amniocentesis and chorionic villus sampling for prenatal diagnosis. Cochrane Database of Systematic Reviews 2003, Issue 3. Art. No.: CD003252. DOI: 10.1002/14651858.CD003252.
7. Mandelbrot L, Mayaux M, Bongain A, et al., for SEROGEST and The French Pediatric HIV Infection Study Group. Obstetric factors and mother-to-child transmission of human immunodeficiency virus type 1: The French perinatal cohorts. Am J Obstet Gynecol 1996;175(3):661-667.
8. Tess BH, Rodrigues LC, Newell ML, et al. Breastfeeding, genetic, obstetric and other risk factors associated with mother-to-child transmission of HIV-1 in Sao Paulo Collaborative Study for Vertical Transmission of HIV-1. AIDS 1999;12(5):513-520.
9. Mandelbrot L, Jasseron C, Ekoukou D, et al.; for the ANRS French Perinatal Cohort. Amniocentesis and mother-to-child human immunodeficiency virus transmission in the Agence Nationale de Recherches sur le SIDA et les Hépatites Virales French Perinatal Cohort. Am J Obstet Gynecol 2009;200:160.e1-160.e9
10. Somagliana E, Bucceri AM, Tibaldi C, et al. Early invasive diagnostic techniques in pregnant women who are infected with HIV: A multicenter case series. Am J Obstet Gynecol 2005;193:437-442.
11. Coll O, Suy A, Hernandez S, et al. Prenatal diagnosis in human immunodeficiency virus-infected women: a new screening program for chromosomal abnormalities. Am J Obstet Gynecol 2006;194:192-198.
12. de Ruiter A, Mercey D, Anderson J, et al. British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women, 2008. HIV Med 2008;9:452-502.
13. RCOG Green-top Guidelines No. 39. Management of HIV in pregnancy, June 2010. Royal College of Obstetricians and Gynaecologists, London. http://www.rcog.org.uk/womens-health/clinical-guidance/amniocentesis-consent-advice (accessed 18 July 2011).
14. European Collaborative Study, Patel D, Cortina-Borja M, Thorne C, et al. Time to undetectable viral load after highly active antiretroviral therapy initiation among HIV-infected pregnant women. Clin Infect Dis 2007;44(12):1647-1656.