Role of the pharmacist in perinatal management of HIV disease

Combination antiretroviral therapy (ART) is recommended during pregnancy to reduce the perinatal transmission of human immunodeficiency virus (HIV) and to improve maternal health. Prevention strategies that include the use of combination ART during pregnancy have helped achieve dramatic decreases in vertical HIV transmission, with reported transmission rates of <2% with optimal ART and other interventions (i.e., C-section delivery when indicated and the avoidance of breastfeeding) versus about 25% with no ART.

Effective perinatal ART has three crucial components. First, the expectant mother should receive combination ART, including at least three fully active antiretroviral drugs, with the goal of achieving an undetectable plasma HIV RNA viral load before delivery. Second, i.v. zidovudine should be administered to the mother at the onset of labor. Third, the infant should receive oral zidovudine immediately after birth and for six weeks thereafter. Other drugs may also be given to the infant in selected circumstances (e.g., the infant is delivered vaginally and the mother has a high viral load at the time of delivery).

While medical advances have yielded remarkable decreases in vertical HIV transmission, optimal outcomes in individual patients may be difficult to achieve, as there are numerous barriers to providing perinatal ART. A lack of prenatal care, the absence of routine prenatal testing, suboptimal ART adherence during pregnancy, and the sociodemographic characteristics of HIV-infected pregnant women, including high rates of homelessness and illicit drug use, continue to contribute to perinatal HIV infection in Canada and the United States.

Because prevention strategies depend on the identification of all HIV-infected pregnant women, the U.S. Centers for Disease Control and Prevention has recommended since 2003 that all pregnant women receive routine “opt-out” screening (i.e., HIV testing after notification of the patient that the test will be performed unless she chooses to decline or defer it, as opposed to “opt-in” screening, in which the test is offered and patients must give permission to proceed).

Routine prenatal opt-out HIV screening has been in place in the province of Alberta, Canada, since September 1998; as a result, more than 95% of all pregnant women who access the antenatal care system each year are tested for HIV. From January 1999 through February 2006, 43% of HIV-infected pregnant women in northern Alberta were diagnosed through prenatal screening. During that period, the rate of perinatal HIV infection in northern Alberta was 0.9%, compared with a rate of 21% during the period 1988–99. Those results compare favorably with data from the Canadian Perinatal HIV Surveillance Program indicating an overall vertical transmission rate of 2.9% nationwide during the first 13 years of the combination ART era (1997–2009) but only 0.9% among patients actually receiving combination ART. The decrease in perinatal HIV infection is likely primarily due to routine
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prenatal opt-out HIV screening and the use of perinatal ART. However, high rates of illicit drug use among HIV-infected pregnant women in our region, coupled with homelessness, psychiatric comorbidities, and cultural and geographic challenges, require significant efforts by a multidisciplinary team to achieve low rates of transmission.

In Alberta, comprehensive health care is provided to all HIV-infected individuals by separate programs respectively covering the northern and southern halves of the province. The Northern Alberta HIV Program operates out of three sites in the capital city of Edmonton and provides care for approximately 1400 patients (30% female) with diverse ethnic backgrounds, including Caucasian (45%), Aboriginal (28%), black (19%), and Hispanic–Asian (4%). The most common risk factors for HIV infection in this patient population are heterosexual sex and illicit i.v. drug use. HIV disease care is delivered by a multidisciplinary team of infectious diseases physicians (adult and pediatric), obstetricians, social workers, pharmacists, nurses, a diettitian, clinical psychologists, and a psychiatrist.

The Northern Alberta HIV Program has a total of five clinical pharmacists, or about 2.8 full-time equivalent (FTE) pharmacists. Three of those pharmacists have residency training, and 2 of them also have postbaccalaureate doctor of pharmacy degrees with advanced prescribing privileges and academic appointments at the University of Alberta Faculty of Pharmacy and Pharmaceutical Sciences. The first pharmacist started with the Northern Alberta HIV Program in a 0.4-FTE position in 1997. Over the subsequent decade, the role of the pharmacist evolved, and additional funding for increased staffing (currently, 2.4 FTE pharmacists) was secured to meet the expanding clinic needs. The pharmacists provide a broad scope of direct patient care services in a collaborative interdisciplinary model of care. Their responsibilities include consultations on ART selection, ART resistance interpretation, management of drug interactions and adverse effects, patient and staff education, adherence support, and management of comorbidities (e.g., smoking, hyperlipidemia, diabetes), as well as the development of patient-care-related protocols and tools.

In the past decade, our program has experienced a significant increase in the number of pregnancies among the HIV-infected women we serve (450 pregnancies during the period 1999–2011ª (Maria Stadnyk, Northern Alberta HIV Program, personal communication, 2011 Apr 6) versus 68 pregnancies during the period 1988–1990), with disproportionate representation of the Aboriginal, black, and i.v. drug user populations. This increase is driven by a shift in the demographics of HIV disease in the province: In addition to a rising rate of HIV infection among Albertan women in high-risk groups (i.e., Aboriginal, i.v. drug users), an economic boom in the province has led to an influx of immigrants from HIV-endemic areas. Although perinatal care is delivered by the multidisciplinary team, a perinatal public health nurse is also designated to closely support and monitor HIV-positive women during pregnancy and after delivery. Data on the estimated date of confinement, the delivery site, the use of ART, the virologic response to therapy, and neonatal outcomes are reviewed at monthly team rounds.

Pharmacists’ involvement in the provision of perinatal HIV disease care has evolved over time; with the increasing volume and complexity of pregnancies, it was evident that there were several gaps in care that pharmacists could help fill. Four key areas where pharmacists have made significant contributions are described below.

Perinatal care protocol. In an effort to standardize the management of these high-risk deliveries among sites, a protocol for perinatal management of HIV-infected women was developed by a pharmacist in 2000; the protocol was subsequently reviewed by clinicians with expertise in adult and pediatric infectious diseases, as well as the regional women’s health program and the program’s pharmacy service and Antimicrobial Subcommittee. In 2008, the development of an updated and more comprehensive protocol was spearheaded by a pharmacist specialist in HIV disease care, who served as a lead author and editor of all sections of the document with the exception of those addressing specific women’s health issues and labor and delivery procedures. Inservice education was provided by a team consisting of a pharmacist with expertise in HIV disease care, a physician, and a nurse, who worked together to educate inpatient pharmacists, obstetrical nurses, and Women’s Health staff at several urban hospitals. All protocol documents were posted on the Alberta Health Services (formerly Capital Health) website.

Major improvements over the first version of the protocol included the addition of a “care map” algorithm, preprinted maternal and infant orders, and comparison tables with guidance on dosing, adverse effects, and special tips for ART administration to pediatric patients. Although a formal audit has not been conducted, it is anticipated that the protocol refinements will likely help to minimize confusion on the delivery ward and prevent medication prescribing errors.

Antenatal care. The pregnant women we serve have diverse backgrounds and often complex health care needs. In addition to women living in very isolated and remote areas, the Northern Alberta HIV Program serves many immigrants from HIV-endemic areas who are affected by social, cultural, and language barriers that complicate ART adherence; other obstacles to medication adherence include addictions and substance use during pregnancy, mental health issues, homelessness, frequent admissions to prison systems and rehabilitation programs, poor access to health services, and fear of disclosure.

The primary goal during pregnancy is to identify and effectively treat HIV-positive women in order to prevent verti-
cal transmission. To achieve this goal, women must take combination ART daily for at least the last two trimesters of pregnancy. For maximal viral suppression and to prevent the development of drug resistance, excellent adherence to ART regimen is required.\textsuperscript{12}

In collaboration with other team members, the program’s pharmacists have major roles in HIV-infected women’s antenatal care. The pharmacists serve as consultants to the medical team regarding the selection of the most effective and least toxic ART regimen. Before therapy is initiated, the pharmacist conducts an extensive counseling session with the patient. The issues covered in those sessions include patient allergies and intolerances, current medications, current symptoms from pregnancy, past antiretrovirals (and potential drug resistance), medication coverage and payment issues, and social issues that may affect a client’s adherence to ART (e.g., language and cultural barriers, housing, family support, confidentiality concerns, substance abuse).

When the pharmacist meets with the patient, strategies to improve adherence are explored. Such strategies might include the use of

- Bubble-packed medications, with weekly dispensing and compliance assessments by the pharmacist,
- Beeper devices that remind patients to take medications,
- Pocket cards and other written materials listing the prescribed medications and administration schedules,
- Daily observed ART administration at a community pharmacy (e.g., if a patient is receiving methadone maintenance therapy),
- “Language and cultural brokers,” who attend clinic visits and assist with the follow-up of patients who speak foreign languages,
- Close follow-up in the community by a family member or outreach nurse, and
- Follow-up phone calls to the patient’s residence.

When possible, pregnant women are seen at least monthly by the team in the clinic. During the clinic visits, the pharmacist reviews all of the patient’s medications, and adverse effects and adherence issues are identified. Closer to the time of delivery, the team develops a birthing plan. Depending on the mother’s HIV viral load and any underlying resistance mutations near the time of delivery, suitable peripartum ART agents for the mother and infant are selected by the pharmacist and treating physicians. If a patient requires complex pharmacotherapy or is delivering in a remote area of the province, the pharmacist can ship the ARTs (maternal and neonatal), along with a communication letter and the perinatal protocol, to the appropriate rural hospital. To help ensure the seamless delivery of care, clinicians and other health care workers receive a copy of this letter.

**Intrapartum care.** As previously mentioned, Northern Alberta HIV Program pharmacists have been instrumental in developing materials and implementing a process to facilitate intrapartum inpatient care. As the intrapartum period is critical in preventing HIV transmission, every effort is made to achieve a smooth transition from the community to the inpatient setting. In a joint effort, the pharmacists and perinatal nurse facilitate inpatient care at the hospitals where most high-risk deliveries occur by communicating the birthing and ART plans for the mother and infant to the maternity ward at each facility. Once the infant is born, the nurse and pharmacist support ongoing maternal and neonatal care by providing discharge ART teaching and prescriptions, observing and reviewing drug administration techniques, and providing programmed beepers. Infant formula is distributed free of charge to the caregivers (breastfeeding is contraindicated due to the risk of HIV transmission). The team nurse discusses issues of future conception with the mother and makes arrangements for outpatient follow-up maternal and infant care.

**Postpartum care.** Immediately after hospital discharge, a designated public health nurse provides in-home follow-up and close consultations with the caregiver and infant. The mother is usually seen in the adult HIV clinic within two to four weeks of discharge, whereas the infant has follow-up in the pediatric HIV clinic at two weeks of age. Pharmacists are consulted by the nurse or clinic physicians to provide infant medication adherence assessments, to review administration techniques, and to manage the adverse effects of ART. Neonates receive a total of six weeks of ART prophylaxis. Infant formula is tracked and dispensed by the dietitian.

**Closing notes.** Despite numerous obstacles to care and medication adherence, the Northern Alberta HIV Program was able to achieve low rates of vertical HIV transmission (<1%) from January 1999 to February 2006.\textsuperscript{8} This success is likely multifactorial and can be attributed to the implementation of opt-out HIV testing during pregnancy, the use of combination ART, and the dedicated support of a multidisciplinary team.\textsuperscript{13}

Canadian consensus guidelines published in 2003 recommended that the optimal care of HIV-infected pregnant women and their children should involve physician specialists in adult and pediatric HIV disease and an obstetrician familiar with HIV disease issues; the guidelines also mentioned the valuable contributions that pharmacists and dietitians can make.\textsuperscript{14} British guidelines published in 2008 further elaborated the need for a multidisciplinary team approach to perinatal management of HIV infection but did not specifically mention the pharmacist as a part of the team.\textsuperscript{15} While current U.S. guidelines provide great detail on drug therapy, a discussion of how the guidelines should be implemented is lacking.\textsuperscript{1}

To our knowledge, the Northern Alberta HIV Program is one of the first to describe the significant contributions that pharmacists have made in this specialized area of practice. The program’s pharmacists have been instrumental in developing and implementing a comprehensive
multidisciplinary perinatal HIV disease management protocol. Pharmacists are involved in providing seamless patient care at all stages of pregnancy and during the postpartum period—services that are critical to optimizing maternal health and decreasing vertical HIV transmission.


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Michelle Foisy, B.Sc.Pharm., Pharm.D.,
Clinical Associate Professor and Clinical Pharmacist
mfoisy@pharmacy.ualberta.ca

Christine Hughes, B.Sc.Pharm.,
Pharm.D., Associate Professor and
Clinical Pharmacist
Northern Alberta HIV Program
Faculty of Pharmacy and Pharmaceutical Sciences
University of Alberta
3126 Dentistry/Pharmacy Centre
Edmonton, Alberta T6G 2N8, Canada

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