Nevirapine (NVP) is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that is used to treat adults and children with human immunodeficiency virus (HIV) infection. The drug was licensed in Canada in September 1998 and has been widely used in combination antiretroviral therapy regimens, usually along with two nucleoside reverse transcriptase inhibitors. NVP is, generally, well tolerated; however, up to 20% of patients may develop rash, with a severe rash occurring in 6% of patients and Stevens-Johnson syndrome reported in 0.5% of patients. A large number of NNRTI mutations have been documented, and a single mutation, K103N, confers a degree of broad NNRTI resistance. Distinctions occur in resistance patterns to different NNRTIs (1).

More recently, NVP has been used during pregnancy, both as a part of combination regimens to treat maternal HIV infection and for perinatal chemoprophylaxis to reduce mother-to-child transmission. The drug has several characteristics that make it attractive for use in perinatal HIV chemoprophylaxis. These characteristics include potent, rapid antiviral activity; rapid absorption across the gastrointestinal tract, placenta and blood brain barrier; a long half-life after a single dose (median 61 to 66 h in pregnant women and 45 to 64 h in infants); availability in both tablet and suspension formulations; and a relatively inexpensive cost.

There have been recent reports of serious adverse events attributed to NVP-containing regimens for postexposure prophylaxis, including hepatotoxicity and skin reactions (2). No serious toxicity has been reported among mother-infant pairs using this regimen for the prevention of perinatal transmission. Combination antiretroviral regimens containing NVP may be used in HIV-infected persons after considering the risks and benefits, and monitoring adverse reactions (2).

A number of studies, designed to assess the potential efficacy of shorter and less expensive perinatal prophylactic regimens, have been conducted in developing countries (3). A recent study in Uganda (HIVNET 012) involving breastfeeding, HIV-infected women, showed that a single 200 mg dose of NVP given to a mother at the onset of labour, combined with a single 2 mg/kg oral dose of NVP given to her infant at 48 to 72 h of age, reduced transmission by nearly 50% at six to eight weeks after birth compared with a very short regimen of zidovudine (ZDV) given orally during labour and to the infant for one week after birth (4). Transmission at age 12 months was 15.7% in the NVP group compared with 24.1% in the ZDV group, with relative risk reduction of 39% (5). Resistance to NVP was detected six weeks after birth in seven of 30 (23%) women and seven of 16 (44%) HIV-infected infants. Resistance patterns in mothers did not always match the patterns in their infants (6).

As a result of the studies on shorter and less expensive chemoprophylaxis regimens mentioned above, there have been recent changes in therapeutic guidelines in the United

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Nevirapine use to reduce mother-to-child transmission of HIV in Canada

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States for HIV-infected women in labour who received no previous therapy (7) and in British Columbia for women who have a detectable viral load at delivery (8). In these situations, a number of options for antiretroviral therapy during labour are available, as follows:

A. A single dose of NVP (200 mg) is given orally at the onset of labour, followed by a single dose of NVP (2 mg/kg) given to the newborn at age 48 h. This regimen is based on the HIVNET 012 study. The efficacy of NVP is unknown if the mother has a NVP-resistant virus.

B. Oral ZDV and 3TC are administered during labour, followed by one week of oral ZDV and 3TC given to the newborn. This regimen is based on the PETRA study (9); it has the potential toxicity that is associated with multiple drug exposure.

C. Intrapartum intravenous ZDV is given during labour based on the AIDS Clinical Trials Group 076 protocol (10), followed by six weeks of ZDV for the newborn. This regimen is based on epidemiological data compared with no ZDV treatment; due to the intravenous therapy component, there are administration and adherence issues.

D. A two-dose NVP regimen is combined with intrapartum intravenous ZDV and six weeks of ZDV for the newborn. This regimen is a theoretical consideration that combines regimens A and C; it has unknown efficacy and limited toxicity data.

NVP may be considered in perinatal chemoprophylaxis in the following circumstances:

- as a component of combination antiretroviral therapy given during pregnancy;
- as a single dose given during labour to women who had no previous therapy or who have a detectable viral load at delivery; and
- as a single postpartum dose administered to infants born to mothers who received no therapy or who received chemoprophylaxis at delivery only. Combined therapy using ZDV and NVP may be beneficial in this circumstance.

REFERENCES

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