Review Article

Perinatal HIV transmission and prevention

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Abstract

Perinatal HIV transmission occurs during pregnancy, labor, delivery or breastfeeding. Maternal factors associated with increased perinatal transmission include timing of infection, immune status, mode of delivery, co-existing sexually transmitted diseases, illicit drug use, increased duration of ruptured membranes, chorioamnionitis, viral load & invasive procedures. Infant risk factors include premature birth, low birth weight, skin & mucous membrane lesions. Preventive measures include anti retroviral therapy, treatment of chorioamnionitis with antibiotics, opting for caesarean section & avoiding breastfeeding. Early appropriate treatment of subclinical chorioamnionitis & virocidal cleaning of birth canal reduces perinatal HIV transmission. Caesarean section before onset of labour & membrane rupture reduces risk of mother–infant transmission by almost 50%. Vertical HIV transmission can occur through breast-feeding mostly during first 6 weeks of life & hence avoiding breastfeeding reduces transmission. Interrupting intrapartum transmission like giving ART in late gestation/ peri-partum & elective caesarean section reduce vertical HIV acquisition. As monotherapy & dual therapy are less effective, current guidelines recommend 2 nucleoside reverse transcriptase inhibitors & either a nonnucleoside reverse transcriptase inhibitor or a protease inhibitor. Perinatal HIV transmission can be reduced through a comprehensive approach including Universal access to prenatal care & routine HIV counselling & testing, access to antiretroviral therapy during pregnancy, at delivery & postpartum, education about treatment options & regimen adherence.

Keywords: Perinatal HIV, Anti-retroviral therapy, Zidovudine

Introduction

Perinatal HIV transmission occurs during pregnancy, labor, delivery or breastfeeding [1]. Only 1.5-2% of mother to child transmission occurs transplacentally during pregnancy, majority occurs during parturition or postnatally during breast-feeding. Risk of perinatal HIV transmission can be reduced from 43% to less than 2% if appropriate treatment is provided [2].

Risk Factors: Risk factors favouring perinatal HIV transmission include both maternal & infant factors. **Maternal factors** associated with increased perinatal transmission include timing of infection [3], maternal immune status [4], low CD4 cell count [5], mode of delivery [6], co-existing sexually transmitted diseases, active genital herpes, illicit drug use, cigarette smoking, unprotected sex with multiple partners, increased duration of ruptured membranes [7], haemorrhage during labour & chorioamnionitis.Invasive procedures like amniocentesis, placement of scalp electrodes, artificial rupture of membranes, episiotomy, forceps delivery increase risk by exposing fetus to maternal blood [5]. Maternal HIV viral load during pregnancy/ delivery has strong correlation with perinatal HIV transmission [8]. Perinatal HIV transmission is less than 1% for women on combination ART with undetectable HIV RNA. Maternal use of illicit drugs increase risk upto 3-fold higher of delivering HIV-infected baby [9]. Primary HIV infection occurring during pregnancy, advanced maternal age, firstborn of twins (born to HIV-infected mother) [10], advanced maternal AIDS-related illness, viral concentration in maternal genital fluids [11] are other risk factors. Maternal Vitamin A deficiency & malnutrition cause immune deficiency & disruption of mucosal integrity & increase HIV transmission [12]. Cigarette smoking during pregnancy also increase transmission [13].

Infant risk factors include premature birth, low birth weight, skin & mucous membrane lesions.

Prevention: Around 50–80% vertical transmission of HIV take place at around time of birth [14]. Preventive measures include anti retroviral therapy, treatment of chorioamnionitis with antibiotics, opting for caesarean section & avoiding breastfeeding.

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Antibiotics: Early appropriate treatment of subclinical chorioamnionitis prior to onset of spontaneous preterm labor reduces perinatal HIV transmission. Antiseptic vaginal & cervical washes have been suggested as an inexpensive way to reduce potential viral exposure to newborns during delivery. Chlorhexidine inhibits HIV viral replication in vitro at concentrations of 0.2% [15]. Virocidal cleansing of birth canal within 4 hours of membrane rupture prior to vaginal delivery reduces intrapartum HIV transmission. Screening & treatment for genital ulcer diseases such as syphilis also reduces HIV transmission [16].

Caesarean Delivery: A meta-analysis of 15 prospective studies showed that elective Caesarean section before onset of labour & membrane rupture reduced risk of mother–infant transmission by almost 50% when compared with non-elective Caesarean section/ vaginal delivery [6]. Pregnant women with HIV on medications throughout pregnancy with a HIV viral load <1000 copies/mL at 34-36 weeks of pregnancy may choose to have vaginal delivery as transmission risk is very low with low maternal viral load.1. For pregnant woman with viral load <1,000 copies/mL- cesarean delivery is not routinely recommended. 2.For pregnant woman with HIV RNA levels of >1,000 copies/mL at/ near time of delivery- delivery by scheduled cesarean section is recommended at 38 weeks gestation [17]. IV Zidovudine (ZDV) should be started 3 hours before scheduled cesarean delivery along with prophylactic antibiotics to decrease risk of maternal infection. 3.For women presenting with onset of labor/ ruptured membranes - it is unclear whether cesarean delivery prevents perinatal HIV transmission & decision should be individualized based on HIV viral load, current Anti-retroviral Therapy (ART) regimen, length of time since membrane rupture, duration of labor & other clinical factors. 4. For pregnant women with HIV infection planned for vaginal delivery- intervention to decrease interval to delivery like administration of oxytocin should be considered as duration of ruptured membranes is a risk factor for perinatal transmission. Procedures potentially increasing neonate's exposure to maternal blood like use of scalp electrodes, artificial rupture of membrane, operative interventions with forceps/ vacuum extractor & episiotomy should be avoided.

Breast Feeding: Vertical HIV transmission can occur through breast-feeding [18]. Viral load is high in colostrum [19]. Risk is high when maternal infection occurs within first few months following delivery [20]. Breast-feeding increases risk of HIV transmission by 5-20% & HIV transmission from breastfeeding is 14% from mothers with established HIV infection & 29% from mothers who acquire HIV after birth [21]. Most HIV infection from breastfeeding occurs during first 6 weeks of life, with a lower risk thereafter [22]. Transmission is increased with low maternal CD4+ cell counts, mastitis & prolonged exposure [23].

Anti-Retroviral therapy: Perinatal HIV transmission has declined by 90% since early 1990s after introduction of ART. Interrupting intrapartum transmission like giving ART in late gestation/ peri-partum & elective caesarean section reduce vertical HIV acquisition [24] by reducing maternal viral load in blood & genital secretions & by providing pre & postexposure prophylaxis for infant. Early treatment can reduce HIV transmission to less than 1% as compared to 16-25% without treatment. HIV-negative mothers with HIV-positive partner should take pre-exposure prophylaxis.

Guidelines on ART: If HIV RNA level is >500-1,000 copies/mL, drug-resistance testing is performed prior to starting/ changing ART. As monotherapy & dual therapy are less effective, current guidelines recommend 2 nucleoside reverse transcriptase inhibitors (NRTIs) & either a nonnucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI)[25].

ART Drugs: Preferred NRTI are Lamivudine & Zidovudine; Preferred NNRTI is Nevirapine; Preferred PI are Atazanavir, Ritonavir & Lopinavir. NVP is to be avoided for treatment of naive women with CD4 counts of more than 250 cells/L due to fatal hepatic toxicity & rash. Efavirenz is not recommended during first 5-6 weeks of pregnancy due to potential teratogenicity; safety data for etravirine, rilpivirine, maraviroc & enfuvirtide during pregnancy is insufficient.

Trials on ART: Zidovudine (ZDV) given orally during last weeks of pregnancy & intravenous (IV) during labor & delivery along with treatment of baby decreased perinatal transmission from 25.5% to 8.3% [26]. Another study showed 68% reduction of vertical HIV transmission with use of zidovudine [14]. ZDV plus lamivudine (3TC) intrapartum & for 1 week postpartum decreased transmission to 8.9% as compared to 15.3% without treatment [27]. Transmission is low with combination of 2 NRTIs. Between Nevirapine (NVP) & ZDV, single dose of NVP at onset of labor along with treatment of baby reduced perinatal transmission to 11.8% as compared to 20.0% with ZDV treatment [28].

Treatment Strategies based on ART status: 1. HIV-infected pregnant women currently receiving ART-continue ART during pregnancy. 2. HIV-infected pregnant women who are Anti retro viral (ARV) naive-

start potent combination ART. 3. HIV-infected pregnant women who previously have received ART but are currently not receiving any ARV medications – do ARV drug-resistance testing prior to initiating ART. 4. HIV-infected pregnant women presenting late in pregnancy-start ART promptly.

Raltegravir is preferred during late pregnancy for women who have high viral loads due to its ability to suppress viral load rapidly. Intrapartum ZDV should be given if HIV viral load is >400 copies/mL near time of delivery. 5.

HIV-infected women who have received no ARV before labour- ZDV should be started as a continuous infusion during labour. Apart from receiving ZDV for 6 weeks, the infant should also be given 3 doses of NVP during 1st week of life (at birth, 48 hours later & 96 hours after 2nd dose).

Intrapartum Management- 1. For women on ART with HIV RNA levels of >400 copies/mL near delivery- IV ZDV during labour can be considered but not compulsory along with usual ARV medications. 2. For women on ART with HIV RNA levels of <400 copies/mL near delivery- IV ZDV is recommended regardless of antepartum regimen. IV ZDV is usually given as 1-hour loading dose of 2 mg/kg followed by continuous infusion of 1 mg/kg/hour until delivery.

Treatment Strategies for infant delivered to HIV infected mother based on HIV RNA Load: 1. Maternal viral load of <50 HIV RNA copies/mL- Twice-daily ZDV monotherapy for 4 weeks. 2. Maternal viral load of >50 HIV RNA copies/mL- 3-drug therapy (ZDV, lamivudine and nevirapine) started within 72 hours after birth for 4 weeks. Perinatal HIV transmission can be reduced through a comprehensive approach including Universal access to prenatal care & routine HIV counselling & testing, access to antiretroviral therapy during pregnancy, at delivery & postpartum, education about treatment options & regimen adherence.

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