Review Article

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HIV infection: Transmission from mother to infant

Reddenna Languluri*, Sai Teja G

Department of Pharmacy Practice, Jagan's College of Pharmacy, Nellore-524346, Andhra Pradesh, India

Abstract

The etiologic mediator of AIDS is HIV, which belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses. HIV infection can be transmitted from an infected mother to her foetus through pregnancy, through delivery, or by breast-feeding. Lack of prophylactic antiretroviral therapy to the mother throughout pregnancy, labor, and delivery, and to the fetus subsequent to birth, the likelihood of transmission of HIV from mother to infant/fetus ranges from 15 to 25% in developed countries and from 25 to 35% in developing countries. Co-trimoxazole is the drug of choice. An effective well-coordinated multidisciplinary team is required to address the changing needs of infected and affected children and their caregivers. Continuity of care between inpatient and outpatient services, local referring-hospitals and the community needs to be developed.

Key words: AIDS; HIV infection; Mother; Fetus

1. Introduction

AIDS was primarily acknowledged in the United States in 1981. The disease became predictable in male and female injection drug users (IDUs) and shortly afterwards in recipients of blood transfusions and in haemophiliacs. It is comprehensible that the main possible etiologic agent of the outbreak was sexual (homosexual and heterosexual) contact and blood or blood products. Human immunodeficiency virus (HIV) was secluded in 1983 from a patient with lymphadenopathy and it was established evidently to be the causative agent of AIDS in 1984. Presently, AIDS is defined as an ill health characterized by one or more marker diseases [1-5].

2. Etiologic agent

The etiologic mediator of AIDS is HIV, which belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses. The human immunodeficiency viruses, HIV-1 and HIV-2, which are cytopathic viruses. On the whole, widespread cause of HIV disease all over the world is HIV-1. The HIV-2 was primarily recognized in 1986 in West African patients and was formerly restricted to West Africa [6]. Transmission of the Virus occurs from mother to child through in utero, at birth and breast milk [7].

3. Maternal-fetal/infant transmission

HIV infection can be transmitted from an infected mother to her fetus through pregnancy, through delivery, or by breast-feeding and it is tremendously significant form of transmission of HIV infection in developing countries, where the fraction of infected women to infected men is approximately 1:1. Virologic study of aborted fetuses shows that HIV can be transmitted to the fetus in the first and second trimester of pregnancy. Conversely, maternal transmission to the fetus happens usually in the peri-natal period. Two studies conducted in Rwanda and the earlier Zaire revealed that the comparative magnitude of mother to child transmissions were 23 to 30% before birth, 50 to 65% during birth, and 12 to 20% via breast-feeding. Lack of prophylactic antiretroviral therapy to the mother throughout pregnancy, labor, and delivery, and to the fetus subsequent birth, the likelihood of transmission of HIV from mother to infant/fetus ranges from 15 to 25% in developed countries and from 25 to 35% in developing countries [8-10].

The majority of observational studies approximate the risk of mother-to-child transmission (MTCT) lacking interventions to be about 15 20% in Europe and the USA and more than 30% in African populations. Other factors autonomously upsetting the rate of transmission comprise the HIV viral load and CD4 cell count of the mother at the time of delivery, extent of rupture of membranes, prematurity and mode of delivery. In the preceding eight years, the MTCT rate was condensed to less than 2% in the USA and in European countries by the prologue of antenatal testing, highly active antiretroviral therapy (HAART) for

*Corresponding author; E-mail: reddennapharmd@gmail.com. Mobile: 9866124220

mother requiring therapy, employment of antiretroviral therapy peri-natally even if not indicated on the reason of the mother's disease position, delivery by optional caesarean section, and abstaining from breastfeeding [11-15].

Women undergoing HAART for their disease who had unnoticeable HIV viral load at delivery have a very low risk of transmitting HIV to their baby and for those women not needing therapy for themselves, many guidelines propose zidovudine and optional caesarean section delivery, which confines exposure of mother and baby to antiretroviral drugs and is allied with a transmission rate of <2%. Current concerns about the probable relation between mitochondrial dysfunction and peri-natal exposure to antiretroviral nucleoside analogues, particularly zidovudine and lamivudine. It was established that the benefits of antiretroviral therapy (ART) in MTCT be more important than the possible adverse effects, but it is vital to prospectively pursue all infants born to infected women as the long-term effects of exposure to ART in-utero is unidentified. A European trial and a meta-analysis of cohort data from the USA and Europe displayed that in women taking no ART or ZDV monotherapy, optional CS delivery decreased the risk of MTCT by about 50% compared with vaginal or emergency CS delivery. This advance was extensively adopted in countries like Europe for women taking mono ART in pregnancy to prevent MTCT but, it has less extensively adopted in some countries such as the USA, where women are more probable to be given triple HAART in pregnancy in order to decrease viral load to below the level of detection. In these circumstances the accompanying benefit of an optional CS delivery remains uncertain [16-20].

In the developing countries, a number of studies have evaluated the efficacy of cheaper and less intricate perinatal ART regimens. These consist of intensive course of ZDV and for the most part particularly the usage of a single dose of the non-nucleoside reverse transcriptase inhibitor (NNRTI) drug nevirapine to the mother in labour and to the infant within the first three days of birth. This enormously inexpensive regimen has revealed to lessen transmission by virtually 40% compared with a regimen of intrapartum and neonatal ZDV for a week, still in breastfeeding women over a period of 12 months. It is currently being implemented together with antenatal HIV testing programmes in numerous parts of the budding world. A apprehension that resistance to nevirapine, which occurred in about 15% of women, might conciliation its employment in following pregnancies is almost certainly unsupported as virus proceeds to undomesticated type in the months subsequent to delivery. Studies had confirmed that curtailed regimens of zidovudine alone or in combination with lamivudine given to the mother during the last few weeks of pregnancy or even only during labor and delivery, and to the infant for a week or less, compact transmission to the infant by 50% compared to placebo.

One imperative study in Uganda established that a single dose of nevirapine given to the mother at the onset of labor followed by a single dose to the newborn within 72 h of birth reduced transmission by 50% compared with a regimen of zidovudine to the mother that began at the onset of labor and continued throughout labor and to the infant for 1 week subsequent to birth. Breastfeeding is an essential modality of transmission of HIV infection in developing countries, predominantly where mothers keep onto breast feed for long lasting periods. The risk factors for mother-to-child transmission of HIV via breastfeeding are not entirely unstated; factors that augment the possibility of transmission comprise noticeable levels of HIV in breast milk, the existence of mastitis, little maternal CD4+ T cell counts, and maternal vitamin A shortage. The risk of HIV infection via breastfeeding is premier in the early months of breastfeeding. In total, elite breastfeeding has reported to carry a lesser risk of HIV transmission than mixed feeding. Definitely, in developed countries breastfeeding by an infected mother must be avoided. Nevertheless, there is

Table 1. Centers for Disease Control revised classification system for HIV infection in children less than 13 years old

Category N:	**Category A:** mildly symptomatic	**Category B:** moderately symptomatic	**Category C:** severely symptomatic
No symptoms	• Lymphadenopathy • Hepatomegaly • Splenomegaly • Dermatitis • Parotitis • Recurrent upper respiratory tract infections, sinusitis or otitis media	• Anaemia, neutropenia or thrombocytopenia • Bacterial infections: pneumonia, bacteraemia (single episode) • Candidiasis, oropharyngeal • Cardiomyopathy • Diarrhoea, recurrent or chronic • Hepatatis • Herpes stomatitis, recurrent • Lymphoid interstitial pneumonia • Nephropathy • Persistent fever > 1 month • Varicella (persistent or complicated primary chickenpox or shingles)	• Serious bacterial infections, multiple or recurrent • Candidiasis (oesophageal, pulmonary) • Cytomegalovirus disease with onset of symptoms at age >1 month • Cryptosporidiosis or Isosporiasis with diarrhoea persisting 1 month • Encephalopathy • Lymphoma • Mycobacterium tuberculosis disseminated or extrapulmonary • Mycobacterium aviumcomplex or M. kansasii, disseminated • Pneumocystis cariniipneumonia • Progressive multifocal leucoencephalopathy • Toxoplasmosis of the brain with onset at age > 1 month • Wasting syndrome [28-32]

divergence concerning recommendations for breastfeeding in definite developing countries, where breast milk is the lone resource of sufficient nourishment as well as immunity against potentially severe infections for the infant. Studies are being conducted to establish whether alternating administration of nevirapine, which has a moderately extended half-life, to uninfected babies born of infected mothers reduces the occurrence of infection via breastfeeding. The most favourable advance to avert transmission by infected mothers who choose to breast-feed would be towards providing continual treatment to the infected mother where reasonable [21-25].

4. Diagnosis

IgG antibodies to HIV are inertly transferred to almost all children born to infected mothers. Detection of proviral HIV DNA by polymerase chain reaction (PCR), 93% of infected infants can be diagnoseb by one month of age, and basically all by three months. Immune complex dissociated p24 antigen assays (ICD p24 ag) are done to identify the nuclear capsid antigen of the virus by a commercial ELISA kit. T-cell subsets and extent of immunoglobulins (Ig) are non-specific tests [26]. Around 70% of perinatally infected children will enclose a few signs or symptoms by 12 months. In the dearth of antiretroviral therapy, the average age at which children upgrading to AIDS are about six years, and 25–30% have died by this age. Disease sequence in children in developing countries is further quick. Generally common clinical description associated with HIV infection includes constant generalised lymphadenopathy,hepatosplenomegaly, chronic or recurrent diarrhoea, fever, and recurrent otitis or sinusitis. Continual oral candidiasis, bilateral parotitis or neurological signs are other explicit of HIV infection. Periodic and repeatedly harsh bacterial infections are common and comprise pneumonia, cellulitis, local abscesses, osteomyelitis, septic arthritis and occult bacteraemia. The widespread contributory organisms are *Pneumococci*, *Salmonellae*, *Staphylococci*, *Streptococci* and *Haemophilus influenzae*. Children with HIV infection recurrently encompass hypergammaglobulinaemia due to dysregulated polyclonal B-cell activation. Pulmonary disease is a central reason of morbidity and mortality. Lymphoid interstitial pneumonitis (LIP), manifested by multiple foci of proliferating lymphocytes in the lung interstitium, happening in 20–30% of vertically infected children. The widespread neurological manifestations are hypertonic diplegia, developmental delay or acquired microcephaly. Malignancy, such as Kaposi's sarcoma or lymphoma, is a comparatively exceptional characteristic of paediatric HIV disease, secretarial for merely 1–2% of AIDS-defining ill health in children. The extensively used surrogate markers for predicting disease sequence in children are the CD4 values and viral load. Very elevated viral loads are commonly established in infected children, principally subsequent perinatal transmission. The endeavour of whichever intervention for HIV-infected children should keep the best achievable quality of life for the children as long as feasible, with the expectation that they will be capable to acquire benefit of budding curative treatment in the upcoming and predictable way pondering the likely benefits of novel treatments next to the necessity for amplified monitoring, achievable toxicities and restraining prospect therapeutic options [33-38].

5. Antiretroviral therapy

Short- and long-term toxicities of particular drugs and drug classes are largely alike in children as in adults. Recent national Italian survey of children revealed that 58% of children presenting with at least one side-effect on HAART. The mainly widespread toxicities are gastrointestinal symptoms and skin rashes [39-41].

Table 2. Issues to consider when starting therapy in children

- Parental (and child) willingness
- Likelihood of excellent long term adherence
- What formulations could this child take?
- What pharmacokinetic data are offered for infants/children/adolescents?
- What understanding have other family members had on antiretroviral drugs?

6. Prophylactic measures

Every child with swiftly failing CD4 counts or counts always less than 15% should be on prophylaxis. Cotrimoxazole is the drug of choice. Routine active immunization schedules should be followed for HIV-infected or -exposed infants, with the exception that BCG should not be given to symptomatically infected children because of the risk of dissemination. Regular intravenous immunoglobulin infusions (400 mg/kg every 28 days) should be reserved for children with recurrent bacterial infections despite good compliance with cotrimoxazole prophylaxis, or those with proven hypogammaglobulinaemia [44].

Table 3. Recommendations for use of HAART in children

- Must start HAART if Clinical stage C or immunological stage 3 disease (CD4 < 15%)
- Consider HAART if Clinical stage B or
  Gradually declining CD4% falling below 25%, or
  High viral load (>106 RNA copies/mL if age <1 year, >105 if age over 1 year) Infant <12 months, regardless of CD4 or viral load
- Suspend HAART if Stage N or A disease CD4>25%
  Low viral load:
  <105 in children between 1 and 30 months
  <50 000 copies/mL in children >30 months [42-43]

7. Supportive care

The parents' own health, their social isolation and feelings of guilt compound the difficulties of caring for a sick child. An effective well-coordinated multidisciplinary

team is required to address the changing needs of infected and affected children and their caregivers. Continuity of care between inpatient and outpatient services, local referring hospitals and the community needs to be developed. Prevention remains the top priority in managing HIV infection in children. Reducing national perinatal transmission rates to below 2% is an achievable target that can only be realized if HIV-infected mothers can be identified prenatally and offered appropriate interventions. This will require continued effort by health professionals, public health planners and community organizations [45-46].

8. Conclusion

An effective well-coordinated multidisciplinary team is required to address the changing needs of infected and affected children and their caregivers. Continuity of care between inpatient and outpatient services, local referring hospitals and the community needs to be developed.

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