Antiretroviral Therapy in Pregnant Women of Florence

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More than 95% of human immunodeficiency virus (HIV) pediatric infections are the result of vertical transmission from mother to child during pregnancy, intrapartum, or in developing countries, through breastfeeding. Antiretroviral therapy, elective cesarean section and no breastfeeding have reduced the rate of transmission below 5%.[1]

In the Infectious Diseases Unit of Careggi Hospital, Firenze, Italy, between 1997 and 1999, 18 HIV-1 infected pregnant women gave birth to 24 children. All the pregnant women received antiretroviral therapy: zidovudine (ZDV) in four cases, two nucleoside reverse transcriptase inhibitors (NRTI) in eight cases, two NRTI combined with protease inhibitors (PI) in five cases, and two NRTI combined with nevirapine (NVP) in two cases (patient 4 switched from nelfinavir to nevirapine). The antiretroviral preferred regimen in three women did not include ZDV. Eight infected pregnant women delivered vaginally, whereas the others delivered by elective cesarean section. In every case, intravenous ZDV was given intrapartum and ZDV syrup was given to infants, as per AIDS Clinical Trial Group (ACTG) 076 protocol.[2]

Table 1 shows CD4 cell counts (last value before delivery), HIV RNA (last value before delivery), antiretroviral regimen, and mode of delivery of the infected pregnant women. Mother-to-child transmission of HIV-1 occurred in only 1 of 18 treated pregnant women (first pregnancy of patient 1). In the infant, HIV polymerase chain reaction (PCR) was found to be positive at 1 week of age; the infected newborn girl was small for gestational age and affected by trisomy 18, a chromosomal disorder producing many developmental abnormalities. In this case, a three-part regimen of ZDV, as per ACTG 076 protocol,[2] and elective cesarean section were carried out.

The antiretroviral regimen in patient 1 (2nd pregnancy), patient 5, and patient 8 did not include ZDV, because of HIV-1 ZDV-resistant strains; genotypic analysis detected gene mutation 70R in patient 1 and patient 8 and detected gene mutations 41Lw, 67N, 215w, 70R, 219Q in patient 5. Stavudine (d4T) + lamivudine (3TC) was the therapeutic regimen, started at 14 weeks, preferred for the ZDV-experienced patient 8; at that time, CD4 cell count was 248 μg/mL and plasma HIV-1 RNA levels were 9600 copies/mL; the woman refused PI and NVP.

Every antiretroviral regimen, including highly active antiretroviral therapy (HAART), was well-tolerated during pregnancy by the 18 women and by the 24 newborns. No short-term adverse effects were observed and follow-up of the infants is continuing. The adverse effects of fetal exposure to antiretroviral drugs are still unknown,[3,4] and long-term follow-up of all children exposed to antiretroviral therapy, beyond that initiated before pregnancy, is important with the increasing use of HAART. Actually, more women become pregnant while already on a combination of antiretroviral therapy, and there are still few data on the use of ZDV, the most used antiretroviral drug in pregnancy, in the first trimester of pregnancy. Studies suggest that ZDV may have a direct toxic effect on the developing mouse embryo in early stages of pregnancy.[5]

The optimal therapeutic regimen for HIV-1-infected pregnant women should be, as far as possible, the same as that for HIV-1-infected nonpregnant women; thus, ZDV cannot always be included as a component of the antiretroviral regimen in HIV-1-infected pregnant women. Actually ZDV-resistant strains of HIV-1, measured by genetic analysis, appear to be an inevitable consequence of antiviral treatment for HIV-1, and virologic failure, dangerous for fetuses, is often associated with resistance.

In conclusion, an antiretroviral regimen that does not include ZDV, in ZDV-experienced individuals, may be required in pregnancy too. Finally, there are no guidelines about the suitable therapeutic regimen or single drug (i.e., d4T or 3TC in pregnancy + NVP intrapartum) for pregnant women not on antiretroviral therapy, ZDV intolerant women, or those unlikely to respond to ZDV (naive

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Table 1. CD4 Cell Count, Viral Load, Antiretroviral Regimen, Mode of Delivery of Pregnant Women and Actual Infection and Clinical Status of the Children

						Children	
Patient	*CD4/mL*	*HIV-RNA (copies/mL)*	*Antiretroviral Regimen*	*Mode of Delivery*	*Note*	*HIV PCR*	*Current Clinical Status*
1	558	35,000	ZDV started at 14 wk	CS	1st pregnancy	HIV+	Trisomy 18
1	692	1,800	d4T-3TC-NFV started before pregnancy	CS	2nd pregnancy	HIV–	No AE
2	756	3,000	ZDV-3TC started at 38 wk	CS		HIV–	No AE
3	1306	<50	ZDV started at 14 wk	CS		HIV–	No AE
4	435	<50	ZDV-3TC-NFV at 6 wk	VD	NFV stopped and NVP started at 15 wk	HIV–	No AE
5	348	4,700	d4T-3TC-IDV started before pregnancy	CS	HAART stopped between 6 and 14 wk	HIV–	No AE
6	639	<50	ZDV-3TC started at 14 wk	CS	Twin birth	HIV–	No AE
7	615	3,700	ZDV-3TC started at 24 wk	CS	Twin birth	HIV–	No AE
8	349	250	d4T-3TC started at 14 wk	VD		HIV–	No AE
9	470	2,700	ZDV started at 14 wk	CS		HIV–	No AE
10	601	4,000	ZDV-ddC started before pregnancy	VD	DDC stopped at 8 wk; pPROM	HIV–	No AE
11	468	4,400	ZDV-3TC-NVP started before pregnancy	VD		HIV–	No AE
12	462	600	ZDV started at 14 wk	VD	ZDV not administered intrapartum	HIV–	No AE
13	1194	<50	ZDV-3TC started at 25 wk	CS		HIV–	No AE
14	1090	120	ZDV-3TC started before pregnancy	CS	Twin birth	HIV–	No AE
15	119	100,000	ZDV-3TC started before pregnancy	VD		HIV–	No AE
16	1191	<50	ZDV-3TC started at 33 wk	VD		HIV–	No AE
17	376	12,000	ZDV-NVP-NFV started at 33 wk	CS		HIV–	No AE
18	442	1,900	ZDV-ddC-SQV started before pregnancy	VD	Triplet birth	HIV–	No AE

ZDV = zidovudine; d4T = stavudine; 3TC = lamivudine; NFV = nelfinavir; IDV = indinavir; ddC = zalcitabine; NVP = nevirapine; SQV = saquinavir; CS = cesarean section; VD = vaginal delivery; HAART = highly active antiretroviral therapy; pPROM = preterm premature rupture of membranes; HIV PCR = human immunodeficiency virus polymerase chain reaction; AE = adverse event; HIV+ = HIV-positive; HIV– = HIV-negative.

with genotypic or phenotypic resistance to ZDV), who would not otherwise start antiviral therapy.

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