

Effective prophylaxis of vertical HIV transmission despite late diagnosis of the mother's infection

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Abstract

A newborn male born was admitted on the second day of life to the paediatric ward of the Provincial Observation and Infectious Hospital suspected of vertical human immunodeficiency virus (HIV) infection. In the mother's study, on the day of delivery, HIV markers were detected, which were confirmed on the following day by Western blotting. In the first day of life, the child was vaccinated against tuberculosis and hepatitis B. Before entering the infectious hospital ward, the newborn was breastfed several times until the second day of life. Laboratory tests showed elevated total bilirubin (6.82 mg/dl) with unincorporated bilirubin predominance (6.4 mg/dl). The viraemia of HIV RNA, which was undetectable, was evaluated by PCR. In accordance with the recommendations of the Polish AIDS Scientific Society, the newborn used triple antiretroviral therapy (ARV): zidovudine (ZDV), lamivudine (3TC), and nevirapine (NVP) in the following doses: ZDV – 2 × 14 mg for each day, 3TC – 2 × 7 mg for each day, and NVP – 2 × 7 mg. Treatment with ZDV and 3TC was continued for four weeks, and NVP for the first two weeks of therapy. In the presented case, during the three- and six-month follow-up visits HIV viral RNA was undetectable, the CD4+ cell amount was normal, and there were no deviations in psychomotor development, indicating that the prophylaxis of vertical HIV was effective.

HIV AIDS Rev 2019; 18, 3: 228-231
DOI: <https://doi.org/10.5114/hivar.2019.85950>

Key words: vertical infection, HIV, newborn, prophylaxis.

Introduction

According to the National Centre for AIDS data, about 101 children infected with human immunodeficiency virus (HIV) live in Poland [1]. Over 90% of them were infected as a result of vertical transmission [2]. Most often, 65-75% are infected in the perinatal period. The most important risk factors include:

- no or unsuccessful antiretroviral treatment of the mother during pregnancy,

- the mother's disease or high HIV viral load above 10,000 copies/ml,
- premature rupture of the membranes,
- exposure of the foetus to the mother's blood and secretions,
- bloody amniotic fluid sucked from the airways,
- pre-term birth before the end of the 37th week of gestation or childbirth after the 40th week of gestation,
- termination of labour within four hours of the discharge of the pregnant women's foetal waters with detectable HIV viral load (over 50 copies/ml),

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Article history:
Received: 17.03.2019
Received in revised form: 25.04.2019
Accepted: 26.04.2019
Available online: 20.04.2019

International Journal
of HIV-Related Problems

**HIV & AIDS
Review**

- a ticking vessel,
- crotch,
- inflammation of the membranes and placenta,
- child's delivery to the mother's blood during Caesarean section, egg through injury.

Thanks to the protective role of the placenta, the risk of intrauterine HIV infection is lower and amounts to 5-10%. The risk of newborn infections during breastfeeding is estimated at 5-10%, but it increases to 40% when the feeding time is prolonged beyond six months [3-5].

The implementation of vertical HIV infection prevention reduces the risk of infecting a child to below 1% [2, 6]. The article presents a case of successful prophylaxis of vertical HIV infection despite the late diagnosis of this infection in the mother.

Case description

The newborn male born at 41 weeks of gestation I, by nature, with a birth weight of 3460 g, rated at 10 points on the Apgar scale, was admitted on the second day of life to the Paediatric Ward of the Provincial Observation and Infectious Hospital, suspected of vertical HIV infection. Only hepatitis B and the syphilis were excluded in the child during the mother's pregnancy. In the study of the mother, on the day of delivery, HIV markers (current anti-HIV-1 and anti-HIV-2 antibodies and the current Ag p24 antigen) were detected, which were confirmed on the following day by Western blotting. On the first day of life, without knowing the mother's serological status, the child was vaccinated against tuberculosis and hepatitis B. Before entering the infectious hospital ward, the newborn was breastfed several times until the second day of life.

At the time of adoption, the boy's general condition was assessed as good. The child was viable, and in the physical examination, yellowing of the skin and sclera was found from the deviations. Laboratory tests showed elevated to-

tal bilirubin (6.82 mg/dl) with unincorporated bilirubin predominance (6.4 mg/dl) (Table 1). The viraemia of HIV RNA, which was undetectable, was evaluated by PCR. The CD4+ lymphocyte count was 1293 cells/ μ l (Table 1). Cytomegalovirus infection, HBV infection, and *Toxoplasma gondii* infection were excluded. Ultrasound of the abdominal cavity and peritoneal cavity of the head gave a correct picture.

In the child's mother, the value of HIV viral load on the second day after delivery was 5.01×10^3 copies/ml and the CD4+ count was 501 cells/ μ l lymphocytes (Table 1).

In accordance with the recommendations of the Polish AIDS Scientific Society, the newborn used triple antiretroviral therapy (ARV): zidovudine (ZDV), lamivudine (3TC), and nevirapine (NVP) in the following doses: ZDV – 2×14 mg per day, 3TC – 2×7 mg per day, and NVP – 2×7 mg (Tables 3-5). Treatment with ZDV and 3TC was continued for four weeks, and NVP for the first two weeks of therapy. During the stay in the ward the newborn baby was fed with modified milk and had a body weight of 400 grams by the 18th day of life. During the treatment, haematological

Table 1. Laboratory tests for mother and child on admission to the hospital

Laboratory test	Newborn	Mother
PCR HIV RNA (copies/ml)	Undetectable	5.01×10^3
The number of CD4+ lymphocytes (cells/ μ l)	1293	501
HIV DUO ELISA (anti-HIV-1, anti-HIV-2 + Ag p24)	Not performed*	Positive
Western blot HIV-1/HIV-2	Not performed*	Positive
Total bilirubin (mg/dl)	6.82	–
Direct bilirubin (mg/dl)	0.40	–

*In children up to 3 years of age, positive results of serological tests do not have diagnostic value

Table 2. Studies performed in a child at week 1-2, 3, and 6 months of age

Laboratory test	Monitoring of antiretroviral therapy		
	1-2 weeks of age – at hospital discharge	3 months	6 months
PCR HIV RNA (copies/ml)	Undetectable	Undetectable	Undetectable
The number of CD4+ lymphocytes (cells/ μ l)	1293	2945	4415
Morphology	Without deviations	Without deviations	Without deviations
ALAT (U/l)	19	18	16
ASPAT (U/l)	30	23	–
GGTP (U/l)	62	27	–
Total bilirubin (mg/dl)	0.42	–	–
Direct bilirubin (mg/dl)	0.33	–	–
Glucose (mg/dl)	76	93	140
Creatinine (mg/dl)	0.37	–	0.21

Table 3. Dosage of zidovudine in the prophylaxis of vertical transmission in newborns [3, 9]

Newborn born \geq 35 weeks of pregnancy	Orally: 4 mg/kg every 12 hours for 4 weeks, or Intravenous: 3 mg/kg every 12 hours for 4 weeks
Premature baby \geq 30 and $<$ 35 weeks of pregnancy	Orally: 2 mg/kg every 12 hours for 2 weeks, later 3 mg/kg every 12 hours for 2 weeks Intravenous: 1.5 mg/kg every 12 hours for 2 weeks, later 2.3 mg/kg every 12 hours for 2 weeks
Premature baby $<$ 30 weeks of pregnancy	Orally (non-preferred route of supply at this age): 2 mg/kg every 12 hours for 4 weeks Intravenous: 1.5 mg/kg every 12 hours for 4 weeks

Table 4. Scheme of nevirapine administration in prophylaxis of vertical transmission in newborns [3, 9]

Birth weight	Administration hours for nevirapine	Oral dose
1.5-2 kg	0-48 hours	8 mg
	48 hours from the first dose	8 mg
	96 hours from the second dose	8 mg
$>$ 2 kg	0-48 hours	12 mg
	48 hours from the first dose	12 mg
	96 hours from the second dose	12 mg

Table 5. Diagram of triple antiretroviral therapy in the prophylaxis of vertical transmission in newborns [3, 9]

Zidovudine	Doses as in Table 2
Lamivudine	Orally: 2 mg/kg every 12 hours for 4 weeks
Nevirapine	Orally: 2 mg/kg every 24 hours for 7 days, later 2 mg/kg every 12 hours for 7 days

parameters, glucose concentration, and hepatic and renal function indicators were monitored – no abnormalities were observed (Table 2). The concentration of total bilirubin on the day of discharge decreased to normal values (0.42 mg/dl) (Table 2). Control laboratory tests (PCR HIV RNA, CD4+ cell count, peripheral blood count, ALT and AST activity, bilirubin, lipid, glucose, creatinine, creatinine clearance, urinalysis) were performed after the child completed the first, third, and sixth month (Table 2). During all control visits, the boy's psychomotor development was assessed as normal, no deviations were observed in the physical examination, the laboratory results remained within the normal range, HIV viral load was undetectable, and the CD4+ cell count was more than 1200 cells/ μ l (Table 2).

Conclusions

Prevention of vertical HIV reduces the risk of this infection from 25-30% to less than 1% [6]. Currently in Poland, in accordance with the Regulation of the Minister

of Health of October 4, 2012 on standards of conduct and medical procedures for the provision of health services, perinatal care exercised over a woman during physiological pregnancy, physiological labour, puerperium, and neonatal care, during pregnancy two tests for HIV infection are to be carried out: the first by the 10th week of pregnancy and the second one between the 33rd and 37th weeks of pregnancy [6-8]. If the tests are not performed during pregnancy, it is recommended that they are performed by the patient on admission to delivery or in the newborn. In the case described, the patient was not tested for HIV infection during pregnancy, and the blood for examination for this infection was taken on the day of delivery.

A pregnant woman diagnosed with HIV requires the implementation of antiretroviral treatment and procedures that minimise the risk of transmission of the virus from mother to child. These include, among others: avoiding groin incision and the use of ticks and obstetric vacuums [2, 6]. The patient should be looked after by specialists in the following: infectious diseases, obstetrics, neonatology, and paediatrics. The goal of antiretroviral therapy is to achieve a full viral suppression (HIV viral load below 50 copies/ml). Assessment of HIV viral load in pregnancy is carried out monthly. The choice of how to terminate the pregnancy depends on the concentration of HIV viral load, and it should be carried out in the 34th-36th week of pregnancy. There is a relationship between HIV transmission in the mother and the risk of vertical transmission, and it is over 41% if the HIV viral load is higher than 100,000 copies/ml, while for HIV viral load less than 1000 copies/ml the risk of rejection is less than 1%. In the case of undetectable viral load, it is recommended to terminate the pregnancy by natural delivery, while for HIV viral load over 50 copies/ml, the solution should be performed in the 38th week of pregnancy with an elective Caesarean section [4, 6]. A pregnant woman diagnosed with HIV late or on the day of childbirth (before the baby is born) should be treated as having a high HIV viral load, and terminated pregnancy by scheduled Caesarean section [4-7]. In the present case, the patient gave birth by natural means, and according to the recommendations, delivery should take place through a planned Caesarean section [4, 6].

In the management of a newborn baby, HIV(+) procedures are different from those of a healthy mother [3, 8]. Children of HIV-infected mothers should be washed imme-

diately after delivery, upper respiratory tract content should be removed, antiretroviral treatment should be started, modified breast milk introduced, and lactation suppressed in the mother; vaccination against tuberculosis should be delayed until HIV infection is excluded [3, 6].

The newborn should receive prophylactic antiretroviral therapy as soon as possible after delivery and no later than 48 hours after birth [3, 8, 9]. The decision to choose medication for prevention depends on the estimated risk of HIV transmission.

In children with uncomplicated births and mothers treated successfully with antiretroviral therapy, with low risk of vertical transmission of HIV, with only detectable HIV viral load, ZDV alone is used for four weeks in doses dependent on foetal age (Table 3) [3, 9].

In cases of increased risk of vertical transmission of HIV, in which the mother received anti-HIV treatment during pregnancy and the HIV viral load at 34-36 weeks of pregnancy is higher than 50 copies/ml, but lower than 1000 copies/ml, and the child was born via nature or prematurely, ZDV and three oral doses of NVP are used for four days for seven days (Table 4) [3, 9].

In the case of high risk of vertical transmission, when the mother was treated ineffectively or too briefly, and the value of HIV viral load in the 34-36 week of pregnancy exceeds 1000 copies/ml, or diagnosis was made shortly before delivery or postpartum, and the patient was not treated with antiretroviral medication in pregnancy, triple regimen is used: ZDV, 3TC, and NVP. ZDV and 3TC for four weeks, and NVP for two weeks (Table 5) [3, 9]. Treatment should be started as quickly as possible.

In the described case, the newborn was not washed immediately after delivery, and contact of the child with the mother for more than two hours was ensured ("skin on skin"), the newborn was placed to the breast and inoculated in the first day of life against tuberculosis. After diagnosing HIV infection in the mother on the second day of the child's life, triple antiretroviral therapy was used: ZDV, 3TC, and NVP.

All children of HIV+ mothers should have completed tests of HIV RNA and designated CD4+ cell counts, and studies should be carried out assessing the side-effects of antiretroviral therapy, including haematological parameters, hepatic and renal function indexes, blood glucose, and lipid levels in the following ages:

- 14th-21st days of life,
- 6-8 weeks of age: when the child has received two- or three-drug therapy,
- 1-2 months: if the newborn only received ZDV for four weeks or after delivery, no prophylaxis was included,
- 4-6 months [3].

Undetectable viral load and normal CD4+ lymphocyte count (≥ 1200 cells/ μ l) in studies performed at 2-3 weeks and 1-2 months of age allow the pre-exclusion of HIV infection in a child. The definitive exclusion of HIV infection in artificially fed children requires measurement of undetectable viral HIV and normal CD4+ count in the blood [3].

In this case, during the three- and six-month follow-up visits HIV viral RNA was undetectable, the CD4+ cell amount was normal, and there were no deviations in psychomotor development, indicating that the prophylaxis of vertical HIV was effective [3, 9, 10].

The majority of HIV infections in children in Poland occur as a result of vertical transmission. Every pregnant woman should have a test for HIV infection. Recognition of this infection in a pregnant woman allows the implementation of AVR therapy, and thus the prevention of vertical transmission of this infection.

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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