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Impact of Art Mother and Child on The HIV Status of the Child Born to HIV-Positive Mothers in Burkina Faso: Towards the Adoption of an Effective Pmtct Policy

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Abstract

Objective: To evaluate the impact of ART of the mother and the child on the HIV status of children born to HIV positive mothers in compliance with the policy of mother-child transmission (PMTCT) adopted in Burkina Faso.

Method: It is a prospective cohort study. 214 HIV-positive mother - infant pairs were involved over a period of 14 months (2011-2013). Early pediatric laboratory biologic diagnosis of HIV infection with children aged from 6 weeks to 18 months was carried out by RNA/PCR of HIV1 (Kit Biocentric®). Children with viral load lower than 300 copies/mL (>2.48 Log) were considered uncontaminated. All the children were clinically and biologically followed up to 18 months, the age at which an immunochromatographic test (Determine®) and an ELISA test (Immunocoomb II BiSpot HIV1 2®) were made to confirm their serological status. We determined the immunological status of positive mothers through a numeration of TCD4 + lymphocytes on a flow cytometer (FacscountV1.5). HIV positive Women were dispatched following treatment systems in accordance with options A and B + (mothers on nevirapine alone, mothers on highly active antiretroviral therapy (HAART)/mothers without HAART).

Results: The median age of the children was 6 months (1.5-18 months). The sex ratio was 0.79. The infection rate was 11.2% (24/214). The MTCT was significantly higher among mothers without HAART on Nevirapine only (22/41) than among those on HAART (2/172) p=0.0000 2. The proportion of children infected through breastfeeding whose mothers were not on HAART (23/23) was significantly higher than those whose mothers were on HAART (0/139) p=0.0000 12.

Conclusion: According to the guidelines combined on the use of antiretroviral for the treatment and prevention of HIV infection (June 2013), we also recommend for Burkina Faso, the abandonment of Option A and the adoption of option B + with all pregnant women whatever their immune-clinical status.

Keywords: HAART; PMTCT; ARV; Burkina Faso

Introduction

The different antiretroviral treatments do not include all the periods of the transmission of HIV from mother to child. Despite WHO recommendations [1], protocols such as the early labor single-dose nevirapine (NVP-du) or zidovudine (AZT) from the 14th week of pregnancy or AZT + lamivudine (3TC) during labour and the 7th day after delivery and the use of NVP with children, up to one week after exposure to breastfeeding are still in use in prevention of mother-child transmission (PMTCT) of HIV infection in resources limited countries, namely Burkina Faso [1-4]. However many worldwide studies from 1994 to 2012 on PMTCT (Test AZT-ANRS 024/1994, Essay Thai-AZT short test Ditrame- ANRS-AZT + short breastfeeding 1998, HIVNET 012 , Uganda single dose NVP 1999, Thai PHPT-1 trial AZT Long vs Short 2000, ANRS DITRAME AZT + 3TC & NVP 2003 Thai PHPT-2 trial AZT & NVP 2004, PEPI NVP + AZT PreP the suckling child 2008, SWEN NVP PreP the suckling child 2008, Mma Bana: CD4<200 (breastfeeding) 2009, BAN: ART vs PreP (breastfeeding) 2010, Kesho Bora prophylactic ART (breastfeeding) 201, ANRS 12174, BAN (Malawi) KIBS (Kenya) Kesho Bora: Burkina Faso, Kenya, South Africa) [4-10] could show all the importance of HIV PMTCT through the adoption of Options B +/(through the benefit of extended breastfeeding) failing that Option B. If in industrialized countries, the eviction of breastfeeding by the HIV positive mother has dropped significantly, HIV PMTCT between 0.5 and 1%, in limited resources context breastfeeding has nutritional immunological economic and social advantages which bring mothers to practice mixed breastfeeding and delay in antenatal examination leads to the starting up of Option A. Which is not justified [11], even if for some authors breastfeeding cancels off the benefit obtained from antiretroviral therapy [12].

In Africa, and in Burkina Faso in particular, cost reasons and the inability to address the side effects of AntiRetroViral treatment with

the parturient limit the prescription of triple therapy to breastfeeding mothers [11,13].

Therefore, the present study while showing the positive impact of HAART treatment on the reduction of PMTCT through option B +; should be an argument for its adoption and harmonization in the guidelines of PMTCT policies and eventually lead to the abandonment of option A.

Methodology

Patients and methods

It is a prospective cohort study which was carried out over a period of 14 months. The recruitment and the clinical monitoring of our patients were carried out in the Pediatrics Department of Centre Hospitalier Universitaire–Souro Sanou from 2011 to 2013. Mothers were categorized as follows:

Mothers on HAART with CD4 < 350 cells/µl (option B +):

With mothers: Association of three ARV during pregnancy and then after taken for a lifetime

- AZT + 3TC + LPV/r
- AZT + 3TC + ABC
- AZT + 3TC + EFV
- AZT + 3TC (or FTC) + EFV

With breastfed infants: Daily administration of AZT or NVP starting from birth, up to 4 to 6 weeks or for some others AZT + NVP.

With non-breastfed Infants: Daily administration of AZT or NVP starting from birth up to 4 - 6 weeks.

Mothers without HAART with CD4 rate >350 Cells/ µl (option A):

Prenatal AZT (from the 14th week of pregnancy)

- NVP- from early labour.
- AZT + 3TC during labor and delivery
- AZT + 3TC for 7 days postpartum

* It is not necessary to give NVP-du and AZT + 3TC if the mother received more than 4 weeks AZT during pregnancy.

With the breastfed infant, single dose NVP at birth, followed with daily administration of NVP from birth up to one week after the discontinuation of exposure whatsoever to breastfeeding, or the same protocol with AZT or AZT+NVP.

Non-breastfed infants: NVP single dose at birth, followed by a daily administration of AZT or NVP for 4 to 6 weeks.

Mothers who received nevirapine only at childbirth:

Option B corresponding to the same principle as option B + except that the triple therapy with mothers is conducted till the exposure of the child to breast milk could not be done.

Data collection on breastfeeding was done with mothers and their caretakers.

Biological investigations were made in the Laboratory CHU-SS and PCR in real-time; RNA HIV-1 was made in the Virology Laboratory of Centre Muraz, Bobo-Dioulasso. A total of 214 HIV-positive child-parents pairs were involved. The inclusion criteria were:

- be at least 6 weeks to 18 months for the most.
- be born to HIV1-positive mother on ART or not.
- to have agreed to take part in the study.

Biological analysis

Preparation of samples

For early diagnosis, we performed the PCR RNA of HIV1 (Kit Biocentric ®) on venous samples at elbow bend of 5 ml of blood with children from 6 weeks to 18 months.

Serology at 18 months was retained as the gold standard from patients' serum. It was conducted using a test immuochromatographie (Determine®) and an ELISA test (Immunocoombs ®).

Immunological status of HIV positive mothers

We conducted the enumeration of TCD4 + lymphocytes on a flow cytometer (FacscountV1.5) from whole blood collected through venipuncture with tubes containing EDTA (ethylene diamine tetra acetic) as an anticoagulant .

HIV-1 biologic diagnostic with children through the measurement of the viral load of plasmatic ARV.

We used an automated test RT-PCR in real-time (ANRS G2) applied to the quantification of HIV1 plasma RNA. It also allowed the diagnosing of HIV-1. The target region, amplified was represented by the LTR gene.

The plasma volume required is 200 µl. The extraction of RNA was done manually using a procedure QIAgen (viral RNA minikit Qiamp, QIAgen, Bandol, France).

The robot which allows the performing of this PCR test was ABI. PRISM 7000 of Applied Biosystems using a 96-pits format. Children with a viral load below 300 copies /mL (>2.48 Log) were considered uncontaminated.

Ethical aspects

Participants in this study were informed about the objectives and constraints related to it. They were informed that the information to be collected in the study will remain strictly confidential and anonymous. The subjects were treated with respect and fairness. It was conducted in accordance with the last revision of the Declaration of Helsinki, especially in agreement with the Geneva Declaration of the World Medical Association and International Code of Medical Ethics.

The study complied with the recommendations on Ethics and Good Practices in Epidemiology passed in 1999 by the Association of French-speaking Epidemiologists [ADELF 1998] and according to the protocol and recommendations of the best practices of Biomedical and laboratory. It met the regulatory requirements in Burkina Faso. The Ethics Committee for Research in Health Burkina granted its approval. So patients were included in the study just after the informed approval of relatives. Test results were given to patients for clinical needs. A participant's fact sheet was developed for all the participants.

Statistical Analyses

Processing and data analysis were made using the software EPI-INFO V15. 01 Excel 2010 for tables and graphs.

The Wilcoxon test was used to compare of rates. The percentages were compared using the Fischer test (t). non parametric tests (Kruskal wallis and Mann –withney)were used when distribution was abnormal. The results were considered statistically significant for values $p < 0.05$.

Results

The sample characteristics: The proportion of HIV-1 and HIV-1/2 was 96.6% and 3.4% respectively. The average age of children was 6 months (6 weeks-18 months). The average age of mothers was 31 years/(21-44 years). Child infection rate was 11.2% (24/214). No serious adverse events were reported.

Impact of the treatment system of the mother on mother-child transmission: Mother-to-child transmission was significantly higher with mother without HAART (option A) than those on HAART (option B+) with a relative risk of 83.6 and an IC [20.79 to 332, 49] p=0.00012. Table 1 reports the impact of the treatment system of the mother on mother- child transmission.

Treatment administered the mother	Number	Children infected	Percentage
HAART	172	2	1.20%
Not HAART	25	22	88%
NVP only	8	0	0%
Unknown*	9	0	0%
Grand Total	214	24	11.20%

Table 1: Impact of the therapeutic regime of the mother on mother to child transmission. *Patients lost to follow-up.

Also, mother to child transmission was significantly higher with children who received NVP system only, than the system AZT + NVP whether it be in the arms of mothers on HAART or without HAART (KHi2=68.54 corrected of Yate , p=0.0016). Table 2 reports the impact of the treatment system of the child and the mother on mother - child transmission.

Treatment of m era	Child diet	Number	Children infected	Percentage
NVP only		8		
	NVP only	7	0	0%
	AZT + NVP	1	0	0%
HAART		172		
	NVP only	169	2	1.20%
	AZT + NVP	2	0	0%
	AZT	1	0	0%
HAART NO		25		
	NVP only	12	9	75%
	AZT + NVP	0	0	0%
	AZT	0	0	0%
	No	13	13	100%
Grand Total		208	24	

Table 2: Impact of therapeutic regimens of the child and the mother on mother to child transmission

Influence of the treatment of the mother and mode of feeding on mother-child transmission: The average age of weaning children was 8 months for children who received breastfeeding. Mother - child transmission was significantly higher in breastfed children exclusively breastfed and with whom mothers were on treatment system without HAART. (Khi2 corrected of Yate=153.90, p=0.00 02). Table 3 shows the impact of the treatment system of the mother and the feeding mode on mother-child transmission.

Breastfeeding mode	Mother diet	Number	Children infected	Percentage
Exclusive breastfeeding		162		
	HAART	139	0	0%

	Not HAART	23	23	100%
Artificial feeding		41		
	HAART	33	1	3.00%
	Not HAART	2	0	0%
	NVP alone	3	0	0%
Mixed feeding		5		
	HAART	0	0	0%
	Not HAART	0	0	0%
	NVP alone	5	0	0%
Grand Total		208	24	

Table 3: Impact of the diet of the mother and of breast-feeding on mother to child transmission.

Immunological status and treatment of the mother: The average of the mother CD4+ was 347 ± 112.4 cells/µl including 623 ± 234.7 cells/µl with infected children mothers and 341 ± 112.4 cells/µl with uninfected non children mothers.

The frequency of mother to child transmission was:

- 0% (0/57) from mothers with a CD4+ rate below 250 cells/µl;

- 0.9% (1/108) from mothers with a CD4+ rate between 250-500 cells/µl;

- 85.2% (23/27) from mothers with CD4+ cell rates higher than 500 cells/µl.

Discussion

Socio-demographic characteristics

The infection rate: The overall infection rate was (11.2%). This result was higher than Namukwaya's, Uganda who found a rate of 6.8% [14].

The high rate we report would be due to the non-inclusion of the taking-in-charge services PLWHA and PMTCT, but also to the fact that mothers in our context come late at the time of delivery, when option A was the most frequently applied and pursued.

The obsession of how to manage the side effects of the triple therapy with parturients and the unavailability of HAART for all eligible parturient are as many hypotheses that could explain the preference choice, sometimes, of option A (without HAART) which is certainly not the best choice for the reduction of HIV MTCT.

The infection rate was 14.3% among female children and 7.4% among male children. The same observation was reported by Namukwaya who found for rates of 8% and 5.7% respectively among female children and male [14]. This observation was also made by Taha in Malawi who reported rates of 12.6% and 6.3% respectively for the female and male children [15]. A genetic susceptibility could be ventured, though in the literature no hypothesis seeking to explain this observation has been found so far.

Impact of the therapeutic diet of mother-child transmission: The mother-to-child transmission was significantly correlated with antiretroviral therapy administered to mothers. The frequency of children infected by mothers without HAART (88%)/ is higher than the mothers on HAART (1.2%). The same observation was made by Simporé in Burkina Faso who found a transmission rate of 7.1% when mothers were on monotherapy and 0% when on HAART [16]. Namukwaya, Uganda reported a mother to child transmission rate of 15.7% if mothers received single-dose NVP, 2.1% when on HAART 5.4%, when they had taken AZT+ NVP/[14].

The effectiveness of the reduction of mother - child transmission by means of a retroviral HAART highly active (HAART) administered to the mother is now shared by almost all the authors who have conducted research works on PMTCT [4-10,14,15] and health policies in developing countries especially Burkina Faso should look forward to implementing this strategy (option B +) .

Pleas should be made to development partners to ensure the availability of ART for eligible mothers (whatever their immuno-clinical stage) to the treatment with the benefit of both improving their life expectancy and avoid the contamination of children born to HIV-positive mothers while maintaining exclusive breastfeeding.

This desire was strengthened by Mayaux's view reminiscent of the non-existence of viral load threshold/below which transmission is null [17,18].

HIV transmission and children treatment diet: In our study the MTCT of HIV infection was strongly related to the treatment system of the child. The frequency of mother to child transmission was higher among children who received single-dose nevirapine/(mother without HAART 75%, mother on HAART 1.2%) than those receiving AZT+ NVP or AZT. Namukwaya, Uganda also reported a TME rate of 15.1% when the child was receiving NVP only, 2.4% if the child received AZT [14].

The high use of single-dose NVP with children conforms to the protocol in force in Burkina Faso for all PMTCT services in Bobo-Dioulasso, whereas Meda in 1997, Burkina Faso could show a resistance pf NVP-du then continues into the period of exposure to breast milk with 90% of children [19].

Impact of the mother treatment system and the breast-feeding mode on mother- child transmission: We found in our study a statistically significant relationship between the mother treatment

system and the exposure of the child to breast milk. Among 162 children exposed to exclusive breast milk, 23 children were infected i.e. a rate of 100% and all had mothers who were not on HAART, and 0% infection was observed in 139 children whose mothers were on HAART.

Simporé, Burkina reported in his work a reduction of TME to 0% when antiretroviral therapy was combined with artificial feeding [16]. As for Namukwaya, Uganda a TME rate of 7.4% was observed if the child was on exclusive breastfeeding lactation and 5.9% when on artificial breastfeeding with mothers on HAART [14].

Thus, strongly convinced of the results reported in our study and as regard to the context of limited resources in Burkina Faso, exclusive breastfeeding should be promoted, while instituting an HAART lifelong treatment with the mother and a prophylactic AZT+ NVP with children till weaning. Pharmacological monitoring metering the antiretroviral levels in breast milk is necessary.

Immunological status of the mother: It is acknowledged by all the authors who have conducted research on PMTCT that a CD4+ rates below 250 cells/µl would be a more important risk factor of mother-child transmission. However discordant results we report i.e. higher transmission rates among mothers having an average CD4+ 623 ± 234.7 cells/µl than those with an average rate of 341 ± 112.4 cells/µl would be due to the fact that primarily eligible mothers to triple therapy were those that had less than 350 CD4+ . Thus, it is strongly recommended that our health policies inform about the not taking into account of the immunological stage of the mother in setting on HAART. All of them, whatever their stage of immune depression should benefit from HAART (strong recommendation)

Conclusion

The frequency of mother - child transmission (1.2%) is reduced when mothers receiving antiretroviral therapy. In fact, exclusive breastfeeding when it is covered by the triple ARV therapy is an effective prophylaxis of the child during the period of exposure to breast milk, effectively reduces MTCT to 0%. Triple therapy is advised with HIV positive mothers whatever their stage of immune depression and whatever the time of first contact of the latter with health structure. A plea to development partners will allow mothers to have a longer life expectancy and uninfected children through the choice of Option B +/(while adding AZT to NVP with children). The value of maternal CD4+ cannot be a criterion for setting on an antiretroviral treatment of HIV-positive pregnant women. The effective choice for reducing MTCT in Burkina would be option B +. In the era of the 21st century it remains inconceivable that, for reasons of resource limitations high risk of HIV MTCT strategies remains in practice. The HIV-positive pregnant woman has a right to life and to conceive under optimum conditions for the reduction of HIV MTCT.

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