
Paediatric HAART where there is no paediatrician

**Way forward for a paediatric primary HIV care and
treatment plan**

MSF January 2005

Challenges

- Children are treated in forefront provinces but much to centralised
- Need for community based ARV pediatric sites an emergency priority for a comprehensive approach:
 - Long term adherence support
 - Family approach
 - Social support (day care centres, “HIV friendly” schools, access to child support grants, orphanages..)
- Essential linkage between MTCT -> early detection of failed MTCT-> prophylaxis and follow-up track according to Cd4 % -> ARV site

Challenges (II)

- Nurses (and MO) are not children confident
 - Not properly trained Not part of their scope of practice
 - Need for coaching and technical support
- Nothing will happen if community sites are not made “ children ARV friendly” (they will keep refering)
 - Dedicated training courses for nurses (IMCI to be reviewed)
 - Dedicated children firendly phlebotomy courses
 - Dedicated coaching for doctors by paediatricians
 - Incentives for Peads Hospital Units to design outreach program with clear responsibility areas
 - Key steps (exclusion of Tb prior to ARV, decision to start ARV...) could be done under supervision of mobile paediatrician (Khayelitsha model) and where not available , paediatric skilled MO (Lusikisiki)

Adherence survey in a community site

(Des Michael , Oct 04, Khayeltsha, qualitative focus groups)

- Main factors impacting on adherence among children
 - Multiple caregivers with unclear roles
 - Age (child and caregiver)
 - Medication formulation (syrup vs pills)
 - Social support to primary caregiver
 - Coping ability of primary caregiver
- Survey did not address adherence barriers when attending a central hospital as all interviewed were treated in Khayelitsha

Key steps for paediatric HIV treatment at community level (I)

1. Reduce vertical transmission .

- Strong PMTCT program is a pre-requisite as it is much easier than ARV RX
- If possible, introduce re-enforced MTCT regimen with ante-natal
- Ex: Khayelitsha: 1000 deliveries/year , transmission measured at 8.8 % (2003), target for 2005 at < 5% makes 50 new HIV infected infants/year
- Strong formula feeding policy where environment makes it feasible

2. Rapid identification of failed MTCT cases

- 50 % will die in 24 initial months while antibody tests only confirm at 18 months -> Early PCR tests 6 weeks (with DBS technique in remote area)
- Monitor closely feeding policy in (-) ones
- All identified (+) children : Cd4 and clinical screening to assure a dedicated follow-up policy and ARV Rx as soon as appropriate

Key steps for paediatric HIV treatment at community level (II)

3. Paediatric ART at community level

- Simplify, simplify and demystify paed Rx
- Children friendly regimen
- Simplified monitoring, adapted tools
- Body weight & weight brackets tables
- Specific training (integrated in IMCI) for nurses including paed phlebotomy
- Paediatric outreach program (supervision) and linkage with referral centre

4. Support structures

- Day care centres
- HIV friendly schools : school based support group, openness and supportive culture
- Facilitated access to child support grant
- Community based small scale orphanages

Problems identified

- Lack of WHO recommended dosing tables based on weight
- Lack of registration of pediatric formulations in most developing countries
- Difficulty to use oral solutions and syrups
- High price of the existing formulations
- Problems linked to formulation: stability, large volumes, breakability
- Regulatory issues: what is needed to register new pediatric FDCs?
- Few WHO pre-qualified pediatric formulations available
- Difficulty to diagnose children under 18 months

Meeting ARV treatment recommendations

Principles of ARV treatment in children with currently available products

Infants above 10-12 kgs

- Switch to solid formulations as soon as possible or tolerated
- Solid formulations of first and second line drugs used for adult regimens should be chosen
- Tablets should not be broken further than in half
- FDCs may provide underdosing of individual components and this should be checked.
- If FDCs are used dual FDC are recommended to reduce chances of under-dosing the NVP???
- There must be a single formulations of NVP as a single agent in addition to dual NRTI FDC
- Dosing changes are required as children grow and catch up on treatment

Recommendations for paediatric ARV product development

Syrups and solutions should be reserved for infants <10-12kg. Where possible sachets, granules, or dispersible tablets would be preferred.

The syrups:

- Should be stable at room temperature; have small dose/volume; have long shelf life at high humidity and temperatures,
- Be available in a range of dosage formulations to provide dosage by 2-3kg weight band for smallest infants, 5kg weight band for bigger ones,
- Be packaged for 28-30 day supply,
- Have suitable masking of bad taste (e.g. AZT)

Solid formulations for use in older heavier children (10-12kgs or more)

- Crushable, granulate or dispersible tablets
- Stable and with long shelf life at high temperature and humidity
- Scored tablets preferable
- Have suitable masking of bad taste

Single drugs priorities

Scaled down dose forms of adult tablets of 3TC, ZDV, ABC, NVP, EFV
Pre-FDC formulation – co-packaging of e.g. ZDV/3TC/EFV: ddi/3TC/EFV

2 drug FDC priorities

D4T/3TC: ZDV/3TC: 3TC/ABC: FTC/TDF

3 drug priorities

Paediatric formulations for FDC already available for adults should be produced:
D4T/3TC/NVP: ZDV/3TC/NVP: ZDV/3TC/ABC

Body weight simplified tables (MSF)

HIV - DRUG DOSES expresses per E

Drug	Product	Name	Strength	5-9 kg	10-14 kg	15-19 kg	20-24 kg
Co-trimoxazole Prophylaxis							
TMP-SMX	Cotrimoxazole	Bactrim®	TMP 80/SMX 400mg	1/2 tab OD	1 tab OD	1 tab OD	1 tab OD
		Co-trim®	TMP 40mg/5mL	5 mL OD			
NRTI (Nucleoside Reverse Transcriptase inhibitors)							
AZT	Zidovudine (ZDV)	Antivir®	100mg caps		1 caps TID	1 caps TID	2 caps BID
			300mg tab				
			10mg/mL	7.5 mL BID			
3TC	Lamivudine	Lamivir®	150mg tab		1/2 tab BID	1/2 tab BID	1 tab BID
			10mg/mL	2.5 mL BID			
d4T	Stavudine	Stavir®	20mg caps			1 caps BID	1 caps BID
			30mg caps	1/4 caps BID*	1/2 caps BID*		
			40mg caps				
			1mg/mL	7.5 mL BID	12.5 mL BID		
NNRTI (Non-nucleoside Reverse Transcriptase inhibitors)							
NVP	Nevirapine	Nevimune®	200mg tab		1/2 tab BID	1/2 tab BID	1 tab BID
			10mg/mL	7.5 mL BID			
EFV	Efavirenz	Aviranz®	50mg caps			1 caps OD +	
			200mg caps		1 caps OD	1 caps OD	
			600 mg caps				1/2 caps OD
Fixed Dose Combinations							
3TC + d4T + NVP		Triviro 30®	150 + 30 + 200 mg tab		1/2 tab BID	1/2 tab BID	
		Triviro 40®	150 + 40 + 200 mg tab			+	1/2 tab BID +
						1/2 tab NVP OD	1/2 tab NVP OD

Future paediatric formulations

ART IN FIXED DOSE COMBINATIONS:

d4T + 3TC + NVP



FORMULATIONS

Adult: d4T (30 mg or 40mg), 3TC 150mg, NVP 200 mg)

Children {
"Junior" (10 - 30 Kg): d4T
12mg, 3TC 60mg, NVP 100 mg
"Baby" (3 - 10 Kg): d4T
6mg, 3TC 30mg, NVP 50mg

Research needs

- pK
 - Simplified dosing regimens
 - Mg/kg versus BSA
 - Rounding off of doses
 - Use of adult formulations
 - ddI
 - Daily vs bid
 - Food with admin
 - 2 tablets for buffering?
 - NVP & 3TC
 - Clarify dose
 - EFV < 3y or 10kg
 - Tenofovir in children