Pediatric ART 2: Characteristics of antiretroviral drugs

Paediatric Antiretroviral Therapy Workshop
Abuja 24-28 July 2006

Goals

- Describe the important characteristics of any antiretroviral drug
- Be familiar with the major characteristics of HIV drugs likely to be used in children in PEPFAR programs

Antiretroviral drug characteristics 1

- Name: Generic, brand, and abbreviation
- Formulations.
  - Liquids: taste issue; large volume; must be measured accurately; suspensions may settle
  - Tabs convenient, can be crushed, a little harder to swallow than capsules
  - Capsules: Humidity a problem; some can be opened (EFV), others contain liquid (LPV/r)

- **Dosage**
  - **Weight-based: Easy to calculate**
  - **Body surface area based: More accurate**

  - So, accurate weights and heights/lengths are necessary for proper dosing

Antiretroviral drug characteristics 2

- Virology
  - Potency: How active is drug against wild-type virus (the virus the patient is initially infected with)?
  - Resistance barrier: How many mutations are needed for resistance?
- Metabolism and elimination
  - Renal versus hepatic (or both)
- Drug interactions
  - Pharmacokinetic: Effects on absorption and metabolism
  - Pharmacodynamic and virologic: Effect on antiretroviral activity
  - Additive or synergistic toxicity

Antiretroviral drug characteristics 3

- Side effects and toxicity
  - What is time course?
  - How common?
  - How serious?
  - Is it reversible?
  - How to monitor?
  - How managed?

Antiretroviral drugs 2006

Nucleoside/nucleotide analogues (NRTI)

- Zidovudine*
- Stavudine*
- Lamivudine*
- Didanosine*
- Abacavir*
- Emtricitabine
- Tenofovir

Non-nucleoside RT inhibitors (NNRTI)

- Nevirapine*
- Efavirenz*
- Delavirdine

Fusion inhibitor

- Enfuvirtide (T-20)

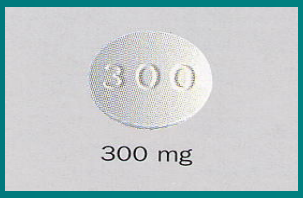
Protease inhibitors (PI)

- Nelfinavir*
- Indinavir*
- Saquinavir
- Amprenavir
- Ritonavir
- Lopinavir/ritonavir*
- Atazanavir
- Fosamprenavir
- Tipranavir

* PEPFAR drugs for children

Zidovudine (AZT, ZDV, Retrovir)

- Formulations:
  - 10 mg/ml syrup
  - 100 mg capsule
  - 300 mg tablet
- Storage: “room temperature”
  - 15-25 deg C
- Taste: fair
- Food: take with or without food



Zidovudine (AZT, ZDV, Retrovir)

- Side effects: generally well-tolerated
  - Common: anaemia, neutropaenia, mild GI intolerance, headache
  - Less common: hepatitis, lactic acidosis, myopathy (muscle aches), cardiomyopathy

Stavudine/Zerit (d4T)

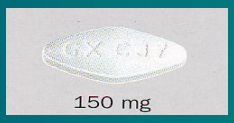
- Capsules: 30 mg, 40mg
- Tabs: 20 mg
- Solution: 1 mg/ml

Stavudine/Zerit (d4T)

- Can be given with or without food
- Capsules can be opened and sprinkled on mashed potatoes, porridge or other soft foods
- Dose
  - > 60 kg 40 mg bd
  - 30-60 kg 30 mg bd
  - < 30 kg: 1 mg/kg bd

Lamivudine/Epivir (3TC)

- Tablets: 150 mg
- 10 mg/ml clear solution



Lamivudine/Epivir (3TC)

- Adolescents/Adults
  - < 50 kg: 2 mg/kg twice daily
  - ≥ 50 kg: 150 mg twice daily or
    300 mg once daily
- Children: 4 mg/kg b.d.

Lamivudine/Epivir (3TC)

- Can be given with or without food
- Store oral solution at room temperature
- Dosage should be decreased in patients with renal impairment

Didanosine/Videx/Videx EC (ddI)

- Capsule:
  - 25 mg
- 10 mg/ml white suspension
- Videx EC:
  - 400mg

Didanosine/Videx (ddI)

- Adolescent/Adult dosing
  - 400 mg OD if ≥ 60 kg
- Paediatric dosing
  - 2 week – 8 months of age
    - 100 mg/m2 BD
  - >8 months
    - 120 mg/m2 BD
- GI disturbances (common), peripheral neuropathy, pancreatitis
- Give on an **empty stomach** at least 1 hour before or 2 hours after meals AND medications

Abacavir/Ziagen (ABC)

- Tablet: 300 mg
- 20 mg/ml yellow oral solution

Abacavir/Ziagen (ABC)

- Adolescent/Adult dosing
  - 300 mg BD
- Paediatric dosing
  - 8 mg/kg BD
- Give with or without food
- Store at room temperature
- $80 per month

Abacavir hypersensitivity

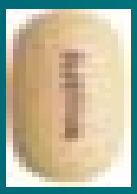
- Teach the signs and symptoms of hypersensitivity reaction
- Instruct patients/care givers to telephone immediately if rash occurs
- Provide medication guide and warning card

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- EFV, Efavirenz (Sustiva)
- NVP, Nevirapine (Viramune)

Efavirenz/Sustiva (EFV)

- Capsules: 50 mg, 200 mg
- Tablets: 600 mg
- No oral suspension



Efavirenz/Sustiva (EFV)

- Adolescents and Adults
  - 600 mg once daily
  - Increase to 800 mg once daily if used with rifampicin
- Children
  - 10- <15 kg: 200 mg
  - 15- <20 kg: 250 mg
  - 20- <25 kg: 300 mg
  - 25- <32.5 kg: 350 mg
  - 32.5- <40 kg: 400 mg
  - >40 kg: adult dose

Efavirenz/Sustiva (EFV)

- Can be administered with or without food, but avoid high fat meals
- Capsules can be opened and added to liquids or foods; grape jelly masks the peppery taste well
- Tolerability of CNS side effects can be improved by bedtime dosing

Nevirapine/Viramune (NVP)

- Oval White tablet 200 mg
- Oral solution 10 mg/ml

Nevirapine/Viramune (NVP)

- Adolescent/Adult
  - Oral: 200 mg every 12 hours
- Paediatric:
  - Single dose for PMTCT:
  - Treatment:
    - * 200 mg/m2/dose if < 4 years or
    - * 150 mg/m2/dose if 4-8 yrs or
    - * 120 mg/m2/dose if > 8 yrs

- INITIATE THERAPY WITH ONCE DAILY DOSING FOR 14 days for ALL patients. If no rash or other problems, then increase to full dose.

- If a patient stops Nevirapine, they need to stop that drug first and continue other medications for a week or more and then stop them. (NNRTI tail)

Didanosine (ddI, Videx)

- Forms
  - 50 mg tablet, 400 mg capsules
- Dose:
  - 100 mg/m2 BD if 2 weeks - 8 months of age
  - 120 mg/m2 BD if > 8 months of age
  - Adults: 200 mg BD or 400 mg OD
- Side effects
  - GI disturbances (common), peripheral neuropathy, pancreatitis
- Other:
  - needs to be taken on empty stomach (selfish drug: no other meds or food to be taken 30-60 min before nor 2 hours after
  - Many drug interactions with other ARVs

Nevirapine-2

Elimination	Hepatic P450 metabolism
Interactions	Rifampin lowers NVP by 1/3- use EFV NVP lowers ketoconazole by 2/3 NVP lowers LPV level- increase LPV dosage
Tolerability, side effects & toxicity	Common: Rash. If mild, check LFTs, continue dosing. If signs of Stevens-Johnson, stop drug. Hepatitis- can be severe, especially with higher CD4 and in women. Monitor LFTs in adults. Risk in children not as well described.
Potency	High
Genetic barrier to resistance	Very low- resistance can develop after single dosage given without other ARVs

Nelfinavir (Viracept, NFV)

Formulations & palatability	**Powder: 50 mg/1.25 ml scoop (mix in milk or water- makes sandy moderately bitter-sweet slurry)** **Tabs: 250 mg (Can be crushed or dispersed; mildly bitter)**
Dosage	**Must take with meal or milk** **Child: <1 year 40-50 mg/kg three times daily OR 65-75 mg/kg BD** **1-13 yr 55-65 mg/kg BD** **Adult: 1250 mg BD**
Side effects	**DIARRHEA – common** **Does cause cholesterol increase**

Lopinavir/ritonavir (Kaletra, LPV/r)

Formulations & palatability	Solution: 80 mg/ml LPV + 20 mg/ml RTV (extremely bitter) Caps: 133 mg LPV/33 mg RTV
Storage	Ideally refrigerated. Stable 25 C X 2 months. Keep caps from moisture
Dosage	Take with food Child > 6 months: 7 kg- <15 kg: 12 mg/kg LPV BD 15-40 kg: 10 mg/kg BD Adult: 400 mg LPV BD Increase dosage by 1/3 if NVP or EFV used
Other	MANY drug interactions – patients and providers must be careful when taking/prescribing other meds while on Kaletra. Most powerful ARV. Side effects: GI disturbances, high cholesterol

Major early or acute-onset ARV toxicities by syndrome

- Anemia, neutropenia: ZDV
- Rash: NVP, EFV, ABC
- Systemic hypersensitivity: NVP, ABC
- Nausea, vomiting: LPV/r >> others
- Diarrhea: NFV > LPV/r
- CNS disturbances: EFV
- Neuropathy: DDI > D4T
- Pancreatitis: DDI >> D4T, ? LPV/r
- Hepatitis: NVP > others
- Myopathy: ZDV
- Lactic acidosis- acute severe (very rare in children): DDI, D4T, ZDV, 3TC