

ZIDOVUDINE (Azidothymidine)

Use

Zidovudine inhibits the replication of the human immunodeficiency virus (HIV), reducing foeto-maternal transmission and slowing the progression of the resultant acquired immunodeficiency syndrome (AIDS).

HIV infection

AIDS is a notifiable disease caused by one of two closely related human retroviruses (HIV-1 and HIV-2) that target T helper (CD4) lymphocytes and macrophages, rendering the patient immunodeficient and vulnerable to a range of chronic infectious illnesses that are not normally lethal. Infection is generally by sexual contact, or the use of contaminated needles. Babies of infected mothers have a 1 in 5 chance of becoming infected around the time of birth if avoiding action is not taken. Contaminated blood infected many haemophiliacs before the nature of the condition was understood. The risk of infection after needlestick exposure is <0.5%.

Care of HIV infected women during pregnancy

Since chemoprophylaxis, and Caesarean delivery before the membranes rupture can almost eliminate risk of materno-fetal transmission, there is an overwhelming case for routine screening in pregnancy, as long as this has the mother's full informed consent. Seek experienced local advice to supplement the guidance provided by the US web site (www.AIDSinfo.nih.gov), and UK web sites (www.bhiva.org and www.aidsmap.com).

Pharmacology

Zidovudine or azidothymidine (AZT) is a thymidine analogue that acts intracellularly, after conversion to triphosphate, to halt retrovirus DNA synthesis by competitive inhibition of reverse transcriptase and incorporation into viral DNA. It inhibits the replication of the HIV virus, but does not eradicate it from the body. It is not, therefore, a cure for the resultant AIDS, but it can delay the progression of the disease, and the drug's arrival in 1987 did much to transform the management of this previously untreatable condition. The most common adverse effects are anaemia and leucopenia (which make regular haematological checks essential), but myalgia, malaise, nausea, headache and insomnia have also been reported. Zidovudine is well absorbed by mouth but first-pass liver uptake reduces bioavailability. The half life is 1 hour, but 3 hours in term babies and 6 hours in preterm babies in the first week of life. Concurrent treatment with ganciclovir (q.v.) increases the risk of toxicity while fluconazole increases the half life. Tissue levels exceed plasma levels (neonatal $V_D \sim 2$ l/kg). Zidovudine crosses the blood brain barrier and the placenta with ease, but there is no human evidence of teratogenicity. Excretion occurs into breast milk, but has not been studied in any detail.

Intrapartum prophylaxis

Mothers: Start giving 300 mg twice a day by mouth, as soon after 28 weeks gestation as possible. Give this dose once every 3 hours as soon as labour starts (or give 2 mg/kg over an hour IV and then 1 mg/kg every hour) until delivery is over. Virus transmission is reduced by also giving nevirapine (q.v.).

Term babies: Give 4 mg/kg by mouth twice a day for four weeks. Start this within 8 hours of birth.

Preterm babies: Give babies of 30–36 weeks gestation 2 mg/kg twice a day for 2 weeks, and then 3 mg/kg twice a day for 2 weeks. Give babies under 30 weeks gestation 2 mg/kg twice a day for 4 weeks. If oral treatment is not possible give 1.5 mg/kg IV once every 12 hours (or every 6 hours if a term baby).

Sustained prophylaxis when bottle feeding seems inadvisable

In situations where hygiene and cost combine to make bottle feeding hazardous *exclusive* breast feeding for 6 months reduces the risk of the baby becoming infected after birth. Risk can also be reduced by continuing zidovudine for six months (4 mg/kg every 8 hrs after 1 month; 6 mg/kg every 8 hrs after 2 months).

Treatment after birth

See the monographs on lamivudine, nevirapine and lopinavir with ritonavir for advice on how to treat babies with known infection. Only give prophylactic co-trimoxazole (q.v.) to babies at serious risk of overt infection.

Case notification

Register all pregnant HIV positive women and their babies in the UK anonymously with the linked RCOG and RCPCH surveillance programmes (e-mail: j.masters@ich.ucl.ac.uk; Tel 020 7829 8686).

Supply and administration

Dilute the content of a 200 mg (20 ml) ampoule (costing £11) to 50 ml with 5% dextrose to produce an IV solution containing 4 mg/ml, and give any IV dose slowly (over 30 minutes). 100 mg and 250 mg capsules cost £1.10 and £2.70 respectively. A sugar-free oral syrup (10mg/ml) is also available (100ml costs £11).

References

- See the Cochrane review of materno-fetal transmission ©
- Lallemant M, Jourdain G, Le Coeur S, *et al.* Single dose nevirapine plus standard zidovudine to prevent mother-to-child transmission of HIV-1 in Thailand. *N Engl J Med* 2004;**351**:217–28. [RCT] (See also 289–92.)
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- Thior I, Lockman S, Smeaton LM, *et al.* Breastfeeding plus infant zidovudine prophylaxis for 6 months vs formula feeding plus infant zidovudine for 1 month to reduce mother-to-child HIV transmission in Botswana. *JAMA* 2006;**296**:794–805. [RCT]
- Coovadia HM, Rollins NC, Bland RM, *et al.* Mother-to-child transmission of HIV-1 infection during exclusive breastfeeding in the first 6 months of life: an intervention cohort study. *Lancet* 2007;**369**:1107–16. (See also 1065–6, and 2073–5.)