AIDS briefs

Co-trimoxazole (CTX) prophylaxis reduces child deaths by preventing bacterial lung infections

The benefits of CTX prophylaxis in adults and children living with AIDS (CLWA) have been confirmed in several African countries. In particular the CHAP study, conducted by the UK's Medical Research Council in Zambia and Malawi, showed that CTX prophylaxis reduced the risk of death in children with HIV by half over 2 years of follow-up. However, researchers in the CHAP study could not explain why CTX prophylaxis reduced illness and death, given that only one case related to PCP could be detected, and so carried out a more detailed analysis of causes of death, hospitalisation and antibiotic use to see if they could detect where CTX might be having a greater effect on morbidity and mortality.

The mortality review was based on case report forms, death certificates, hospital notes, postmortem findings, and laboratory data. Hospital admission case report forms were validated against hospital notes by an independent trial manager and trained data monitor.

Investigations such as nasopharyngeal aspirates (NPAs) for suspected respiratory infections, blood cultures, chest X-rays, thin/thick films for malaria parasites, cerebrospinal fluid (CSF), urine, and other samples for microscopy and culture were carried out, on CLWA admitted to hospital, whenever possible. Postmortems were carried out in only 12 cases.

TB was diagnosed by examination for acid-fast bacilli in NPAs, sputa or gastric washings. All NPAs were examined for *Pneumocystis jiroveci* using immunofluorescence and polymerase chain reaction (PCR).

Overall, 28% and 42% of CLWA on CTX and placebo, respectively, died. This included 15% and 21% of hospital deaths in the CTX and placebo groups, respectively, and 28% and 42% of deaths outside hospital in the CTX and placebo groups, respectively. The number of days spent in hospital was significantly higher in the placebo group compared with the CTX group.

There were 91 hospital deaths, the leading causes of which were serious bacterial infections (49.5%), diarrhoea (13.2%), and malnutrition (7.7%). Pneumonia or empyema accounted for 29% and 39% of hospital deaths in the CTX and placebo groups, respectively. There was no evidence that mortality reductions in the CTX group varied by the cause of disease.

When hospital admission by cause was considered, pneumonia/empyema was the most predominant, either singly or concurrently with TB, malaria, and malnutrition. *Staphylococcus aureus* and Salmonella species were the major bacterial isolates identified from blood cultures. Most malaria (51/55) and TB (43/47) diagnoses were presumptive and not laboratory confirmed. *P. jiroveci* was rare, with 1/115 and 0/73 NPAs being positive by immunofluorescence and PCR, respectively.

Serious bacterial infections and malnutrition admission rates were reduced in the CTX group compared with the placebo group. By 2 years, the cumulative probability of first admission to or death in hospital with serious bacterial infections was significantly reduced in the CTX group.

These data provide additional evidence for the protective effect of CTX prophylaxis in CLWA irrespective of the CD4 count and against a background of high antibiotic resistance in Zambia. CTX prophylaxis reduced bacterial infections, hospital admissions and days of hospitalisation, and antibiotic use in CLWA.

Mulenga V, *et al. AIDS* 2007; 21: 77-84.

Maternal nevirapine-based ART is more effective if delayed for more than 6 months after single dose at delivery

Women who received single-dose nevirapine at the time of childbirth had better outcomes from nevirapine-based triple combination therapy if they started ART more than 6 months after delivery, researchers in the USA report in the *New England Journal of Medicine*.

Concern about the effectiveness of nevirapine-based ART for women previously exposed to the drug at the time of delivery centres around the risk that a single dose of the drug may be enough to cause long-lasting resistance. This is because nevirapine levels can take 10 - 14 days after a single dose to fall below the limits of detection in many women, and throughout this period the potential exists for a nevirapine-resistant virus to emerge.

In order to study the effect of peripartum nevirapine exposure on subsequent response to nevirapine-based ART, US researchers from the Botswana-Harvard School of Public Health AIDS Initiative looked at 218 postpartum, HIV-infected women who had received nevirapine or placebo at delivery plus a short course of zidovudine (AZT) during pregnancy in the previous MASHI study. Sixty women started nevirapine-based ART within 6 months of giving birth, and the remaining women began the regimen after 6 months.

Of the 60 women who started nevirapine-based ART within 6 months of giving birth, 24 had received a single dose of nevirapine during labour, while 36 had received a placebo. (All of the women in the study were given AZT from 34 weeks into their pregnancies through delivery.) Of the women in this group who received a single dose of nevirapine during labour, 41.7% subsequently experienced treatment failure, or 'virologic failure', within 6 months of starting therapy – compared with 0% among the women in this group who had received placebo during delivery. Similar differences were found at follow-up visits 1 and 2 years after therapy had started. Among women who had delayed ART for 6 months, there were no differences in failure rates, regardless of whether or not they had received a single dose of nevirapine during labour.

Advice about nevirapine-based regimens also applies to efavirenz-based regimens, since nevirapine and efavirenz are cross-resistant.

Treatment response was also measured among 30 infants in the study who received nevirapine-based ART. More than three-quarters of the 15 infants who were exposed to single-dose nevirapine as newborns did not respond adequately to the triple-drug treatment (compared with 9.1% of the 15 infants without prior nevirapine exposure).

Lockman S, *et al. N Engl J Med* 2007; 356 (2): 135-147.

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