AIDS BRIEFS

ZINC SUPPLEMENTATION IN CHILDREN WITH HIV INFECTION

Zinc is an essential trace element that is important for growth, development and immunity. Zinc deficiency is associated with impaired immune function and an increased risk of infection, particularly diarrhoea and pneumonia. We know that zinc supplementation in children in poor countries can reduce the incidence and severity of diarrhoea and pneumonia and may reduce the morbidity associated with malaria. These findings have introduced the idea of mass zinc supplementation in poor areas. However, the situation in children with HIV-1 infection is not clear-cut. As Raziya Bobat and colleagues point out in a recent paper in the *Lancet*, there are structural elements in the HI virus that require zinc for normal function. Zinc also activates lymphocytes and activated CD4+ T lymphocytes are major target cells for HIV-1 replication. An increase in these cells could potentially enhance HIV-1 replication. If mass supplementation with zinc is going to be recommended in areas with a high prevalence of HIV-1 infection, zinc's safety in children infected with HIV-1 needs to be established. The team carried out a trial of zinc supplementation in HIV-1-infected children to assess the effect on plasma HIV-1 viral load and morbidity from infectious diseases.

They carried out a randomised, double-blind, placebo-controlled equivalence trial of zinc supplementation at Grey's Hospital, Pietermaritzburg in 96 HIV-1-infected children, who were randomly assigned either 10 mg of elemental zinc sulphate or placebo daily for 6 months. Their HIV-1 viral load and CD4+ T lymphocyte counts were established at baseline and measurements were repeated at 3, 6 and 9 months after supplementation started.

USING TOTAL LYMPHOCYTE COUNT

The team found that the average HIV-1 viral load was 5.4 for the placebo group and 5.4 for the zinc-supplemented group 6 months after supplementation started. The corresponding figures 3 months after supplementation ended were 5.5 and 5.4, a difference of only 0.05. The average percentage of CD4+ T lymphocytes and median haemoglobin concentrations were also similar in the 2 groups after zinc supplementation. There were 2 deaths in the zinc supplementation group and 7 in the placebo group. They also found that children given zinc supplementation were less likely to get watery diarrhoea than those given placebo.

The conclusions were that zinc supplementation does not result in an increase in plasma HIV-1 viral load and can reduce morbidity caused by diarrhoea. This suggests that programmes to enhance zinc intake in populations assumed to be deficient in zinc with a high prevalence of HIV-1, can be started without any concerns about adverse effects on HIV-1 replication. The team also suggest that zinc supplementation should be implemented as adjuvant therapy for children with HIV-2 infection, given the reductions in the morbidity associated with diarrhoea and pneumonia.

Bobat R, *et al. Lancet* 2005; **366:** 1862-1867.

In the developed world the decision about when to start antiretroviral therapy in adults and children is based on clinical symptoms and CD4 T-cell count or percentage and HIV RNA viral load. However, these tests are often not routinely available in poor countries and total lymphocyte count is used by the World Health Organization, in their 2003 guidelines, to provide the threshold at which adults and children should be started on antiretrovirals. Most of the studies assessing the value of total lymphocyte count as a marker of disease progression have been cross-sectional and done in adults. The authors of this paper in the *Lancet* describe an analysis of almost 4 000 children, followed up longitudinally in studies in Europe and the USA, before they first received antiretroviral therapy. They developed a

model to estimate the 12-month risks of death and progression to AIDS on the basis of age and the most recent total lymphocyte count. They also assessed the consistency of thresholds of total lymphocyte count and CD4-cell percentage used for starting antiretroviral therapy, as recommended in the WHO 2003 guidelines. Finally, they compared the clinical outcomes that would have been seen if the rules for the initiation of antiretroviral therapy had been based only on monitoring total lymphocyte count or only on CD4-cell percentage.

The team used a longitudinal study of 3 914 children with HIV infection, who were pooled from observational and randomised studies in Europe and the USA. They found that total lymphocyte count was a powerful predictor of the risk of disease progression, even though it showed only a weak correlation with CD4-cell percentage. For children older than 2 years, the 12-month risk of death and AIDS increased sharply at values less that 1 500 - 2 000 cells per µl. There was little increase at higher total lymphocyte counts. However, total lymphocyte count was less prognostic in younger children. The team also found that the risk of mortality was substantially higher at the thresholds of total lymphocyte count recommended by the WHO than at corresponding values of CD4-cell percentage. When the two types of marker were compared at approximately equal mortality risks, total lymphocyte count was as effective as CD4-cell percentage at identifying children before death, but resulted in antiretroviral therapy being started earlier.

The conclusions were that, in this population, the total lymphocyte count was a strong predictor of short-term disease progression and was only marginally less predictive than CD4-cell percentage. However, the authors point out that confirmatory studies are needed in poor environments to identify the most cost-effective markers to guide the start of antiretroviral therapy.

HIV Paediatric Prognostic Markers Collaborative Study. *Lancet* 2005; **366:** 1868-1874.

Bridget Farham

SINGLE SUTURE

MIND CONTROL

People could learn to suppress chronic pain by learning to control the activity of certain areas of the brain. This is the conclusion of Christopher deCharms, who is part of an imaging technology firm, Omneuron, in California. Working with colleagues from Stanford University, he showed that 8 patients suffering from chronic pain managed to control their pain through visual feedback from real-time MR images of the rostral anterior cingulate cortex (rACC) – a pain centre in the brain. All patients had complicated conditions such as fibromyalgia and neuropathic pain, that had not responded to conventional treatment. Using only 3, 13-minute sessions in the scanner, 5 of the patients managed to suppress the activity of the rACC and reduce their pain by more than 50%. A control experiment showed that healthy people who were given painful heat stimuli on their hands could not control this pain without seeing the brain scan feedback or when shown brain scans from a different region of the brain or from a different person.

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