PCP Prophylaxis in Perinatally HIV-Exposed Infant

CDC and WHO recommendations for PCP prophylaxis for HIV-exposed infants state that co-trimoxazole is indicated for HIV-exposed infants at 4-6 weeks and it needs to be continued till HIV PCR DNA tests on the infant on 2 occasions are negative; one done after 1 month of age and second after 4 months of age(1). With introduction of PACTG 076 protocol, risk of perinatal transmission of HIV infection has shown a dramatic decline from 24 to <5%(2). This implies that out of 100 mothers who are HIV-positive and on PACTG 076 management, only 5 unlucky infants will develop HIV infection. If above WHO PCP prophylaxis recommendations are followed, 95% of infants would have unnecessarily received PCP prophylaxis when in fact they are not infected with this deadly virus. Such a mass usage of co-trimoxazole carries with it risk of causing bacterial and malarial resistance. Besides, co-trimoxazole is not devoid of adverse-effects. I personally feel that some sort of a risk scoring should be done and co-trimoxazole prophylaxis offered only to those with high risk of acquiring the vertical infection. What is the recent opinion on it?

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Reply

The recommendations for cotrimoxazole prophylaxis to infants born to HIV-positive mothers are mainly based on the following facts: high number of deaths from *Pneumocystis carinii (jirovecii)* pneumonia (PCP) in HIV-infected infants (especially between 2-6 months of age), efficacy of cotrimoxazole in preventing PCP in adults, and difficulties in determining the HIV infection in exposed infants due to persistence of maternal antibodies(1). Cotrimoxazole prophylaxis not only prevents PCP infection, but also prevents other opportunistic parasitic infections (toxoplasmosis, isosporiasis, etc), bacterial infections and malaria, and also decreases HIV-related mortality(1-3).

The side effects of cotrimoxazole-like rashes, fever, leucopenia, hepatitis, thrombocytopenia, etc. rarely require discontinuation of the prophylaxis (exception-Stevens Johnson syndrome) or therapy as most of these side effects are easily treatable(1,4). The drug appears to be better tolerated in children and risk of toxicity has been considered to be negligible(1,2,4,5). Desensitization and supportive therapy allow us to continue the prophylaxis. Other alternatives (dapsone, atovaquone, or pentamidine) are available in patients with severe adverse reactions. The dose of cotrimoxazole used for PCP prophylaxis is much lower than that used for treatment of PCP.

Resistance of *Pneumocystis jirovecii* to sulfonamides (and resistance of malarial parasite to sulfadoxine-pyrimethamine) is a possibility, but is usually not associated with treatment failure(3). Gill, *et al*.(1) (in a conceptual model of benefits and risks of cotrimoxazole prophylaxis) argue that the empirical prophylaxis is justifiable only at a higher level of HIV prevalence and by reduction of perinatal transmission (by drugs like nevirapine), the PCP risk is also indirectly lowered. However, the clinical importance of these theoretical concerns of drug resistance is not well understood or well

substantiated; and as most of these effects are expected to be delayed in their appearance, this risk of resistance has not been quantified(1,2). Using a risk scoring to decide about the PCP prophylaxis seems to be a novel idea but may not be practically applicable in field conditions especially on a national scale.

There is paucity of randomized trials proving the efficacy of cotrimoxazole in HIV exposed infant, but there are ethical and methodological concerns in planning such studies(1,2). Gill, *et al.*(1) have suggested that improved strategies for preventing perinatal transmission coupled with early identification of the infected infants will be better than mass empiric prophylaxis to prevent PCP. Short duration of cotrimoxazole prophylaxis (till age of 6 months) has been proposed, thus preventing most cases of PCP and minimizing the risk of resistance by reducing the duration of the prophylaxis(2,5). Chokephaibulkit, *et al*.(5) have successfully used clinical criteria indicative of HIV disease to decide continuation of cotrimoxazole prophylaxis beyond the age of 6 months in these infants; a strategy that can be considered in other developing countries with limited access to diagnostic and treatment facilities. Blinded studies comparing low dose cotrimoxazole to the currently recommended dose are warranted and there is a need to quantify the risk supposed to be associated with the cotrimoxazole prophylaxis(1,2,4). Prospective monitoring of the adverse effects and microbiological effects of the mass prophylaxis is needed in various populations along with cost-effectiveness studies(1,2). A serious reappraisal of the strategy of using cotrimoxazole in all the infants born to HIV-positive mothers is certainly required(3).

As for our country, considering the following facts that (*i*) cotrimoxazole prophylaxis prevents many other infections in addition to PCP; (*ii*) the incidence of breastfeeding by HIV-positive mothers is still high (with continued risk of HIV transmission to the infant) and; (*iii*) the availability of HIV-DNA PCR test (to prove HIV negativity) is still limited; it appears that we need to continue the strategy of administering cotrimoxazole prophylaxis to all infants born to HIV-positive mothers. It may be better to prevent the PCP infection rather than trying to treat it as many of our patients present late to the medical care facility. I feel it is necessary for us to continue the PCP prophylaxis till we can improvise on availability and affordability of the diagnostic methodology for HIV (i.e. DNA PCR) in infancy and till more clinical research is available on this issue.

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