CASE STUDIES

Case Study 6

Background

The wider implications of preventing mother-to child transmission of HIV, and subsequent management of women and children, in rural Uganda.

Epidemiological studies have shown that about 8% of the adult population in rural Uganda is HIV positive and that this rate is steady or declining slightly over time. The HIV prevalence in pregnant women is just over 10%.

Although many trials have been conducted to evaluate the effectiveness of interventions designed to reduce rates of HIV transmission from mother to child, there has not been an intervention trial in a rural part of Africa.

Studies have shown that treatment with zidovidine (AZT) can significantly reduce the rate of vertical transmission of HIV but the regimens shown to be successful in developed countries are too costly (about $300 per woman) and too technically demanding (i.e. in training, human resources, infrastructure, facilities) to be useful in developing countries. A simpler, more practical, regimen-which involved no post-delivery treatment and required that women did not breast feed-has been shown to be effective in Thailand for about $75 per woman. Although these results are promising, they may not generalize well to rural Africa where there are few reliable alternatives to breast feeding.

Two studies of the same short course AZT regimen in breast feeding populations in Africa have been published recently. These studies showed reductions of HIV from transmission of 37 and 38%. A third African study (the PETRA study) has also been reported. This study found that treatment with AZT and 3TC reduced transmission by 50% when the drugs were given from 36 weeks gestation, intrapartum and postnatally for 1 week, and by 37% when treatment was given intrapartum and postnatally only. The cost per woman of the two regimens was $150 and $25 respectively.

A study from Uganda has shown that 200 mg of nevirapine to the mother at /'the onset of labour and 2mg/kg to the neonate within 3 days of birth reduced vertical transmission by 48% more than AZT (600 mg at the onset of labour and 300mg doses every 3 hours during labour for the mother followed by 4mg/kg given to the neonate twice daily for 1 week). The cost of this nevirapine regimen is $4 per woman. The nevirapine regimen is more appropriate to the African situation, being more affordable and technically feasible in the context of rural Ugandan health services and a government annual per capita health expenditure of under $6. It is therefore deemed imperative that this intervention is investigated in the rural African context, since most Africans live in rural settings.

Research proposal

Programmes implementing interventions to reduce the risk of rnother-to-child transmission of HIV in areas where there has not been a trial, and where antenatal testing programmes are not in place, require a large degree of preparation to ensure that infected women are appropriately identified and that the population at large understand the benefits of treatment. In order to determine the feasibility of a new Nevirapine treatment programme to prevent mother-to-child transmission of HIV, researchers from Uganda, U.K. and U.S.A. plan to conduct a two-year pilot project in a designated rural area of Uganda.

In the pilot study women will receive the nevirapine regimen and they will also be advised to

breast feed exclusively for 3 months post-partum and then to wean their children completely. This pilot project is necessary to determine the feasibility of a widespread treatment program for rural Uganda. Counselling facilities, social science expertise, and a community development programme are already available. The counselling section offers individual HIV testing and counselling at five offices within the sub-county (research region). However, less than 10% of adults wish to learn their HIV status, generally because of fear and stigma. The researchers have built up the necessary infrastructure for the study in the area and already employ experienced staff there. A clinic has been established within the community, and drug supplies are obtained at regular intervals and stored securely and safely.

The pilot project will involve a social science component investigating the feasibility of delivering the nevirapine regime to prevent vertical transmission and of exclusive breast feeding for 3-6 months followed by early weaning. As well, the study will aim to determine the feasibility of a counselling and community development initiative to promote the benefits to mothers of knowing their HIV status, to counsel them about the possibility and benefits of nevirapine treatment if they are HIV positive, advise them on how to access treatment, and provide support for exclusive breast feeding for 3-6 months followed by complete weaning. Furthermore the logistics of providing nevirapine therapy through one central maternity clinic in the sub-county will be assessed, as will trends over time in both breastfeeding and nevirapine interventions.

The intervention will be evaluated by assessing the proportion of women accessing the HIV testing and counselling services, the proportion of HIV-positive pregnant women accessing the nevirapine treatment regimen, vertical transmission rates in treated and untreated women, and the proportion of HIV-positive women following the guidelines for safer breast "/feeding. Expectant HIV positive mothers attending the clinic will be told about the pilot project. Those women who wish to access the intervention will be asked to provide informed voluntary consent before being started on the nevirapine regimen. 200mg as early as possible in labour and a 2mg/kg dose to the baby within 3 days of birth.

No further post-natal treatment will be given, but this will be reassessed in the light of future research findings from studies elsewhere. Mothers (and their infants) declining to take up nevirapine treatment will be given clinical care and support. They will be seen routinely by a clinician at 3 monthly intervals and encouraged to attend the clinic at other times if sick. All conditions identified will be treated using medications approved by the Uganda Ministry of Health. Currently the Ministry of Health has no specific plan to provide antiretroviral therapy to non-pregnant adults or children. If necessary the patient will be referred for investigation and treatment to nearby hospital facilities.

If pregnant women are found to be HJV positive in the study they will be encouraged by the counsellor to attend a designated maternity clinic in the area for antenatal care and delivery. Staff at the maternity clinic will be trained and supported by the project staff to deliver the nevirapine regimen, to respect the confidentiality of the mothers' HIV status, and to provide appropriate and safe maternity care for HIV positive women.

Children will be seen as close to birth as possible when they will be assessed clinically, and blood taken for serological testing and storage on filter paper for subsequent polymerase chain reaction (PCR}. Children will be seen at 3, 6, 9, 12, 15 and 18 months and on each occasion assessed clinically and blood taken for serology and stored for PCR. Children will be managed by a paediatrician and nurse as part of the on-going research programme. Children will be seen routinely every 3 months and their parents will be encouraged to bring them to the clinic at other times if they are sick. Management will be on the same basis as mentioned above for adults.

Questions

You are the Minister of Health for Uganda. Because of the importance of the study you have been closely involved in the preparations, discussions and negotiations with the researchers. As the

final preparations are taking shape, your staff calls a meeting with you to discuss some difficult ethical questions that have surfaced late in the discussions that that must be resolved before any final agreement may be reached, specifically:

1. When should consent be sought from the mothers?

2. Should the children's test results routinely be made available to the: "mothers/parents? If so, how?

3. Nevirapine has great potential for saving children's but many surviving children are likely to become orphans. How should this issue be addressed??

4. What are the prospects on the nevirapine treatment, if successful, being taken up across the country? What are your obligations as Minister of health? What should you propose to do?

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