

South African study highlights importance of research involving children

More clinical trials involving children are needed to improve access to essential medicines. However, such trials pose ethical, scientific and practical challenges for researchers.

When 24-year-old Zama heard that her one-month-old baby girl had tested HIV positive, she did not believe it.

“To be honest, I found it difficult to accept that my baby and myself were HIV positive. I’m fit and my baby was not sick,” she said, explaining her initial hesitation at joining a clinical trial for early antiretroviral (ARV) treatment of infants with HIV.

But Zama quickly accepted that both she and her baby were HIV positive, told her boyfriend and her sister, and enrolled her baby in the study.

One year later, Zama is one of seven mothers, feeding and playing with their healthy children in a bright room at Chris Hani Baragwanath Hospital. Mothers there told the *Bulletin* that they were glad to be part of the clinical trial.

Initial results from the Children with HIV Early Antiretroviral Therapy (CHER) study found a significant increase in survival among infants who received immediate ARV treatment. The trial started in July 2005 and is designed to continue through 2011. But a routine review by the trial’s data and safety monitoring board in June this year, found that of the 377 babies enrolled, 96% were alive in the early treatment group compared to 84% in the delayed

treatment group. The results were so striking that the board recommended that no additional infants be placed in the delayed treatment group and all babies be evaluated for initiation of ARV treatment.

The trial, sponsored by the National Institute of Allergy and Infectious Diseases (NIAID), highlights the importance of diagnosing HIV-infected children within the first six weeks of life and facilitating early access to ARV treatment.

Zama said: “I did it for the sake of my child after she tested [HIV] positive. I gave informed consent when she was six weeks old. She has had no complications on treatment and is doing fine.”

Another mother from Soweto, 26-year-old Ntebo, said it was

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Zama, an HIV-positive mother from Soweto.



Claire Keeton

HIV-positive mothers, with nursing sister Valerie Kemesse, hold up their babies and toddlers, who have been participants in a groundbreaking antiretroviral treatment trial for infants.

difficult to disclose her HIV status to loved ones, however, it was necessary in order to treat her baby with anti-retrovirals every day.

She said: “The support we get here has made life easier. I trust the doctors and nurses, and my baby has had no sickness.”

Dr Avy Violari, lead investigator of the Soweto arm of the treatment trial, said disclosure of their HIV-positive status to partners and family was the main challenge for many mothers joining the study.

“You can’t hide the big bottles of syrup for treatment, which has to be taken twice a day,” said Violari of the University of Witwatersrand’s Perinatal HIV Research Unit. “Some mothers were scared to take them home ... [but] these babies were way too young to swallow a pill.”

Getting true informed consent can be another obstacle. All the mothers recruited in the trial took part in group screening sessions and individual sessions to help them understand what joining the trial would mean.

“They were also given a summary of the treatment to take home and when they came back they had another individual session with the doctor,” said Violari. “We would use diagrams and ask them questions to see if they understood. They also had a long informed consent form to sign. The forms were in seven different languages.”

The success of this trial – both its high participation and positive results – shows the huge potential benefits of doing clinical trials to develop and test medicines on children, despite the risks and challenges involved.

The World Health Organization (WHO) recently finalized the first list of essential medicines for children, which will be released in November. Dr Sue Hill, WHO’s technical expert on the list,

said the limited availability of appropriate children’s medicines contributes to childhood mortality.

The development of medicines for children lags years behind that of adults. Pharmaceutical companies, whose research agenda is mostly driven by commercial imperatives, do not always see a sufficient market to be gained among children.

The number of clinical trials among children has gone up in the United States of America where such trials are required by law, said Hill.

Davina Ghersi from WHO’s Clinical Trials Initiative said

her office is working towards a global standard register for clinical trials and would like to see more transparency in trials worldwide.

“Participation in a trial should not just be for the greater good of the community – it should be for the good of the individual too. It should not carry greater than minimal risk for the children either.”

Dr Avy Violari of the University of Witwatersrand’s Perinatal HIV Research Unit.

She said the two core issues in trials involving children are: Who is asking the questions and driving the research agenda? And, are the answers relevant to the public health needs in the countries doing the trials?

Hill said that more research into children's medicines is needed. One

focus is developing different dosage forms besides liquids, which are bulky, heavy to transport and tend to have a shorter shelf-life than tablets. She said some medicines tasted unpleasant and were difficult for children to swallow, for example the ARV drug ritonavir.

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Claire Keeton, *Soweto*
