Prevention of mother-to-child transmission of HIV in Africa: uptake of pregnant women in a clinical trial in Abidjan, Côte d'Ivoire

Monotherapy with zidovudine (ZDV) has been widely used to prevent mother-to-child transmission (MCT) of HIV-1 in developed countries since the positive results of the AIDS Clinical Trials Group (ACTG) 076/Agence Nationale de Recherches sur le SIDA (ANRS) 024 trial have become available [1]. Several alternative interventions trials have been designed and implemented since then in developing countries to overcome the difficulties of use of the ACTG 076 ZDV drug regimen when prenatal care services are limited and breastfeeding a common practice [2].

The main objective of these ongoing large-scale clinical trials is to assess the efficacy of interventions that could be acceptable, efficient and affordable in settings with limited resources [3]. A prerequisite is to assess the acceptability and the feasibility of these interventions. Indeed, it is still uncertain whether HIV voluntary counselling and testing (VCT) can be routinely accepted by pregnant women in developing countries. Other impediments may even render the recruitment of pregnant women more problematic in the clinical trials themselves.

In order to implement a tolerance and efficacy trial of ZDV in Abidjan (Côte d'Ivoire) and Bobo-Dioulasso (Burkina Faso) [4], we systematically proposed the HIV test to pregnant women in selected prenatal clinics. No VCT existed in these clinics prior to the project [5].

Here, we describe how the selection process for this double-blind trial of ZDV versus placebo was conducted in Abidjan from 16 September 1996 to 3 March 1997 (Fig. 1). Of the 3000 pregnant women who consulted the Yopougon Health Centre for their first prenatal visit during this period, 28 women had language barriers that made them ineligible for the proposal of an HIV test, and 753 women were not eligible for the trial itself (427 women were aged under 18 years, 21 women had ≥ 32 weeks of amenorrhea, and 305 women had delivery planned outside Abidjan). When proposed during individual pretest counselling, the serological HIV test was refused by 395 (17.8%) out of 2219 women, mainly because of fear of the result.

Amongst the 1824 pregnant women who agreed to be tested and had blood samples taken, 279 were HIV-positive (15.3%): 249 for HIV-1, 21 for HIV-2, and nine with dual reaction. Of the 258 HIV-1-infected and dually reactive women eligible for the trial, 204 came back for post-test counselling and to receive their test result. Of these women, three refused the confirmation test and 29 were lost to follow-up after this second test, leaving 172 women who came to the appointment to be formally pre-included. Amongst these 172 pre-included HIV-positive women, one was excluded for clinical reasons and none for severe anaemia or leukopenia. Two women came back too late in their pregnancy to be included and 18 delivered before the time of inclusion. Twelve changed their mind and delivered outside Abidjan. Three women reported an abortion. Twelve women, often after a discussion with their husband, decided not to enter the trial and two did not attend the inclusion appointment. We were unable to obtain any information about 51 other women who were lost to follow-up before formal inclusion. In total, 71 women were formally recruited and received the trial treatment.

When we compared the characteristics of the 71 women who were included to the trial with the 101 women who were lost to follow-up between the post-test counselling session and inclusion in terms of age, marital status, level of education, and obstetric history, the only significant difference was age: women included were older than those lost to follow-up (26 versus 24 years; $P = 0.02$). When compared with the HIV-infected women who did not seek their test

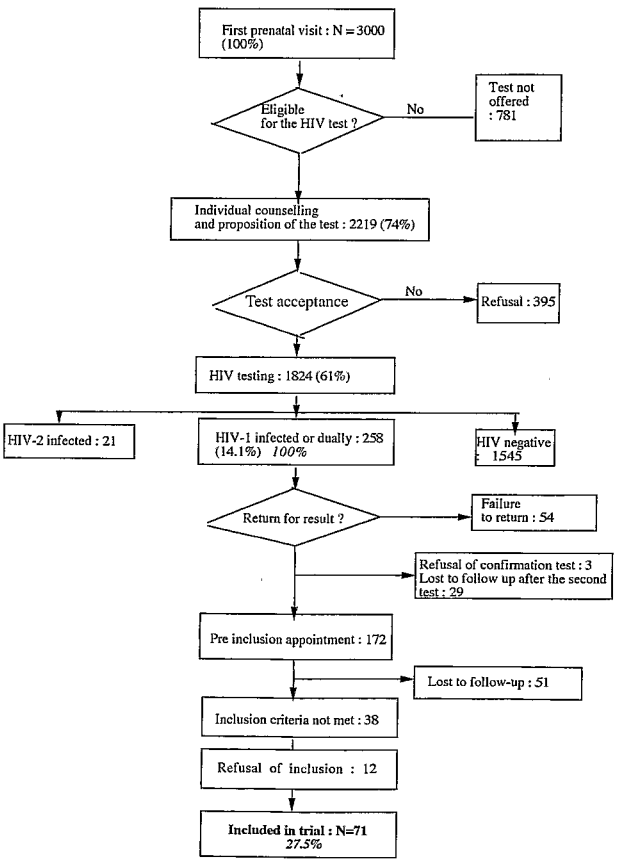

Fig. 1. Selection process in a double-blind placebo-controlled trial of zidovudine for the reduction of vertical transmission of HIV-1 (ANRS 049a, Abidjan, Côte d'Ivoire, 1996–1997).

results or refused the confirmation test (86 women), the only difference was gestational age at the first contact with the team: women who were included came in contact with the team earlier than the others (22 versus 24 weeks of gestation; $P = 0.045$).

In this setting, it was necessary to organize pretest counselling for 3000 pregnant women, to perform HIV tests in 1824 women, in order to recruit 71 women for a clinical trial in which medical care and treatment were free.

The prevalence of HIV infection in this sample of pregnant women was 15.3%, slightly higher than in previous estimates in the same population of Abidjan [6]. This shows the magnitude of the public health problem already represented by MCT of HIV in some developing countries if one assumes that, without intervention, one-quarter to one-third of these children will be HIV-infected.

Test acceptance, after individual counselling and after informed consent was obtained, was high in this population (82.2%), even if lower than expected in a feasibility study conducted in the same population [7].

There was a significant difference between the number of pregnant women who could have benefited from this intervention, had it been efficacious in at least the 258 HIV-infected pregnant women who were identified, and the actual number of women enrolled in the trial. Whether trial conditions and restrictions created more impediments than advantages, compared with routine procedures as they could have been implemented in a routine programme, was unknown.

If feasible and effective antiretroviral treatment is shown to prevent HIV MCT in developing countries [8], information programmes about MCT and its prevention will have to be designed for women of childbearing age and pregnant women. Integrated programmes of prevention of vertical transmission will then need to be elaborated to translate the trial results into public health measures, providing an optimal package of care adapted to the local situation and including VCT.

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