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REPORT FOLLOWED BY RECOMMENDATIONS

INTERNATIONAL

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PROMOTING ACCESS TO ANTIRETROVIRAL THERAPY FOR PREGNANT WOMEN WITH HIV/AIDS IN DEVELOPING COUNTRIES

INTRODUCTION

Every year throughout the world, some 700 000 children, i.e. almost 2000 per day, are infected by HIV. The great majority of these infections result from mother-to-child transmission (MTCT) during pregnancy, during labour or through breastfeeding. Without treatment, the transmission rate can vary from 15 % to 30 % if the infant is not breastfed, and from 30 to 45 % if the infant is breastfed.

In developed countries, where women get global care with access to treatment and to milk substitute, transmission rates of the virus from the mother to the child are now very low: roughly 1 % to 2 % in France for instance.

As early as 1998, in its Statement on access to treatment in Sub-Saharan Africa, the Council advocated global access to ARVs, which was not, then, a widespread approach. Its position was not based on purely ethical consideraations, but also on public health criteria: there can be no efficient prevention actions without global care. In a context where generalized access to treatment is now acknowledged by most of the local and international bodies and with the evolution of knowledge on treatments, the Council considers that the time has come to assess actions now implemented in programmes for the prevention of mother-to-child transmission (PMTCT).

1 LIMITATIONS OF CURRENT PROGRAMMES FOR THE PREVENTION OF MOTHER-TO-CHILD TRANSMISSION IN DEVELOPING COUNTRIES

In developed countries, where treatment is widely available, an increasing number of pregnant HIV+ women are monitored and given combination therapy; this explains the low percentage of infected children. Protocols for the prevention of MTCT have improved over the years and benefit from the latest research findings. In France, for instance, updated recommendations take into account the recent data which show that combination therapy is the most efficient prevention of mother-to-child transmission. It is therefore recommended to continue multitherapy for pregnant women or to initiate it at the end of pregnancy so as to quickly reach the lowest possible viral load . Furthermore, if the woman needs treatment for herself, it can be started earlier during pregnancy. Lastly, ARV-related risks for the infant do exist, but as knowledge stands today, they do not outweigh the risk/benefit ratio of treatment.

As we write, such recommendations are not applied in developing countries where only simplified PMTCT programmes were set up as of 1998. Few and far beteween, they consist for the main part of short regimens of a few weeks, or even single-dose treatments for the mother and the infant.

Such programmes, carried out mainly in Sub-Saharan Africa, are still often presented as having a good cost/efficieny ratio, even if some contenders, especially NGOs, questioned their implementation conditions from the outstart. Numerous instances strongly advocated these programmes which are now part of their fight against HIV/AIDS in developing countries. Despite this mobilization, available data on the way in which prevention programmes are carried out show evidence of certain limitations.

1.1 STILL TOO MANY INFECTIONS

The gap between the number of women who have a PMTCT prenatal visit and the number of women given treatment is considerable. At each stage of the process (first information-and-counselling visit; agreement to test; communication of test result; complete and effective treatment; artificial feeding) the number of women followed up decreases. Several studies find a proportion of about 30 %

of HIV + women seen at a prenatal consultation and who accept to be treated (5) . Now, treatment is only 50% efficient, owing mainly to exclusive breastfeeding or mixed feeding. Subsequently, only 10 to 15 % of the infants born to the women who had a prenatal visit in these programmes actually benefit from prevention.

Causes of the lack of recourse to artificial feeding are now identified: strong stigma of women who do not breastfeed, all the more so as the practice itself now spells HIV infection in many places ; the lack of financial resources when baby formula is not distributed free of charge and for a sufficient length of time by the PMTCT programme ; hygiene problems that increase infants' health risks. Moreover, campaigns in favour of exclusive breastfeeding, which are justified in terms of nutrition, have been carried out for over 20 years by various international organizations. These campaigns do not sufficiently take into account both the changes due to the development of the HIV/AIDS epidemic or the fact that breastfeeding is seldom exclusive and therefore entails almost as many health risks as milk substitute.

1.2 RISKS OF CAUSING RESISTANCES WITH INSUFFICIENTLY POTENT TREATMENTS

In developing countries, the number of treatments used for the prevention of mother-to-child transmission is relatively limited. Most programmes now use AZT (or zidovudine), sometimes combined with 3TC, but more often with nevirapine. WHO now recommends a first-line triple combination (AZT + 3TC + NVP) if the pregnant women can access care early enough. However, WHO also recommends, despite their lesser efficiency and related resistance risks, a double combination (AZT + 3TC), or single-dose nevirapine for the mother and the infant if care starts really late. In actual fact, most of the programmes implemented in developing countries use nevirapine monotherapy due to its availability, low cost and simple use.

However, current use of nevirapine monotherapy for women in those countries may strongly reduce the efficiency of future treatments. Various trials show that utilization of nevirapine monotherapy causes resistance mutations in a number of patients; this is not the case when it is appropriately combined with other ARVs. Depending on the protocols chosen in the trials, the percentage of women with resistance mutations varies from 20 to 70 %. Even if for the mothers, the initial form of virus becomes dominant again over time, the resistance mutations have, so to speak, been " archived " by their bodies and could impede the activity of future treatment. 30 to 60 % of patients treated with nevirapine only at childbirth experience treatment failure six months later when they get certain other combination therapies. Lastly, infants who are born infected to mothers with mutant viruses also get those resistances.

With 80 % of long-term therapeutic programmes in Africa using Triomune, a triple therapy combining nevirapine, AZT and 3TC, it can be thought that a great many women treated with nevirapine monotherapy, and their infants if they are infected, will not benefit from long-term treatments. Furthermore, most of the women are not informed on the toxicity risks related to the use of nevirapine, such as liver disease and drug eruptions . Lastly, resistance mutations caused by nevirapine monotherapy are not only resitances to that drug but to the whole non-nucleoside class. Generalizing treatments based on nevirapine monotherapy therefore highly jeopardizes chances of successful therapy with triple combinations currently available in developing countries and so, in the long run, the survival of these women and their infants.

2 INTEGRATING PROGRAMMES FOR THE PREVENTION OF MOTHER-TO-CHILD HIV TRANSMISSION INTO GLOBAL CARE

There are effective treatments in developed countries and they have enabled to significantly reduce the transmission risks. Likewise, with state-of-the-art knowledge on toxicity risks to both mother and child, and resistance risks, guidelines have changed and treatments recommended have been adjusted.Why should guidelines for developed countries not apply to developing countries ?

2.1 GIVING ACCESS TO ARVS TO PREGNANT WOMEN AND THEIR FAMILIES

As the Council emphasized in its Statement of 1998, there can be no efficient promotion of testing if there is no access to treatment. Such results have been noted in the North and in the South. In programmes where testing is proposed along with long-course treatment, the number of patients who consent, collect their test results and actually start treatment, is much higher than the 10 % usually observed when no treatment is offered (10) . Including HIV positive women in long-term treatment programmes would very likely reduce the rate of 'lost-contact' patients.

Within the PMTCT programmes, follow-up and treatment of these women are too often designed for the unborn babies and maybe future orphans, rather than for the women themselves. They are seen not as infected persons in need of care but as potential sources of transmission. Lack of care for these persons as such is both ethically unacceptable and therapeutically inefficient. Indeed, for lack of treatment, pregnant HIV positive women are only requested to have no other babies and to use contraception. Now, child-bearing and the desire for children are so essential to their social identity that the approach turns them away from the PMTCT programmes and they give birth outside any prevention and care system.

Moreover, because of the very strong social constraints on these women, they very often refuse bottle feeding which ostracizes them as infected persons. And those who do try to reduce the transmission risks for their infants often mix breast feeding and bottle feeding, which for lack of satisfactory hygiene conditions and adequate care, entails for the infants cumulated risks associated to each of these practices. On the other hand, women who get triple therapy during pregnancy and continue it while breast-feeding, will see their viral load go down. Risks of transmission to the infant through breast-feeding could be reduced.

Lastly, extending access to medication to the fathers and other family members, along with information and prevention messages, would help fight stigma and the pressure experienced by people with HIV who subsequently conceal their disease and even discontinue treatment.

Currently, the principle of generalized access to treatment for people with HIV in developing countries has been accepted by the main international and national outfits involved in fighting HIV/AIDS. Proof of this is the development of initiatives such as the 3 by 5 programme or the many projects on access to ARVs that request funds from international bodies, and namely the World Fund. So, it appears necessary to include the existing PMTCT programmes in the various programmes of global access to treatment and to provide triple therapy to pregnant HIV positive women. PMTCT programmes should be designed as an initial stage in access to combination therapy for these pregnant women and their families (" PMTCT + "). WHO in its latest guidelines acknowledges the proven dangers of using nevirapine but draws incomplete conclusions, while what is required is a complete revision of strategies and recommended treatments.

2.2 PREPARING THE CHANGE OF DIRECTION AND SCALE OF PMTCT PROGRAMMES.

For lack of global access to care, except in some countries such as Brazil or Thailand where PMTCT actions are completed with ARV access programmes, less than 1 % of women with HIV in developing countries benefit from such prevention. It is therefore necessary both to change the nature of PMTCT programmes implemented in those countries and to increase their number.

For the National AIDS Council, care for these women with an early combination therapy during pregnancy and continued after delivery, must become one of the basic parts of the programmes of generalized access to treatment in developing countries. The Council is aware of the difficulties entailed by such a change of direction and scale. Nevertheless, the necessary adjustments are to a large extent obvious to all the global access programmes if they are to achieve their goals.

The first condition is the presence, stability, training and monitoring of health care teams. Programmes for access to care are too often understaffed, underpaid and undertrained. The change of scale will not be achieved without teams' involvement and recognition.

Furthermore, the change means reinforcing the network between health care teams in charge of mother-and-child health, and health care teams specialized in HIV/AIDS : within far too often poor and socially discriminating health care systems, prenatal consultations and delivery are a sometimes unique opportunity for contact with a health care facility and therefore access to primary care and health education messages. Childbearing must thus be a privileged time for global access to care : basic essential care should be offered so as to reduce not only infant mortality but also maternal mortality and especially mortality that can, sooner or later, be related to HIV/AIDS. It also necessary to support these women within in their families so as to get its adherence to and involvement in the programmes.

Lastly, the practical conditions of programme implementation must be addressed, so as to improve their efficiency, especially by preventing losing contact. Thus, the issue of the cost of treatment for the patients but also of transportation and consultations will have to be tackled, as will the issue of interaction between heath carers and patients in order to propose a realistic but fundamental change in the programmes.

3 THE NATIONAL AIDS COUNCIL'S RECOMMENDATIONS

The National AIDS Council considers that if the introduction of simplified protocols for the prevention of mother-to-child transmission was an important step in the awareness of the issues of the fight against AIDS, it no longer seems sufficient. With the ongoing initiatives in favour of global access to treatment, mothers must benefit from treatment when they need to. Also, the evolution of knowledge on efficiency and side-effects of medication, entails new recommendations.

In such a context, the Council once again stresses that respecting people's rights is a key element in making HIV/AIDS programmes work. The underlying definition of prevention in the programmes currently implemented to reduce MTCT, must be reappraised so that pregnant women with HIV be considered as persons whose situation requires global care and not just as potentially contaminating future mothers. Pregnancy must therefore be one of the privileged times for access to care, the goal of which is to reduce both infant mortality and maternal mortality.

Consequently, the National AIDS Council recommends efficient and prophylactic combination therapy for pregnant women: that is how the highest reduction in transmission rates is achieved and how future treatment options are best ensured for the mothers and the infants. It recommends their inclusion in programmes for global access to ARVs : the Council considers that including programmes of care for pregnant women in programmes of global access to ARVs will have beneficial consequences both in terms of prevention of HIV transmission from mother to child and in terms of care for women with HIV. It once again stresses that testing must be linked to a direct benefit for the person. In such conditions, the availability of treatments should significantly increase the number of women benefitting from long-term therapeutic care.

The Council considers that treatment should be offered to pregnant women but also to the fathers and other members of the family within the framwork of global care. Moreover, feeding modalities should be better taken into account in these programmes.

Furthermore, the National AIDS Council is concerned about the development of resistances that can be entailed by an insufficiently potent treatment, both among infected mothers and infants. Such resistances compromise the efficiency of future treatments. The Council considers that it is no longer acceptable, owing to new knowledge, to make infected pregnant women and infants run that risk while there is a new perspective of future access to efficient ARV treatment for them.

The Council subsequently recommends a revision of currently recommended protocols in developing countries and the development of efficient therapeutic strategies adapted to the specific situations of those countries.

The National AIDS Council is however quite aware of the practical grass roots difficulties and of the need to monitor the measures it recommends, particularly through supervision of and training courses for health carers. All international cooperation programmes for access to ARVs must increase efforts for the improvement of the parctical implementation conditions.

LIST OF INTERVIEWEES

The National AIDS Council is endebted to the following persons who agreed to be interviewed by the Standing Committee on International Issues :

- madame le docteur Alice Desclaux, laboratoire d'Ecologie humaine et d'anthropologie, Université d'Aix-Marseille III, Aix en Provence ;
- madame le docteur Isabelle De Vincenzi, Organisation mondiale de la santé (OMS), Genève ;
- madame le docteur Catherine Dollfus, praticien hospitalier, Service d'hématologie/oncologie, Hôpital Trousseau, Paris ;
- madame le docteur Marie-Josée Mbuzenakamwe, coordinatrice du centre Tuhiro de l'Association nationale de soutien aux séropositifs et sidéens (ANSS), Burundi ;
- madame le professeur Christine Rouzioux, responsable du secteur virologie, Hôpital Necker-enfants malades, Paris ;
- monsieur le docteur Jean-François Chambon, secrétaire général de la Fondation GlaxoSmithKline France ;
- monsieur le professeur François Dabis, Institut de santé publique, d'épidémiologie et de développement, Université Victor Ségalen, Bordeaux ;
- monsieur le docteur Marc Lallemant, directeur de recherche, Institut de recherche pour le développement (IRD), Perinatal HIV Prevention Trial, Thaïlande ;
- monsieur le docteur Jean-Elie Malkin, responsable de la veille médicale et scientifique, Ensemble pour une Solidarité Thérapeutique Hospitalière En Réseau (ESTHER), Paris ;
- monsieur le professeur Philippe Van De Perre, chef du laboratoire de bactériologie et de virologie, CHRU Arnaud de Villeneuve, Montpellier.