

The experience of providing universal access to ARV drugs in Brazil

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INTRODUCTION

The Brazilian HIV/AIDS drug policy has been extensively discussed and even criticized, particularly at the time of its implementation by the Government in the early 90s. However, after a decade of action, the success of the Brazilian response to HIV is evident and achieved worldwide recognition, based on a concerted early governmental response, a strong and effective participation of civil society, a multi-sector mobilization, a balanced prevention and treatment approach and the advocacy of human rights in all strategies, particularly with the policy of wide access to antiretroviral (ARV) drugs.

In order to improve quality of life for people living with HIV and AIDS, the Brazilian Ministry of Health (MoH) implemented a policy of universal free of charge access to antiretroviral therapy in the mid 90's. This effort was

initiated in the early 1990's with limited distribution of the ZDV capsules, and was strengthened with a 1996 presidential decree that ordered all HIV-infected citizens to have free access to essential medication to combat HIV. The distribution of protease inhibitors began between December 1996 and January 1997. The same presidential decree stipulated that the criteria for dispensing HIV treatment would be established by the Ministry of Health, which had two task forces working on the problem, one focusing on HIV therapy for adults and adolescents and one for children. The two task forces gathered at least once a year to review established criteria and to discuss new medical breakthroughs and the availability of new treatments.

BRIEF OVERVIEW

By the end of 2001, approximately 113,000 patients received ARV

through the public health system, representing roughly US\$ 232 million in expenditures to buying a list of 14 drugs that make up the so-called "anti-HIV cocktail". These expenditures with antiretroviral drugs represent 1.6% of the total budget for the Ministry of Health and less than 0.05% of Brazilian GDP in 2001. In addition, the Brazilian Government established national HIV treatment guidelines for adults, children and adolescents and implemented a logistic control system of these drugs in more than 400 ARV dispensary units throughout the country and, in order to adequately monitor treatment, it also established a National Network of Viral Load Laboratories and a Network of TCD4+TCD8+ Lymphocyte Counting laboratories, with 73 and 65 units, respectively. Concomitantly, a network of approximately 900 public alternative HIV/AIDS care services was built up based on

regional and administrative divisions according to the complexity of the care needed, in order to improve the monitoring of HIV infection and for diagnosis and medical observation of opportunistic diseases. It is also important to say is that the acquisition of drugs to treat AIDS-related opportunistic diseases was established as an attribution of states and municipalities.

FIRST RESULTS

After five years, the results of these strategies were impressive. From 1996 until now we have observed a striking reduction on mortality, morbidity and hospitalization rates for HIV+ patients in Brazil, with cost-reduction for this antiretroviral therapy policy.

The occurrence of HIV-related opportunistic infections decreased by 60-80%. Tuberculosis in HIV+ patients, for instance, dropped 75% in the last four years, in the State of São Paulo, which accounts for roughly 50% of all AIDS cases reported in Brazil. Moreover, a change in the profile of HIV health care services was observed, with a significant demand increase for outpatient, home care and a decrease for in-patient and day-hospital services.

Another figure that reflects the impact of the Brazilian policy of universal access to antiretroviral drugs is the phenomenon of partial immunological reconstitution promoted by

the treatment. This was demonstrated by the evolution of the mean TCD4+ cell count in HIV+ patients on ARV therapy after widespread use of HAART in Brazil. In a small study conducted by MoH in 2002, we observed that the mean cell counts rise progressively from 267 cel/mm³ to 426 cel/mm³ after 24 months of treatment with combined ARV regimens. This improvement seems to significantly contribute to the reduction in frequency and severity of opportunistic diseases associated to HIV and to be a good indicator of the better quality of life of patients treated in the public health network.

RECENT DATA

All of these aspects are consequences of an evident reduction in the number, time of duration and complexity of treatment in hospital admission episodes, suggesting a significant welfare profit for these patients after a more disseminated use of antiretroviral combined therapy. It is also worth noting a reduction of more than seven fold in hospitalization rates and 358,000 avoided AIDS-related hospital admissions, resulting in an overall saving to the Government of more than US\$ 1.1 billion for the 1997-2001 period.

By the end of 2001, the Brazilian MoH distributed 14 antiretroviral drugs of three different pharmacological classes to all HIV infected patients that meet the criteria estab-

lished by national guidelines. Of these, we have eight locally produced anti-retroviral formulations, with pharmacological specifications for generic versions of these groups. A new drug, an association of Lopinavir/ritonavir (LPV/r), was added to this MoH list in March 2002.

Furthermore, prices of antiretroviral drugs purchased by the Brazilian MoH have been declining quite significantly over the last few years. This is mainly thanks to, firstly, investments made by the MoH to set up domestic national laboratories and, secondly, effective negotiation of drug prices with international pharmaceutical drug companies that are exclusive producers of certain anti-AIDS drugs. At this moment, we have 6 federal ARV pharmaceutical producers and one of them, the Farmanguinhos/Fiocruz Pharmaceuticals (from Brazilian MoH), is responsible for approximately 40% of the total amount of antiretroviral drugs used in Brazil. In fact, prices of drugs produced within Brazil, fell on average 82% between 1996 and 2001, however, imported drugs fell only 25% during the same period. In 1999, the expenditures with imported ARV drugs represented 81% of total MoH budget for ARV drugs, but in 2001 it has dropped to approximately 57% and 63% of ARV consumption in the Public Health System are locally produced versions of these drugs.

NEGOTIATION STRATEGIES

To avoid the use of compulsory licensing in certain situations, the Brazilian MoH also has used a negotiation strategy with some exclusive producers based on tiered or differentiated prices. An agreement with Merck Sharp & Dhome Laboratories to reduce the prices of two anti-retroviral medicines produced by that company was announced in April 2001. Indinavir underwent a price cut of 64.8%, Efavirenz had its price reduced by 59% and another negotiation occurred in 2001 with Roche Laboratories which cut Nelfinavir prices by 40%. Recently, an agreement with Abbott Laboratories has also reduced the price of its new protease inhibitor (LPV/r) by 46%. With these strategies, the average cost for patient/year in antiretroviral therapy decreased by half in recent years, in spite of the proportional increase in the number of patients needing more expensive, complex treatments.

The average cost for patient/year in antiretroviral therapy decreased a full 48% between 1997 and 2001 (from US\$4,860 in 1997 to US\$2,530 in 2001). It is also important to emphasize that local production of HIV-drugs is being done only for domestic consumption. Negotiations are the Brazilian Government's first option when dealing with drug companies. The compulsory license is only a safeguard and last option in order to provide

access to medicines for the Brazilian people and has never been used, up to now.

ARV ANTIRETROVIRAL DISTRIBUTION AND CONTROL

The Brazilian MoH also has implemented a specific computerized system for logistic distribution and control of anti-retroviral drugs named SICLOM. At this moment, SICLOM is fully implemented in 111 antiretroviral dispensary units, and covers around 65% of total patients on ARV treatment in the Public Health System. The major objectives of this logistic control system are:

- to control drugs stock at national, state and municipal levels;
- to assure efficiency and safety in the provision of drugs;
- to plan the purchase of drugs; and
- to assure general management of drugs.

All these strategies and tools certainly contributed to promote sustainability and maintenance to the universal access to ARV policy adopted and when we analyze the final costs of ARV expenditures and the savings of hospitalizations/opportunistic infections treatment avoided, we can see that the Brazilian ARV access policy is cost-effective.

We estimate that the Brazilian policy for national production of ARV drugs has represented an economic

saving of approximately 490 million dollars in the 1996-2000 period. With the start of local production of Nevirapine and Indinavir, the Brazilian Government has saved approximately US\$ 80 million in a one-year period, which represented 30% of global expenditures in 2000. Another new strategy that we are now evaluating is the local production of a generic version of new co-formulation and presentations of ARV that will reduce the daily pill burden, which will improve adherence to treatment and can promote an additional cost reduction.

ADHERENCE TO TREATMENT

The Brazilian MoH has also created an advisory committee to establish the official recommendations for treatment with antiretrovirals. Accordingly with the most recent review of Brazilian antiretroviral guidelines, the use of potent antiretroviral therapy was established as standard of care. Antiretroviral treatment is recommended for all symptomatic (AIDS) individuals, regardless of laboratorial parameters, and if patients are asymptomatic, it is indicated only if the CD4 cell count is lower than 200/mm³. However, these guidelines consider the use in asymptomatic patients if the CD4 cell count is between 200 and 350/mm³.

Another important topic is adherence to antiretroviral treatment. Recently we conducted a multicentric trial in 27 care units in the State

of São Paulo, with a follow up of almost 9,000 HIV+ patients. The study considered the capacity to take more than 80% of prescribed pills as a definition of good compliance. At the end of the study we calculated an adherence rate of 69%, which is very similar with the results found in international studies. In this study, the major factor associated with good adherence was the quality of medical service. Now, we are starting a new complementary study, in order to evaluate the quality of care in AIDS outpatient services and its relation to patient adherence to antiretroviral therapy.

Until this moment, the prevalence and profile of drug resistance mutations in Brazilian patients under HAART has been very similar to what have been found in international studies. However, the prevalence of primary resistance in first time drug patients is less than 8%, significantly lower than the rates seen in Western Europe and the US. Together with striking reduction on mortality, morbidity and hospitalization rates for HIV+ patients, the quality, safety and efficacy of generic antiretroviral drugs are reinforced and so is the policy of universal access to ARV therapy adopted by the Brazilian Ministry of Health in the last decade. However, considering the impact that this aspect can have on the Brazilian HIV treatment policy, the MoH decided to establish a National Network of Genotyping Test

(RENAGENO) able to perform and interpret the results of HIV-1 resistance tests using an adequate and rational criteria. For the initial implementation of this network, 12 laboratories were accredited and 60 reference genotyping expert physicians from different parts of the country were trained to act on a regional basis.

EXPRESSIVE MEASURES TAKEN BY BRASIL

It has been a long process to arrive at these achievements, and some lessons were learned. Firstly, some adherence strategies to optimize the antiretroviral therapy are needed. Pilot studies in Brazil have demonstrated that feasibility, efficacy and adherence rates with antiretroviral treatment are similar to those obtained in high-income countries, even among patients with low education or with important social limitations. Training projects for health care workers and organization of patients groups to improve adherence also have been identified as important factors that explain the success of this process, that used simple clinical and laboratorial tools for diagnosis, treatment monitoring and approach.

Secondly, the participation of civil society at every level of decision-making and during the elaboration of relevant strategies is of paramount importance. I have to emphasize that this is one of the key as-

pects of the Brazilian STD/AIDS Program and has served to help guarantee the human rights of patients with HIV/AIDS and other STD, and the execution of community projects and the building of partnerships with the private sector.

However, some challenges are coming. In the near future, the Brazilian Government must improve the diagnosis of HIV infection in early stages, ensure mother to child transmission prevention for all pregnant HIV+ women around the country, expand the CD4 and viral load laboratory networks so as to decentralize it, and better monitor adherence and viral resistance, particularly in 'hard to reach' groups.

Brazil also has made its voice heard in several international forums worldwide promoting the expansion of access to ARV. Among them, it is worth highlighting the Brazilian participation at the 57th Session of the United Nations Commission on Human Rights, held in April 2001, advocating the provision of treatment and care to HIV/AIDS patients as a fundamental human right. Brazil has also consistently pushed for the flexibility of the WTO-based TRIPS (Trade Related Aspects of Intellectual Property Rights) Agreement, and the IV Ministerial Meeting of the World Trade Organization, held in November 2001, is a cornerstone example of success of the Brazilian policy. As a member at the Transitional Working Group of the Global

Fund to fight Aids, Tuberculosis and Malaria, Brazil has also played a very important role to ensure the participation of developing countries and civil society actors in its decision-making structure. Finally, it should be said that Brazil articulated and collaborated, in partnership with the Horizontal Technical Cooperation Group of Latin America and the Caribbean, in the elaboration of an international Databank of Prices of Aids Drugs.

Considering all aspects described above, it is now clear that past objections to HIV treatment in developing countries is not persuasive anymore and there are strong arguments in favor of the effort for widespread treatment access. A considerable amount of evidence suggests that an effective Aids treatment is possible even in low-income countries. Contrary to what the World Bank expected in early 90's, that 1.2 million people would be infected by the year 2000 in Brazil, recent estimates have placed the figure at 597,000 HIV carriers, or in other words, approximately half the number predicted some years ago. This performance is highly significant, even taking into account possible statistical errors and epidemiological trends, and represents a result of balanced efforts in prevention and care. Reducing prices of antiretroviral drugs and promoting other strategies to expand effective access to them can dramatically alter the economics of

HIV/Aids treatment, and possible obstacles to adequate treatment such as poor infrastructure can be overcome through a well designed and supported international effort to improve the approach to Aids both in rich and poor nations of the world.

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