Review Article
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Antiretroviral effectiveness with Cuban generics in patients with HIV/AIDS in the province of Santiago de Cuba

Abstract

The HIV/AIDS epidemic continues to be a real health problem; one of the most significant progresses in the fight against the epidemic is the highly effective antiretroviral treatment. A descriptive and transversal study was carried out, with retrospective collection of the sample. We used a study universe consisting of all patients with AIDS of the mentioned province, selecting a simple random probabilistic sample of 60 patients with HIV/AIDS, belonging to the province of Santiago de Cuba who graduated from the Internal Medicine service of the General Teaching Hospital Dr. "Juan Bruno Zayas Alfonso" (clinical immunology). Clinical and therapeutic variables were used according to the national program and expert criteria, arriving at precise estimations in the variations of the effectiveness of the therapeutic used of this medication through selected clinical and hematological parameters. The female sex predominated in the conglomerate of patients and there was a greater percentage of recoverability of the evolutionary parameters studied for the male sex. Scheme I showed to be the most used with figures of 41.7%, modifying the parameters of studies such as CD4 and viral load in a beneficial and staggered manner according to the quarters analyzed. The effectiveness of the therapeutic scheme used became evident, based on a marked increase in the values of CD4 lymphocytes, and the relevant decrease in viral replication, which translates into a significant decrease in opportunistic diseases.

Keywords: AIDS, antiretroviral effectiveness, viral load, CD4 lymphocytes

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Introduction

The HIV/AIDS epidemic is still a real health problem, the reality is that more than 80% of AIDS patients in most nations die severely immunocompromised, suffering multiple opportunistic infections and extremely aggressive neoplasms. One of the most significant advances in confronting the HIV/AIDS epidemic has been the development of highly active antiretroviral therapy (HAART), which prevents or slows the progression of the disease, with the positive impact of reducing the burden circulating viral, restore the immune system and improve the quality of life.1 Despite the controversy that this issue still results, there is solid evidence that HAART has revolutionized the horizons of these patients. Systematic improvements are known in the prognosis and quality of life, as well as in important reductions in AIDS-related morbidity and mortality, especially in North America and Europe.[1,2] Recent statistics referring to the end of 2017 report that 36.9 million [31.1 million-43.9 million] people lived with HIV worldwide, about 1.8 million [1.4 million-2 , 4 million] people became infected with HIV and 940,000 [670 000-1.3 million] people worldwide died from AIDS-related diseases, compared to 1.9 million [1.4 million -2.7 million] in 2004 and 1.4 million [1 million-2 million] in 2010.[3,4]

In Cuba, the essence of the social system and political will have implemented multisectoral strategies aimed at prevention, diagnosis, treatment and everything related to the HIV/AIDS issue. At the end of 2017, this Caribbean region exhibited an estimated prevalence rate in the sexually active population of 0.24%, which continues to be one of the lowest in the region, as reflected in the Annual Report of the Prevention Program and Control of STIs / HIV/AIDS.[5] All the above requires, on the part of the medical staff, not only the clinical knowledge of their causes, but also the uptake of the patient with the positive result and their initial clinical evaluation, as well as the referral to the specific unit of specialized care, where you will be diagnosed and the appropriate treatment will be indicated.[6]

Antiretroviral drugs (ARVs) are drugs that act as inhibitors at different stages of the viral life cycle. To date, the most commonly used are those that interact with enzymes: reverse transcriptase (IRT), protease (IP) and integrase or in the fusion mechanism of the virus with the host cell. These ARVs are used in combination in therapeutic schemes, which is known as highly effective antiretroviral therapy (TARVAE).[7,8] The TARVAE, manages to reduce the viral load (CV) to undetectable levels, increase or stabilize the number of T-CD4 + lymphocytes (LT-CD4 +), significantly decrease the incidence of opportunistic infections (OI), with a notable impact on the decrease of mortality and an increase in the quality of life.[7,8] The correspondence between viral infection and the use of ARVs has been demonstrated, with the incidence of haemochemical and hematological alterations in patients. This fact reflects changes that are mostly nonspecific, in the function of the organs and systems that could be the cause or consequence of the pathophysiological state of the disease process generated by the virus.[7-9]

The effectiveness of ARVs has become a topic discussed by experts in comprehensive care for people with HIV/AIDS. In our province there are few studies that reflect this problem, so a question arises, will the effectiveness of HAART with the Cuban generic schemes in our conglomerate of patients be remarkable? In this sense, the preparation of this work, in order to estimate the variations in their effectiveness, in relation to selected clinical and hematological parameters.

Method

A descriptive and cross-sectional study was carried out, with retrospective collection of the sample, using a universe of study constituted by all patients with AIDS of the mentioned province, a simple random sample of 60 adult patients with HIV/AIDS was selected, with clinical and humoral follow-up, carried out in the "Dr. Juan Bruno Zayas Alfonso" Clinical and Surgical General Hospital, of

the province of Santiago de Cuba, in the period January 2015-2017, with the objective of estimating the variations in the effectiveness of antiretroviral treatment with generic drugs. Effectiveness of the applied therapeutic plan: To the effects, the antiretroviral treatment was conceived of the following way:

Effective: it was considered as such when the global CD4 + count and the viral load at the end of the treatment imposed by the investigation period were adequate, and when the patients presented a satisfactory clinical response to antiretroviral treatment.

Not effective: it was considered as such when the response measurement parameters, previously described, were not adequate, accompanied or not by adverse reactions to all types of drugs (first and second lines), which prevented it from continuing.

The global CD4 + lymphocyte count was considered adequate when it exceeded 50 cells / mm3 after 4-8 weeks of medication, and the viral load was 50% lower, compared to what was initially found before starting antiretroviral therapy and inadequate when this first decreased riskily and the second doubled. Regarding the evolution of the clinical response, it was satisfactory when the initial symptoms and signs improved, new opportunistic infections did not appear if they had or recurred, and the carriers gained in body weight; and it was considered unsatisfactory when the systemic manifestations of the disease worsened or other pathogens were contracted. The average and the standard deviation were used as a summary measure for quantitative variables and the percentage as a summary measure for the qualitative variables. The x2 homogeneity test was used to identify a statistically significant association between the criteria of interest. A level of significance $\alpha = 0.05$ was selected. The Test Statistician was used:

To identify significant differences between the evolutionary quantitative parameters (CD4 and viral load) non-parametric variance analysis for related samples was applied (Friedman's test). In this case, the statistical hypotheses to be tested were: H0: $\mu1 = \mu2 = \mu3 = ... \mu K$ and H1: $\mu i \neq \mu k$, for at least one pair of i, j. The Test Statistician was used: $X2 = [12/N^* K^* (K + 1)^* (\Sigma R.j) 2-[3^*N^*(K + 1)]] \rightarrow \chi2$, with (k-1) degrees of freedom. The participation of individuals in the investigation depended on the ethical principles contained in various documents, namely: principles of beneficence, non-maleficence, justice and autonomy, based on the Nuremberg Code (1947), and the Declaration of Helsinki (1989).

Results

Table 1 shows that schemes I, II and IV required the highest percentage magnitudes, with 25 (41.7%), 20 (33.3%) and (10) 16.7%, respectively, not applying the Scheme VI to no patient. The analysis of humoral parameters associated with the disease (CD4 and viral load), requires significant evolutionary differences in the three quarters analyzed for both indicators: increase for the first and decrease for the second; only no marked differences were found for the CD4 count corresponding to treatment scheme V, (Table 2). Table 3 reflects the association between the clinical evolutions of the patients according to the different treatment schemes. It is identified that, for the first four schemes, the preponderant percentage magnitudes corresponded to a satisfactory evolution of the patients, the least important being the one corresponding to scheme V, with 50.0%. There were 53 patients representing 88.3% who progressed satisfactorily, regardless of the antiretroviral treatment regimen imposed. Table 4 identifies high percentages of effectiveness of the different antiretroviral therapies, with percentages equal to or greater than 70.0%, except for scheme V, which only reaches 50.0% effectiveness. In 8 out of 10 patients, the effectiveness of the imposed treatment was verified.

Table 1 Distribution of the conglomerate of patients according to the type of antiretroviral treatment with Cuban generic drugs used

Antiretroviral treatment	No.	%
Scheme I	25	41,7
Scheme II	20	33,3
Scheme III	1	1,7
Scheme IV	10	16,7
Scheme V	4	6,6
Total	60	100,0

Source: Clinical history and specialized consultation control card.

Discussion

Pharmacological treatment consists of the consumption of antiretroviral drugs in the amounts, hours and doses indicated. This treatment is highly complex, especially because of its unpleasant side effects and the continuity and long period in which they are consumed. It also requires the person to make significant changes in their lifestyle.[10,11] The treatment of HIV infection is based on combinations of three drugs, as it delays the progress of the disease, improves the quality of life of people, by suppressing the replication of the virus in a maximum and lasting, restoration or preservation of immune function, hospital admissions decrease, associated costs and significantly increases survival. The number of available antiretroviral drugs allows multiple combinations of treatment. When selecting treatment, since many of these combinations have a similar efficacy, it is necessary to assess other aspects such as the number of tablets, the frequency of administration, the appearance of adverse reactions, tolerance and adherence of previous treatments, Potential drug interactions and cost.[10,11] Morbidity and mortality in HIV-infected patients has changed dramatically since 1996 with the inclusion of protease inhibitors (PI), and more recently with the inclusion of IP-sparing schemes with non-nucleoside reverse transcriptase inhibitors, 11-13 includes nevirapine, in our research scheme I using nevirapine was used in a large proportion of patients, recent studies have used this scheme, which also use zidovudine (AZT) and lamivudine (3TC). Our research series reflects the majority of patients' consumption due to several factors, including better global accessibility, better adherence and less toxic effects.

However, it is important to mention that the improvements in the new antiretroviral drugs have succeeded in suppressing more opportunistic infections.[12-14] These data coincide with our research, which improved the results of CD4 and viral load globally for the prescribed schemes with Cuban generics, during the first three months of antiretroviral treatment. Studies report that in the first months this aspect, especially mortality, is 4 times higher if the CD4 count is less than 100 cells/ml compared with patients with CD4 greater than 200 cells/ ml, as well as the mortality after the first three months of ART,

regardless of the CD4 count remains constant over time, these figures are similar to the mortality rates reported in some chronic diseases such as diabetes mellitus or arterial hypertension.[15,16]

Table 2 Distribution of sick patients with AIDS according to the treatment schemes with Cuban generics and selected humoral parameters (CD4) and (viral load)

Schemes of treatments	Selected parameters						Signif. (prob.)
	I Quarter		II Quarter		III Quarter		
	CD4		CD4		CD4		
	Media	Desv.st.	Media	Desv.st.	Media	Desv. st.	
I	235,6	64,3	269,2	57,6	297,5	61,2	0,004
II	200,6	64,3	216,5	57,7	269,4	47,6	0,000
III	198	0,0	220	0,0	315	0,0	0.000
IV	190,1	18,2	216,3	37,0	270,4	52,9	0,000
V	200.0	24.5	213.0	13.2	292.3	48.2	0.074
Schemes of treatments	**Viral load**		**Viral load**		**Viral load**		**Signif. (prob.)**
	Media	**Desv.st.**	**Media**	**Desv.st.**	**Media**	**Desv.st.**	
I	55390.5	238725.1	3422.6	5383.4	811.7	1840.3	0.000
II	41014.4	74022.6	4501.5	7070.1	139.8	194.1	0.000
III	23444	0.0	24	0.0	0	0.0	0.000
IV	101719.5	273525.4	3039.0	4016.1	40.3	107.5	0.000
V	5492.5	4987.8	25.3	32.1	17.5	21.1	0.038

Source: Clinical history and specialized consultation control card.

Table 3 Distribution of the clinical evolution of patients suffering from AIDS according to antiretroviral treatment schemes with Cuban generics

Scheme of treatment	Clinical evolution					
	Satisfactory		Not satisfactory		Total	
	No.	%	No.	%	No.	%
I	23	92,0	2	8,0	25	100,0
II	19	95,0	1	5,0	20	100.0
III	1	100,0	0	0,0	1	100,0
IV	8	80,0	2	20,0	10	100,0
V	2	50,0	2	50,0	4	100,0
Total	53	88,3	7	11,7	60	100,0

Source: Clinical history and specialized consultation control card.

p = 0.103 (not meaning).

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Table 4 Distribution of patients suffering from AIDS according to antiretroviral treatment regimens with Cuban generics and therapeutic effectiveness obtained.

Scheme of treatment	Therapeutic effectiveness					
	Cash		No cash		Total	
	No.	%	No.	%	No.	%
I	22	88,0	3	12,0	25	100,0
II	17	85,0	3	15,0	20	100.0
III	1	100,0	0	0,0	1	100,0
IV	7	70,0	3	30,0	10	100,0
V	2	50,0	2	50,0	4	100,0
Total	49	81,7	11	18,3	60	100,0

Source: Clinical history and specialized consultation control card.

p = 0, 327 (not meaning).

Our research shows how the immunological elements through their markers (CD4 and viral load) are useful when they are used to establish early prophylactic and therapeutic measures, as well as the evaluation of the efficacy and monitoring of treatments in HIV-AIDS infection. For a biological marker to fully satisfy the definition of a substitute marker in HIV infection, it must meet two requirements: a) variations in marker values over time must correlate with the risk of clinical progression of the infection; and b) any effect of a treatment on the risk of clinical progression should be explainable and predictable due to its action on the substitute marker (Colburn, 1997) .[16-19] Our research demonstrated that the use of ARV treatments with locally produced drugs , in our small sample, has fulfilled the main purpose of therapy, which is to achieve the maximum reduction in viral load for as long as possible, the decrease in the appearance of opportunistic infections and a significant increase in the CD4 count.

Our series also shows that the analysis of the humoral parameters associated with the disease (CD4 and viral load), requires significant evolutionary differences in the three quarters analyzed for both indicators: increase for the first and decrease for the second; only marked differences were not found for the CD4 count corresponding to the treatment scheme V. This drug-immunological analysis coincides with series of studies on this topic.[18,19] Regarding the clinical evolution of the patients according to the different treatment schemes, they were not significant from the statistical point of view (p=0.103) (it does not mean.), although from a medical-assistance perspective. The first two treatment schemes were effective, not only in the sense of the clinical evolution of these patients, which could be corroborated by not having presented any of the typical clinical signs of AIDS marker. A study in South Africa reported coincidence with our investigation, reflecting that of 2 446 patients on ART, 749 (30.6%) achieved immune reconstitution (CD4 200 cells / mm3 or more) and 1021 (41.7%) state of virological suppression (viral load <400 RNA copies / mL).[20]

Conclusion

In total, 576 cases reached both therapeutic objectives, so that the total number of patients with relevant quantifiable efficacy according to the laboratory monitoring of CD4 and viral load was 1 194, almost half of the cases under treatment (48, 8%), while only 201 cases of the treaties died in the period, with an effectiveness/ decease rate of 5.9/1.20 In other words, for every 7 patients on ART in which 1 died, another 6 filed relevant immunological and/or virological improvement, evidencing the clinical improvement and the consequent antiretroviral effectiveness. If a critical and detailed analysis of these data is made, it can be seen that most of the members of the casuistry improved the symptoms and initial signs of the condition, which for many were opportunistic diseases, disappeared the same after one year of treatment. , with no recurrences, with some well-defined manifestations such as those caused by lack of sleep,[17-18,20] while the improvement in CD4 and viral load values remained evident. This work shows the population effectiveness of the implementation of different therapies against HIV, not so much the individual efficacy, which is already known by clinical trials. This analysis allows evaluating how the introduction, since 1996, of the therapies against HIV has markedly improved the progression of the infection to different AIDS events. Individual treatment variables were not used, but the calendar period as a variable that change over time, in order to evaluate the population effectiveness of treatment inclusion. As a colophon, it can be corroborated in our research, that the antiretroviral effectiveness is still connoted in the schemes available to patients in our country with Cuban generics, estimating favorable variations of the therapeutic schemes, but unquestionably based on a marked increase in the values of CD4 lymphocytes, and the relevant decrease in viral replication, which translates into a significant decrease in opportunistic diseases and with it the morbidity and mortality due to AIDS.

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Conflict of interest

The authors declare that there are no conflicts of interest.

References

1. Betancourt Gambino J. Adherence to antiretroviral treatment in seropositive patients. *Cuban Journal of Comprehensive General Medicine*. 2019;34(3):955.
2. Espinosa Aguilar A, Avila Sánchez M, Gibert Lamadrid Md. An updated conception of adherence to antiretroviral treatment. *Cuban Journal of Nursing*. 2018; 34(1).
3. Statistical yearbook of health. Address of medical records and health statistics. Ministry of Public Health. Cuba, 2017.

4. Information sheet. Latest statistics on the state of the AIDS epidemic, 2017.
5. Mendo Alcolea Neity, Mesa Perez Eduardo de Jesus, Neyra Barrios Rafael, et al. Adverse reactions to antiretroviral drugs in patients with human immunodeficiency virus. *Medisan*. 2018;22(8):674–682.
6. New advances in research and development on HIV, 2014.
7. Gil del Valle, L, Lezcay Rizo M, Castro Perigó Y, et al. Evaluation of effectiveness and follow-up of Cuban AIDS patients with late diagnosis treated with antiretrovirals. *Cuban Journal of Pharmacy*. 2016;50(4):1561–2988.
8. Lamotte J. HIV/AIDS infection in today's world. *Medisan*. 2014;18(7):993–1013.
9. US Department of Health and Human Services. 2018.
10. Espinosa Aguilar A, Avila Sánchez M, Gibert Lamadrid Md. An updated conception of adherence to antiretroviral treatment. *Cuban Journal of Nursing*. 2018;34(1).
11. Betancourt Gambino J. Adherence to antiretroviral treatment in seropositive patients. Cuban Journal of Comprehensive General. *Medicine*. 2019;34(3).
12. Montalvo Raul, Mejia Jhonatan, Ramirez Percy, et al. Mortality in patients with HIV/AIDS infection in antiretroviral treatment in Huancayo, Peru 2008-2015. Minutes Peruvian [Internet]. 2016;33(2):119–125.
13. Collazo M, De la Cruz B, Tapanes R. Pharmacoeconomics: Should it be of interest to evaluate antiretroviral therapy in HIV/AIDS? Pharmacoeconomics-Spanish Research Articles. 2010;7(3):142–150.
14. Álvarez Payero M, Martínez López de Castro N, Ucha Samartín M, et al. Medication non-adherence as a cause of hospital admissions. *Farm Hosp*. 2014;38(4):328–333.
15. Arévalo B Arturo Raúl, Mattos Pablo, Gonzales Janeth, et al. Effectiveness of triple antiretroviral therapy in a young infant diagnosed with AIDS category c. *Rev Méd La Paz*. 2014;20(2):50–56.
16. Tello Velásquez Jorge Renzo, Díaz-Llanes Bruno Eduardo, Mezones-Holguín Edward, et al. Poor sleep quality is associated with lower adherence to highly active antiretroviral therapy in Peruvian patients with HIV/AIDS infection. *Cad Saúde Pública*. 2015;31(5):989–1002.
17. Moraes Danielle Chianca de Andrade, Oliveira Regina Célia de, Prado Adriana Vitorino Arruda do, et al. The knowledge of people living with HIV / AIDS about antiretroviral therapy. *Sick glob*. 2018;17(49):96–141.
18. Besse Díaz R, Puente Saní V, Martínez Cantillo L, et al. Clinical and epidemiological aspects in patients with acquired immunodeficiency syndrome in the province of Santiago de Cuba. *Medisan*. 2018;22(3).
19. Hernández Requejo Daymé, Pérez Ávila Jorge, Can Pérez Adriana. Opportunistic diseases in HIV/AIDS patients with AIDS debut receiving antiretroviral treatment. *Rev Cubana Invest Bioméd*. 2015;34(3).
20. Besse Díaz R, Romero García LI, Cobo Montero E, et al. Clinical and epidemiological approach of patients with HIV/AIDS treated in an emergency and emergencies service. *Medisan*. 2018;22(7).

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