Lack of Effect of Motivation on the Adherence of HIV-Positive/AIDS Patients to Antiretroviral Treatment

Rosa Garcia[1], Milena Pondé[2], Manuela Lima[2], Alba Regina de Souza[3], Silvia Maria de O. Stolze[3] and Roberto Badaró[1]

Federal University of Bahia[1]; Medical School of Bahia (FBDC)[2]; CREAIDS[3]; Salvador, BA, Brazil

As a result of the potent drug combinations of reverse transcriptase inhibitors and protease inhibitors currently available, it is now possible to achieve extreme reductions in the numbers of viral particles in the peripheral blood of HIV-positive patients undergoing treatment, to the point that they are undetectable. Moreover, the immunological recovery resulting from continued and prolonged use of these drugs significantly reduces both mortality and the incidence of opportunistic infections. However, the strict therapeutic regimens required, the number of pills, adverse events and the stigma of a disease that requires the patient to introduce pill-taking into his/her lifestyle brings into question one aspect of mental health, which is motivation to do that which is being proposed. We investigated the influence of each of the components of the adherence trilogy: information, motivation and behavioral abilities, as risk factors in a population of HIV-positive/AIDS patients undergoing antiretroviral treatment in the city of Salvador, Bahia, Brazil. Material and Methods: An intervention study was carried out by introducing motivational assistance into the routine recommendations for the treatment of patients who were initiating antiretroviral (ARV) therapy. Seventy-six treatment-naive patients, who had been selected to initiate ARV therapy, were included. These patients were divided into two groups. Group A, in which the regular routine of the institution was followed, received information on the disease and its treatment;patients in group B had the same routine, but they were also followed-up fortnightly and given motivational intervention. Evaluations of viral load and CD_4 count before and following treatment were used to measure adherence. Results: There was no significant difference between the two groups. Conclusions: As the rates of non-adhesion were at the lower limits of the ranges reported in the literature, it would appear that providing motivation and information can be of help to the patient.
Key Words: Motivation, adherence, HIV-Positive/AIDS, treatment.

In human immunodeficiency virus (HIV)-positive patients who develop acquired immunodeficiency syndrome (AIDS), the course of the disease, its prognosis and treatment are quite different today from 10 years ago. AIDS used to be a disease that led inevitably to death, as there was no possibility of any pharmaceutical interference capable of altering its course. The evolution of the disease was continuous and progressive, its prognosis poor and the options of treatment few. Today, the course of this disease remains chronic, but its prognosis has been improved through effective treatment. However, no clear limits for the duration of this treatment have been defined. The criteria for the administration of antiretroviral (ARV) medication are determined by three fundamental parameters: the clinical manifestations of opportunistic diseases, measurement of HIV plasma viral load (VL), and CD_4/CD_8 cell counts in peripheral blood. These criteria define the therapeutic model of the combination of drugs in regimens referred to as highly active antiretroviral therapy (HAART). The need to use at least 90-95% of the medication contained in HAART continuously and regularly leads to another issue in anti-HIV therapy, adherence to treatment.

Received on 05 October; revised 22 November 2005.
Address for correspondence: Dr. Rosa Garcia. Avenida Garibaldi, 1477, sala 106, Garibaldi. Zip code: 40170-130, Salvador, BA, Brazil.

The Brazilian Journal of Infectious Diseases 2005;9(6):494-499

Adherence, an essential component for measuring response to ARV, has been examined in recent studies that evaluated the degree of adherence necessary to achieve a sustained response to ARV [1,2]. Measurement of HIV-1 viral load is the paradigm of response to treatment and is considered indirect proof of the degree of the patient's adherence [3]. The higher the number of tablets taken, the higher the percentage of patients reaching undetectable viral load over the weeks of treatment [4,5]; however, the higher the number of tablets that have to be taken, the less likely it is that the patient will adhere to treatment [6-8]. It is calculated that between 30 and 50% of all patients fail to adhere to treatment [9,10]. More recently, reports have suggested that adhesion to a medication depends on a trilogy of factors: information, motivation and behavioral abilities. This trilogy is interdependent, and adhesion cannot be evaluated without studying these components both individually and collectively. Information refers to knowledge on the physiopathology of the disease and the effects of treatment on immunity. Behavioral abilities refer to the patient's lifestyle and behavior. The motivation component is the essential link between information and behavioral abilities. Motivation refers to the patient's desire to be treated. This desire gives origin to values that reason transforms into willpower [11]. These values guide and control human behavior, establishing a life project and motivating the effort required for achieving established goals. One of the ways to stimulate motivation in the patient is through structured or semi-structured motivation interviews.

We evaluated the effect of stimulating motivation on patient's adherence to ARV treatment.

Material and Methods

An intervention study was carried out in patients undergoing ARV therapy at the Bahia State AIDS Referral Center (CREAIDS). Seventy-six HIV-positive, treatment-naive patients, who had been selected to initiate ARV therapy in accordance with current guidelines for the prescription of ARV therapy in adult HIV-positive or AIDS patients, were included in the study. Inclusion criteria comprised: patients over 18 years of age, with a diagnosis of HIV confirmed by ELISA/WB or HIV plasma viral load. Patients undergoing concomitant treatment for chronic opportunistic diseases or diseases that would require the use of medication for more than 60 days were excluded from the study. The patient was considered to have adhered to treatment when a reduction in HIV plasma viral load to levels < 400 was achieved at the end of the study, and when the CD_4 count after six months of treatment was twice that registered prior to initiation of treatment. The patients were randomly allocated to two different groups. Group A followed the current routine established for the prescription of ARV therapy in which information regarding the disease and therapy was provided. A team comprising of a physician, a social worker, a nurse and a pharmacist participated in the Information item. This team provided information to the patient regarding the importance of treatment, therapeutic regimen, how to adapt this regimen to the patient's lifestyle, and how to deal with side effects. Group B was the intervention group, in which, in addition to current practice for the prescription of ARV therapy, *motivation* was provided for six months during fortnightly visits of 20 minutes each made by a social worker. The sessions were based on the FRAMES model of brief intervention (Feedback, Responsibility, Advice, Menu of Strategies, Empathy, Self-Efficacy), [11,12].

Feedback

Refers to the feedback given by the health worker to the patient. In addition to discussing situations that affect the patient's behavior, the patient is reassured that care will continue to be given regardless of adherence.

Responsibility

Refers to the points the staff member should raise with the patient regarding his/her change of behavior, his/her choices, emphasizing that it is not the wishes of

others but the wishes of the patient him/herself that should prevail. The objective is to motivate the patient by keeping the discussion focussed on him/her.

Advice

This refers to the advice and guidance that should be given to the patient to change this behavior.

Menu of strategies

Refers to the type of behavioral changes that may be achieved.

Empathy

Means putting yourself in the patient's place, being available and honest, acting authentically.

Self-efficacy

Consists in strengthening the patient's self-esteem and confidence in him/herself [11,12].

Results

Seventy-six patients were included, 41 being allocated to group A and 35 to group B. The sociodemographic data on the patients of both groups are shown in Table 1.

Another variable was constructed, "adherence based on CD_4 count", based on the CD_4 variables before and after AIDS treatment. Adhesion was considered to have been achieved when the CD_4 count following treatment was twice as great as the CD_4 count prior to treatment. The provision of motivational intervention failed to result in any significant change in adhesion to treatment, defined as adherence based on CD_4 count (Table 2). Among the patients who were submitted to the intervention, 35.5% adhered to treatment and 65.5% did not; whereas in the group of patients who were not submitted to this intervention, 52.5% adhered to treatment and 47.5% did not. There was no significant difference between the two groups (Pearson's chi-squared test, p=0.138, Table 2).

Considering CD_4 as the parameter of adhesion, the power of the study was calculated using a significance level of 0.05, with a sample size of 40 patients in group A and 29 in group B. Since the proportion of the event in group A was 52.5% and in group B it was 34.5%, the resulting power was 31.28%.

Another parameter of adhesion was also used: the viral load before and after treatment. Adherence to treatment was considered to have taken place when viral load fell to levels <400 following treatment. Among the patients who were submitted to intervention, 64.3% adhered to treatment and 35.7% failed to adhere to treatment; whereas among the patients who were not submitted to intervention, 71.8% adhered to treatment and 28.2% did not. No significant difference was observed between the two groups (Pearson's chi-squared test, p=0.513, Table 3). Considering this parameter, the power of the study was 9.72%.

Discussion

The phenomenon of HIV resistance to ARV therapy is a mainstay of the study of adhesion [13,14]. ARV inhibits replication; however, at low levels, it allows the virus to incorporate codons conferring resistance, and consequently a new epidemic begins [15,16]. Studies on the forms of development of genetic barriers, performed by investigating the pharmacodynamics involved in preventing the development of HIV-resistance to ARV, suggest that blood levels of the drugs used are very close to toxic levels [17,18]. The toxicity of ARV drugs, which has been well documented in studies on metabolic complications [19,20] and mitochondrial toxicity, [21,22] is another parameter for evaluating adhesion. A new challenge has therefore to be met in the studies on adhesion to therapy in the AIDS patient: to maximize efficacy and minimize toxicity [23].

Undetectable viral load is proof of the degree of patient adhesion [7]. In a study controlled by the measurement of serum levels and direct control of the ingestion of tablets by patients (directly observed

Table 1. Sociodemographic data of all patients enrolled in the study

Variable	All Patients	Group A No intervention	Group B Intervention
Gender (male/female)	38 (50%) / 38 (50%)	19/22	19/16
Age (mean ± SD)	37 ± 10	37 ± 11	36 ± 9
Viral load (mean ± SD)	400893 ± 981614	258394 ± 485576	567820±1339756
CD_4 1 (mean ± SD)	179 ± 135	166 ± 152	194 ± 111
CD_8 1 (mean ± SD)	807 ± 488	717 ± 423	909 ± 541
Number of visits		25 ± 12	15 ± 9
Sexual orientation:			
heterosexual	38 (50%)	17	21
homosexual	7 (9%)	5	2
bisexual	2 (3%)	0	2
Marital status			
single	49 (64%)	24	25
married	16 (21%)	9	7
widowed	2 (3%)	0	2
separated	3 (4%)	2	1
CD_4 2 (mean ± SD)	333 ± 198	304 ± 172	373 ± 227
CD_8 2 (mean ± SD)	946 ± 451	956 ± 462	930 ± 445
Viral load 2 (mean ± SD)	610000 ± 19380	10773 ± 32909	31369 ± 116479
Total number of patients	76 (100%)	41	35

Table 2. Adhesion to treatment (based on CD4 measurement), according to group

Patient Group	Adhesion to Treatment		
	Yes	No	Total
A: No intervention	21 (52.5%)	19 (47.5%)	40 (100%)
B: Intervention	10 (34.5%)	19 (65.5%)	29 (100%)
Total	31 (44.9%)	38 (55.1%)	69 (100%)

Table 3. Adhesion to treatment (*viral load after treatment)* according to group

Patient Group	Adhesion to Treatment		
	Yes	No	Total
A: No intervention	28 (71.8%)	11 (28.2%)	39 (100%)
B: Intervention	18 (64.3%)	10 (35.7%)	28 (100%)
Total	46 (68.7%)	21 (31.3%)	67 (100%)

therapy - DOT), the results indicated that > 95% adhesion is required to achieve an undetectable viral load in more than 80% of the patients [7,8].

When we evaluated adhesion by checking CD_4 counts, the patients who adhered comprised 45% of the sample, whereas those who did not adhere made up 55% of the total sample. When adhesion was evaluated according to viral load, 68% adhered and 31% did not. These results are in agreement with other data published in the literature, in which estimates indicate that between 30 and 50% of patients fail to adhere to treatment [9,10].

Motivation applied as an intervention to improve adhesion did not prove to be any more effective than providing the information routinely given to all patients as a regular part of the CREAIDS program. As the power of the study was very low, the sample size may have been insufficient to achieve statistical significance. Based on the data, no significant difference was found between the intervention group and the group that was not submitted to motivation. This leads to the hypothesis that the information routinely provided to patients does, in itself, provide motivation for adhesion, and that no additional benefit would be obtained by investing in a specific member of staff for the purpose of providing motivation as part of the FRAMES model of brief intervention.

Conclusion

The rates of non-adhesion to treatment, as evaluated by viral load and CD4 counts, are in agreement with those reported in the literature although they are below the maximum limits published. As an auxiliary factor for improving adhesion, the provision of motivation failed to provoke any difference in adhesion rates when compared with the provision of information alone; there was no significant difference between the two groups. Since the rates of non-adhesion were at the lower limits of the ranges reported in the literature, it would appear that both psychological interventions, such as providing motivation, and educational interventions, such as the provision of information, may be of help to the patient.

References

1. Singh N., Bernab S.M., Swindells S., et al. Adherence of human immunodeficiency virus-infected patients to antiretroviral therapy. Clin Infect Dis **1999**;29:824-30.
2. Tuldra A., Ferrer M.J., Fumaz C.R., et al. Monitoring adherence to HIV therapy. Arch Intern Med **1999**;159:1376-7.
3. Hecht F.M. Measuring HIV treatment adherence in clinical practice. AIDS Clin Care **1998**;10:57-9.
4. Moyer T.P., Temesgen Z., Enger R., et al. Drug monitoring of antiretroviral therapy for HIV-1 infection: method of validation and results of a pilot study. Clin Chem **1999**;45:1465-76.
5. Montaner J.S.G., Raboud J.M., Rae S., for the INCAS and AVANTI Study Groups. Adherence to treatment increases duration of virologic suppression regardless of p VL nadir [abstract LB-10]. 38th ICAAC, San Diego, CA, **1998**.
6. Friedland G.H. Adherence: The Achilles' heel of highly active antiretroviral therapy. IAS-USA **1997**; 5(1): 3-15.
7. Deeks S., Beatty G., Cohen P.T., et al. Viral load and CD4+ T cell changes in patients failing potent protease inhibitor therapy. 5th Conference on Retroviruses and Opportunistic Infections. Chicago, IL, **1998**. (Abstract 419).
8. Paterson D., Swindells S., Mohr J., et al. How much adherence is enough? A prospective study of adherence to protease inhibitor therapy using MEMS caps (abstract 92). In: Program and abstracts of the 6th Conference on Retroviruses and Opportunistic Infections (Chicago). Alexandria V.A.: Foundation for Retrovirology and Human Health, 1999; 84: Lamotte C, Peytavin G, Farinotti R. Determination of Nelfinavir, a potent protease inhibitor, and its active metabolite M8 in human plasma by high-performance liquid chromatography with photodiode array detection. J Chromatogr B Biomed Sci Appl **1999**;735:159-70.
9. Cramer J.A., Mattson R.H., Prevey M.L., et al. How often is modification taken as prescribed? A novel assessment technique. JAMA **1989**;261:3273-277.
10. Mostashari F., Riley E., Sclwyn P.A., Altice F.L. Acceptance and adherence with antiretroviral therapy among HIV-infected women in a correctional facility. J Aquir Immune Defic Syndr Hum Retroviral **1998**;18:341-8.
11. Tamayo A., Schwartz S. Estrutura Motivacional dos Valores Humanos, Psic Teor Pesq, Brasília **1993**;(9)No.2: 329-48.
12. Cheever L. Adesão à Terapia Antiretroviral e Assistência aos Pacientes HIV + Usuários de Drogas. 4ª Conferência Anual Brasil AIDS. Universidade John Hopkins hopkins-aids.edu/educational/events/brazil **2000**.

13. Yerly S., Kaiser L., Race E., et al. Transmission of antiretroviral-drug-resistant HIV-1 variants. Lancet **1999**;354:729-33.
14. Little S.J., Daar E.S., D'aquila R.T., et al. Reduced antiretroviral drug susceptibility among patients with primary HIV infection. J Am Med Assoc **1999**;282:1142-9.
15. Baxter J.D., Mayers D.L., Wentworth D.N., et al. CPCRA 046 Study Team. A pilot study of the short-term effects of antiretroviral management based on plasma genotypic antiretroviral resistance testing (GART) in patients failing antiretroviral therapy. In: 6th Conference on Retroviruses and Opportunistic Infections. Chicago: Abstract LB8, **1999**.
16. Murphy R.L., Brun S., Hicks C., et al. ABT-378/ritonavir plus stavudine and lamivudine for the treatment of antiretroviral-naive adults with HIV-1 infection: 48-week results. AIDS **2001**;15:p. F1-9.
17. Boubaker K., Sudre P., Flepp M., et al. Hyperlactatemia and antiretroviral therapy in the Swiss HIV Cohort Study. 7th Conference on Retroviruses and Opportunistic Infections. San Francisco, CA, **2000**. (Abstract 57).
18. Mokrzycki M.H., Harris C., May H., et al. Lactic acidosis associated with stavudine administration: a report of five cases. Clin Infect Dis, **2000**;30:198-200.
19. Dube M.P. Metabolic complications of antiretroviral therapies. AIDS Clinical Care, **1998**. 10: p. 41.
20. Eastone J.A., Decker C.F. New-onset diabetes mellitus associated with use of protease inhibitor. Ann Intern Med **1997**;127:948.
21. Visnegarwala F., Krause K.L., Musher D.M. Severe diabetes associated with protease inhibitor therapy. Ann Intern Med **1997**;127:947.
22. Ter Hofstede H.J., de Marie S., Foudraine N.A., et Al. Clinical features and risk factors of lactic acidosis following long-term antiretroviral therapy: 4 fatal cases. Int J STD AIDS **2000**;11:611-6.
23. Lorenzi P., Yerly S., Abderrakim K., et al. Toxicity, efficacy, plasma drug concentration and protease mutations in patients with advanced HIV infection treated with ritonavir plus saquinavir. AIDS **1997**;1:F95-9.