Review

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Quality of life and adherence to HAART in HIV-infected patients

ABSTRACT

A review on adherence to highly active antiretroviral therapy and the quality of life of patients living with HIV in the scientific literature, indexed in MEDLINE between 1998 and 2008, was performed. Studies published in Portuguese, Spanish or English with patients over 18 years of age were included. Reviews, case reports and letters were excluded. Of the 21 studies found, 12 were included (three clinical trials, three prospective cohorts and six cross-sectional studies). The relationship between quality of life and treatment adherence remains controversial, despite descriptive studies indicating the possibility of a positive association. The results may have been influenced by the specific characteristics of the described clinical trials and do not show a consensus regarding the impact of treatment adherence on patients' quality of life.

DESCRIPTORS: HIV Long-Term Survivors. Anti-HIV Agents. Medication Adherence. Acquired Immunodeficiency Syndrome, prevention & control. Quality of Life. Review.

INTRODUCTION

The acquired immune deficiency syndrome (AIDS) and infections of human immunodeficiency virus (HIV) are a global public health problem. With the advent of antiretroviral therapy, there was a significant increase in life-expectancy and, therefore, in the expectation of improved quality of life (QoL) related to health.

During the 1990s, there were improved awareness of the disease, more therapeutic resources, increased survival and changes in the epidemiological profile.[8] With advances in pharmaceutical research and the advent of antiretroviral protease inhibitors in the second half of the 1990s, a new phase of antiretroviral therapy began, known internationally as highly active antiretroviral therapy (HAART).[10]

In 2008, the estimated number of new HIV infections was 30% less than in 1996, and the total number of people living with the virus was 20% greater than in the year 2000 (a prevalence three times greater than in 1990). The increase in people living with HIV reflects the beneficial impact of HAART, since the estimated number of AIDS related deaths in 2008 is 10% less than in 2004.[a]

Antiretroviral medications began being offered in Brazil in the middle of 1992. HAART was introduced in the Brazilian health system in November of 1996, as part of the national policy of free access to health services and medicines and is offered to the entire population that is indicated for treatment.[10] The introduction of HAART allowed for a reduction in mortality of 33%, which has remained stable.[20]

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[a] Programa Conjunto das Nações Unidas sobre HIV/AIDS. Relatório Global sobre a Epidemia de AIDS 2009: sumário geral [internet]. Brasília, DF; 2009 [cited 2010 Feb 9]. Available from: http://www.onu-brasil.org.br/doc/2009-Relatorio-Global-Aids-Sum-rio-Geral-Port.pdf

Given this new global reality, it is relevant to understand the correlations that exist between the QoL of these patients and adherence to HAART. Even though the relationship between these two factors has not yet been extensively studied, it is known that adherence to HAART improves clinical results, controls the progression of disease and reduces mortality rates, which supposedly should result in improved patient QoL.[4] In contrast to these benefits, the side effects of HAART include fatigue, nausea, vomit, diarrhea and lipodystrophy. These symptoms contribute to non-adherence to the medication, which results in increased blood viral load and decreased counts of CD4+ T lymphocytes (CD4). This can increase resistance of HIV to the medications, resulting in treatment failure, opportunistic infections and loss of financial resources.[21,24]

QoL is an aspect to be considered throughout the long therapeutic process of AIDS and is one of the most utilized subjective aspects in evaluating the impact of chronic diseases. It can be used as a parameter for decision-making concerning treatment and the approval of new therapeutic regimens.[23] According to the World Health Organization, the concept of QoL is defined as: "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".[28] QoL is determined by the extent that ambitions and expectations correspond to personal experience; by personal perception about one's position in life, considering the cultural context and value systems in which people live; and in relation to personal goals, expectations, standards and beliefs through the evaluation of the current state in relation to the ideal, as well as to what people consider as important factors in their lives[3] Not only health, as represented by physical and functional attributes, is important for understanding the quality of life for a person facing a disease, but other social and emotional aspects carry equal value.[17]

The objective of this study was to analyze the scientific literature for the relationship between treatment adherence while on HAART and QoL for patients living with HIV.

METHODS

A systematic review was conducted of published articles, indexed in the MEDLINE (PubMed) database over the past ten years, concerning adherence to HAART and about QoL of patients living with HIV. This review therefore concerns studies performed after the beginning of HAART as a therapy for patients living with HIV/AIDS, thereby guaranteeing that the studies

about treatment adherence homogenously describe the difficulties with the HAART scheme.

The review was restricted to the MEDLINE database, since it includes the main studies published in the international health sciences literature. Descriptions from the Medical Subject Headings (MeSH) were utilized to create the following strategy for advanced search of PubMed (("Antiretroviral Therapy, Highly Active"[MeSH] AND "Patient Compliance"[MeSH]) AND "Quality of Life"[MeSH]) AND "HIV Infections"[MeSH] AND ("last 10 years"[PDat] AND (Humans[MeSH]) AND (adult[MeSH])). Studies involving patients greater than 18 years old and published in Portuguese, Spanish or English over the last ten years (during the period from 7/1/1998 to 7/1/2008) were included, and review articles and letters were excluded.

The data extraction from the selected articles was done by just one reviewer and tabulated with the following information: authors, study location, year of publication, study period, study type, tool utilized, sociodemographic characteristics, main findings and limitations.

RESULTS

There were 21 articles identified, of which nine[2,9,11,14,18,19,22,25,27] were excluded for not describing the relationship between treatment adherence and the QoL of patients living with HIV. Of the 12 studies that met the inclusion criteria (Table), six were cross-sectional, three were prospective cohorts and three were clinical trials. Among the 12 included studies, ten showed a positive correlation between adherence and QoL, with a concomitant increase in treatment adherence and QoL.[1,4,7,12,13,16,17,23,24,26]

In the three prospective cohort studies,[7,13,27] the success of treatment adherence over time was associated with greater QoL. In the cross-sectional studies,[1,12,17,23,24,26] it was also possible to observe positive correlations between QoL and adherence.

According to Manheimmer,[13] QoL can influence treatment adherence since people with a higher QoL also have a greater tendency of adhering to treatment. Both QoL and treatment adherence are affected by the same determinants: both are associated with viral load, disease stage and symptoms.[5,13,b] The harm from treatment adherence is associated with higher viral load, which is associated with lower level scores in QoL. On the other hand, having an AIDS diagnosis and symptoms associated with the disease are aspects related to lower QoL and higher treatment adherence. Treatment adherence is an important component for the success of therapy in HIV infection and is associated

[b] Hecht FM, Colfax G, Swanson M, Chesney MA. Adherence and effectiveness of protease inhibitors in clinical practice. In: Abstracts do 5th Conference on Retroviruses and Opportunistic Infections; 1998; San Francisco, United States; 1998. p.151.

Table. Description of the scientific publications about the relationship between adherence to HAART and QoL in people living with HIV during the period from 1998 to 2008.

Authors and publication year	Type of Study	Objectives	Tools	Sociodemographic characteristics	Conclusions
Goujard et al[6], 2003	Clinical trial	Evaluate the impact of an educational intervention on adherence and its influence upon QoL[a] and therapeutic response	PMAQ7,[b] HIV-46,[c] knowledge score, NAF,[d] clinical data	N=367; 80% Men; average age = 40.5; 33% AIDS	The intervention increased adherence but did not show increased QoL
Chiou et al[4] 2005	Clinical trial	Evaluate QoL and adherence in a program to control symptoms	Clinical data, adherence questionnaire, QoL index[e]	N=67; 95% men; average age= 34.2; 27.3% AIDS	Adherence and QoL increased after the intervention to control symptoms
Wu et al[29] 2006	Clinical trial	Evaluate the impact on QoL after using a device to remind to take medication	Device, Neuropsychological tests, clinical data MOS-HIV,[f] CES-D[g] and more	N=62; 54.8% men; average age = 38.4	The use of an electronic device to remind patients increased adherence and decreased QoL
Jia et al[8] 2004	Cohort	Evaluate the direct and indirect effects of social support, help with coping and depression, on QoL of patients with HIV.	Demographic data, HCSUS,[h] SS-A,[i] CES-D, Coping Questionnaire, PMAQ7	N=226; 100% men; average age = 45.7; 30.3% AIDS; 96.9% adherent	The effects of social support and coping support are related to symptoms of depression and associate with all the dimensions of QoL
Mannheimer et al[13] 2005	Cohort	Evaluate the therapeutic aspects associated with improved QoL and its relationship to adherence	SF12,[j] CPCRA[k]	N=1050; 80% men; average age = 39 years; 29% AIDS	Adherence to HAART is associated with increased QoL
Parsons et al[16] 2006	Cohort	Study the relationship between QoL and neuropsychological functioning in treatment adherence	Neurological and neuropsychological evaluation, neuro QoL,[l] CD4 count for adherence	N=86; 68% men; average age = 42.5; 68% AIDS	The success of HAART is connected to improved psychological state and cognitive QoL
Penedo et al[18] 2003	Cross-sectional	Evaluate the relationship between personality trait and QoL upon adherence	Sociodemographic data, Clinical data, NEO-PI-R,[m] HAT-QoL,[n] ACTG[o]	N=116; 55% men; average age = 39.2; 72% adherent	Personality traits are associated with QoL, which is associated with treatment adherence
Ruiz-Pérez et al[23] 2005	Cross-sectional	Evaluate the association between sociodemographic data on treatment adherence	Questionnaire on social support and overall health, MOS-HIV	N=320; 73.4% men; average age = 39.7; 35.6% AIDS	Sociodemographic aspects, including QoL, have an influence on increasing treatment adherence
Ruiz-Pérez et al[24] 2006	Cross-sectional	Evaluate QoL over time and how it is related to adherence	Questionnaire on social support and overall health, MOS-HIV	N=320; 73.4% men; average age =39.7; 35.6% AIDS; 88.1% adherent	Treatment adherence and clinical status are associated with difference QoL dimensions
Barder et al[1] 2006	Cross-sectional	Evaluate the relationship between adherence, coping, QoL and physical symptoms	TSK,[p] MOS-HIV, Soc-fart,[q] Psc[r]	N=100; 65% men; 78% between 30-50 years; 55% AIDS	Autonomy in treatment adherence leads to increased QoL
Luszczynska et al[12] 2007	Cross-sectional	Investigate if QoL and social support are related to adherence	Adherence questionnaire, SES,[s] BSSS,[t] BFS,[u] MOS-SF 20[v]	N=104, 635% women, average age 34.7	Personal and social resources and QoL increase adherence
Sherr et al[26] 2007	Cross-sectional	Investigate the psychological implications of potential changes in treatment regimen	Demographic, clinic and sexual behavior questionnaire. Optimism, scale. MSASSF,[w] EQ5D,[x] adherence and treatment regimen data	N=778; 75.8% men	Patients that do not change medication have a greater QoL than patients that change or stop treatment

[a] Quality of life; [b] Patient medication adherence questionnaire 7; [c] HIV QoL Questionnaire; [d] non-adherence factor; [e] Quality of Life index; [f] Medical outcomes study HIV health survey; [g] Center for epidemiologic studies depression scale; [h] The HIV cost and services utilization study; [i] Social support appraisals scale; [j] Heath survey instrument; [k] Antiretroviral medication self-report; [l] Neuropathy and Foot-Ulcer-Specific Quality of Life Questionnaire; [m] NEO personality inventory; [n] HIV/AIDS –targeted quality of life; [o] Adherence to combination therapy guide; [p] The Trier Scales on coping with physical illness; [q] Social Factors of ART; [r] Physical Symptom Checklist; [s] Self-efficacy scale; [t] Berlin social support scales; [u] Benefit find scale, physical function subscale; [v] Medical Outcomes Study 20 item questionnaire; [w] Memorial Symptom Assessment Scale Short Form; [x] EuroQoL questionnaire

with the level of viral load, CD4 lymphocytes, the level of viral resistance to medication and the quality of the services that provide care.[13,15]

In a clinical trial developed by Chiou et al,[4] 67 patients were divided into three randomized groups (individual classes, group classes and control group). The patients, who attended classes, participated in a program to manage symptoms once a week during three weeks. In this study, greater treatment adherence after counseling for management of symptoms was associated with greater QoL in the experimental group.

Two clinical trials did not show a positive correlation after the interventions. One of the studies showed a worse QoL after increased adherence,[27] and the other did not show any correlation between these factors.[6]

Wu et al[29] evaluated the impact on QoL of a medication reminder device for patients with HIV. The experimental group received the device, which verbally reminded the patients about the time and dosage of the medication, and in addition to this, the group received 30 minute adherence counseling sessions, monthly. The control group only received counseling for treatment adherence. At the end of six months, the group that received the intervention showed an improvement in treatment adherence, but a considerable decrease in QoL. The authors considered the possibility that this worsening was due to the actual device, which operated as a stressful event.

Clinical trials undertaken by Goujard et al[6] compared an experimental group that participated in an educational program with a control group with out-patient care. The patients in both groups underwent HAART for at least the first three months of the study. QoL was evaluated at three time points in both groups: at the sixth, 12th and 18th months. An increase in adherence was seen at the 12th month, but no significant impacts were found on QoL throughout the study period. The health status (CD4 cell count and viral load) of the patients improved in 56% of the experimental group and 50% of the control group, but this impact was not significant for CD4 count and for viral load. The study showed that an educational intervention improves adherence to HAART and health status, especially when began at treatment enrollment. The study found an increased level of adherence after the educational intervention but did not show a statistically significant impact upon QoL.

DISCUSSION

There were 12 articles that addressed the relationship between QoL and adherence to HAART, which can be considered a small number considering the importance of the issue. However, seven of these were published in the last three years, which reveals the growing importance of the topic. In analyzing these studies, we should consider the heterogeneity of the samples and the methods utilized.

Three clinical studies showed conflicting results, possibly due to bias from the specific conditions of each of the studies. The study by Wu et al[29] suggested that the most plausible reason for decreased QoL was the actual medication device used to remind patients, which could have limited patient QoL due to reduced privacy, since they complained that the size and noise of the device bothered them in social situations. The increase in side effects may have also lowered QoL, since greater adherence to medication may lead to greater side effects from medication. Also, the small sample size (N=62) may have negatively impacted the randomization process and thereby failed to show similar samples.[29] Nonetheless, methodological failures were not identified.

The study by Goujard et al[6] may have not shown a change in QoL despite the increase in adherence, due to patients being asymptomatic at the beginning of the study and having high QoL. Therefore, there was little room for improvement in QoL after the intervention.

Such discordant results in the three clinical studies suggest that the issue has not been explored well. Even so, the three studies indicate that QoL tends to be greater when the chronic disease interferes less with daily activity, possibly due to the patient being asymptomatic or not being forcibly reminded to take medicine.

The association between high treatment adherence and greater QoL in the cross-sectional studies does not allow for a causal relationship to be established. Despite the positive correlations in the studies, some factors should be considered, such as the use of non-randomized convenience samples,[1,7,12,16,17,23] sampling of only male patients[23] and utilization of QoL instruments not specific to HIV/AIDS patients.[4,12,13,16,26]

The relationship between treatment adherence and QoL should be more thoroughly explored. Ideally, these two aspects should occur simultaneously, with adherence improving treatment outcomes. This may not occur in such a straightforward way, though, in the life of a patient living with HIV and using HAART. The few studies identified revealed a paradox: increased treatment adherence (which is an investment in the likelihood of increased survival) can lead to worse overall QoL. Increased survival, due to the development of the disease's chronic stage, may not improve QoL because higher adherence may increase the side effects of the medication. Another possibility is that QoL, since it is a very broad and all-encompassing concept, may not be the best measure for the impact of treatment upon the patient. Nonetheless, the average value of QoL can not be ignored but should be critically understood. QoL consists of the evaluation of diverse aspects of an

individual life, including physical, psychological and social aspects. It is possible that increased adherence to HAART may have led to a reduction in the relative importance of the physical aspects in QoL. This possibility allows us to question if the benefit from adherence upon QoL comes from a subjective improvement in well-being, a sensation of vitality or improved social and emotional bonds. In other words, we can consider the hypothesis that more resilient patients are able to overcome physical damage, on behalf of increased emotional and social QoL.

This study sought to analyze the studies that reported on QoL and treatment adherence from 1998 to 2008. While new medications delayed opportunistic infections and their symptoms, they did not fully protect patients from the constant threat of death, the stigma of the disease and the side effects of the medication. On average these patients are living longer, making it even more important for health teams to recognize and provide for increased QoL among this population. This evaluation compares the overall impact of HIV/AIDS and of diverse treatments on overall patient well-being.

Additional studies should be encouraged, especially prospective cohorts using QoL evaluation tools and addressing other social and emotional aspects, such as strategies for coping, self-efficacy and resilience.

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