UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO

FACULTAD DE MEDICINA

REDUCTION IN HOSPITALIZATION COSTS, MORBIDITY DISABILITY, AND MORTALITY IN PATIENTS WITH AIDS

T E S I S
ESPECIALIDA EN MEDICINA LUTERNA

P R E S E N T A:

JOSÉ LUIS ESTRADA AGUILAR

MEXICO, D.F. 2002

ELSEVIER

Archives of Medical Research 31 (2000) 515–519

Archives of Medical Research

ORIGINAL ARTICLE

Reduction in Hospitalization Costs, Morbidity, Disability, and Mortality in Patients with AIDS Treated with Protease Inhibitors

Carlos Lavalle,* Juan Carlos David Aguilar,* Francisco Peña,** José Luis Estrada-Aguilar,** Juan Antonio Aviña-Zubieta** and Mario Madrazo***

*Hospital de Infectología Dr Daniel Méndez Hernández, Mexico City, Mexico
**Unidad de Investigación en Epidemiología Clínica, Hospital de Especialidades, Centro Médico Nacional La Raza, Instituto Mexicano del Seguro Social (IMSS), Mexico City, Mexico
***Dirección de Prestaciones Médicas, IMSS, Mexico City, Mexico

Received for publication May 20, 1999, accepted April 17, 2000 (99/073)

Background The objective of this study was to analyze hospitalization costs, morbidity, disability, and mortality in patients with acquired immunodeficiency syndrome (AIDS) treated with protease inhibitors (PI).

Methods. This is a self-controlled, ambispective study of a total of 581 patients with human immunodeficiency virus (HIV)/AIDS seen at the Hospital de Infectología, Centro Médico La Raza, IMSS, in Mexico City during 1997. A total of 210 (36.14%) patients initiated protease inhibitor (PI) treatment at the onset of the study. Thirty-eight patients satisfied the inclusion criteria for this study and were analyzed retrospectively during the year prior to PI treatment, and then prospectively throughout the year on PI treatment. As concerns main outcome measures, financial costs, number of hospitalizations, number of infections, and productivity and laboratory parameters ($CD4^+$ counts and viral load) were analyzed during the year prior to PI treatment and then prospectively during the year on PI prescription. Our hypothesis was that the hospital costs, morbidity, disability, and mortality of patients with AIDS decreased while on PI treatment.

Results. During the year prior to PI prescription, the 38 patients enrolled in the study were admitted on a total of 59 occasions (1.55 hospitalizations/patient), whereas during the year on PI therapy, all 38 patients had only seven admissions (0.18 hospitalizations/patient). Hospitalization costs decreased 35% when annual PI costs for the 38 patients studied were taken into account. The number of microorganisms detected during hospitalization decreased from 24 prior to PI to five on PI. The number of disability days involved in patients on PI decreased significantly ($p < 0.0002$). None of the 38 patients studied died during the year of follow-up under PI treatment. Mortality decreased significantly, from 481 (23.2%) in 1996, to 77/581 (13.2%) in 1997, to 40/740 (6.4%) in 1998. There were no deaths among the 38 patients studied during the 1-year follow-up period; when the observation period was extended 1 additional year, only one patient died (2.63%). Only six (3.48%) of the 172 PI-treated patients with AIDS not included in the study died during the same period. $CD4^+$ cell counts increased from 190.56 ± 169.5 cells/mm^3 to 235.00 ± 112.65 cells/mm^3 ($p < 0.05$) after 12 months of PI treatment. Viral loads decreased from 5 logs to 2.4 logs at 12 months of PI treatment ($p < 0.001$).

Conclusions. Introduction of PI to antiretroviral treatment in patients with AIDS was associated with a lower rate of hospital admissions, lower costs, and a lesser number of infections/year, disabilities, and mortalities. Increase of $CD4^+$ cell counts and decrease in viral loads in the 38 patients were associated with decreased morbility and mortality. © 2001 IMSS. Published by Elsevier Science Inc.

Key Words: Costs, HIV/AIDS, Protease inhibitors, $CD4^+$, Viral load.

Address reprint request to Dr Carlos Lavalle M., Coordinador, Coordinación de Educación Médica, Centro Médico Nacional Siglo XXI, IMSS, Av. Cuauhtémoc #330, Colonia Doctores, 06725 México, D F., México Tel (+525) 761-0747, Fax: (+525) 761-0596, E-mail: ncem@imss.gob.mx

0188-4409/00 $–see front matter Published by Elsevier Science Inc
PII S0188-4409(00)00097-7

2002

2

Introduction

Since the surge of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) in humans, there has been constant concern for offering better and more opportune treatment alternatives that include antiretrovirals, as well as drugs, to treat the complications generated by the disease itself (e g., opportunistic infections, neoplasms). Unfortunately, the prescription of more potent antiretrovirals and combinations of the latter has led to greater expense in the treatment of patients. In this context, it is mandatory to determine cost-benefit and cost-effectiveness in short-term and long-term studies in developing countries for prescribing these drugs on a rational basis.

Initially, treatment for patients with HIV/AIDS was eminently in-hospital care and included mostly patients with AIDS-related complex diseases (e.g., *P. carinii* pneumonia, Kaposi's sarcoma, wasting syndrome), with little or nothing to be done concerning the disease's prognosis and the patient's quality of life

The majority of the studies on treatment costs for patients with HIV/AIDS are carried out in developed countries. In the U.S., costs of ambulatory care for patients with HIV/AIDS is around $1,500 U.S. dollars (USD) monthly per patient, with costs ranging between $20,000 and $46,000 USD annually when hospitalization costs are added (1). The long-term cost per patient has been estimated to be from $55,000 to $150,000 USD (2,3). In London in 1986, average annual costs per patient were $10.000 USD/£6,800 (pounds Sterling) (4,5).

In Mexico, there have been few studies analyzing the economic impact of HIV/AIDS treatment. In 1992, an evaluation of direct treatment costs was carried out in five public hospitals. Hospital admission costs/patient ranged between $1,430 and $7,350 USD, with an average cost of $2.565 USD (6). In 1998, the annual cost per patient in Mexico ranged between $10,424 and $14,520 USD, and total cost per admission was $3,212 USD (our hospital, unpublished data). These costs are 31–50% lower than those reported in developed countries (1) Nevertheless, the costs are still very high for developing countries such as Mexico and therefore, a cost/effectiveness study must be carried out to investigate direct and indirect costs of AIDS treatment in short-term and long-term studies.

Protease inhibitors (PI) are new drugs introduced recently (June 1997) into the Mexican market. The main goals for prescribing these drugs are disease control and improvement in productivity, quality of life, and increased life expectancy. At the beginning, there was hope for complete virus eradication with PI, but at the last World Congress on AIDS in Geneva, Switzerland (1998), this hope seems to have vanished indefinitely We report herein our experience with a select group of patients under PI treatment and the effects of such treatment in terms of hospitalization costs, morbidity, disability, and mortality in Mexican patients with AIDS.

Methods

We reviewed the medical records of all patients with HIV/AIDS actively seen at the Hospital de Infectología in 1997. From among these, we selected for further review those who met the following inclusion criteria: (1) patients treated with PI; (2) patients who had received reverse transcriptase inhibitors during the year prior to PI therapy, and (3) patients with complete information on the following data: number and days of hospitalizations/year, causes for admission, record of drugs prescribed; laboratory tests and radiographic studies performed; number of consultations and surgeries performed (major and minor), and number of disability days. Cases with incomplete or missing information were not included in the study. In addition, at time zero (at initiation of PI treatment), the patients were also followed prospectively for 1 year to collect the parameters mentioned previously.

The behavior of $CD4^+$ cells (flow cytometry) and viral load (NASBA-Organon-Teckmica, sensitivity limit: 400 copies/mL, 2 4 $\log_{10}$ copies/mL) was also examined to assess the host's immunologic status and therapeutic response.

Results

A total of 581 patients with HIV/AIDS were actively seen at our hospital in 1997. From among these we selected 210 patients (36%) classified as clinical stage C3 who received PI. Of these, only 38 (18%) patients met inclusion criteria. Thirty-four patients were males (89.2%) and four were females (10.8%), with a 10:1 male/female ratio. Patient mean age was 36 years (16–46 years). One hundred seventy-two cases (82%) were not included in the analysis due to missing medical record information.

Sexual transmission was the mechanism of HIV infection in 34 patients (89.4%), followed by transfusion in two (5.3%), and perinatal transmission in another two (5.3%). Among patients with HIV sexual transmission, 18 were homosexual (52.94%) and 16 were heterosexual (47.06%).

In the year prior to use of PI, 27 patients were hospitalized once (45.7%), five patients twice (16.9%), three patients three times (15.2%), two patients on four occasions (13.5%), and one patient on five occasions (8.4%), for a total of 59 hospitalizations: the number of admissions was 1.55 per patient. Once patients were on PI, only seven admissions were registered during the follow-up year with 0.18 admissions per patient ($p < 0.001$) (Table 1).

Crude hospitalization costs while on PI treatment decreased 84.6%; however, when PI costs were added to the total number of patients studied ($n = 38$), the cost reduction fell to 35% (Table 2).

The total number of hospitalization days/year decreased from 481 to 100 after the use of PI, although the number of days/hospitalization/patient (14 days) (1–20) was not statis-

Introduction

Since the surge of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) in humans, there has been constant concern for offering better and more opportune treatment alternatives that include antiretrovirals, as well as drugs, to treat the complications generated by the disease itself (e g., opportunistic infections, neoplasms). Unfortunately, the prescription of more potent antiretrovirals and combinations of the latter has led to greater expense in the treatment of patients. In this context, it is mandatory to determine cost-benefit and cost-effectiveness in short-term and long-term studies in developing countries for prescribing these drugs on a rational basis.

Initially, treatment for patients with HIV/AIDS was eminently in-hospital care and included mostly patients with AIDS-related complex diseases (e.g., *P. carinii* pneumonia, Kaposi's sarcoma, wasting syndrome), with little or nothing to be done concerning the disease's prognosis and the patient's quality of life

The majority of the studies on treatment costs for patients with HIV/AIDS are carried out in developed countries. In the U.S., costs of ambulatory care for patients with HIV/AIDS is around $1,500 U.S. dollars (USD) monthly per patient, with costs ranging between $20,000 and $46,000 USD annually when hospitalization costs are added (1). The long-term cost per patient has been estimated to be from $55,000 to $150,000 USD (2,3). In London in 1986, average annual costs per patient were $10.000 USD/£6,800 (pounds Sterling) (4,5).

In Mexico, there have been few studies analyzing the economic impact of HIV/AIDS treatment. In 1992, an evaluation of direct treatment costs was carried out in five public hospitals. Hospital admission costs/patient ranged between $1,430 and $7,350 USD, with an average cost of $2.565 USD (6). In 1998, the annual cost per patient in Mexico ranged between $10,424 and $14,520 USD, and total cost per admission was $3,212 USD (our hospital, unpublished data). These costs are 31–50% lower than those reported in developed countries (1) Nevertheless, the costs are still very high for developing countries such as Mexico and therefore, a cost/effectiveness study must be carried out to investigate direct and indirect costs of AIDS treatment in short-term and long-term studies.

Protease inhibitors (PI) are new drugs introduced recently (June 1997) into the Mexican market. The main goals for prescribing these drugs are disease control and improvement in productivity, quality of life, and increased life expectancy. At the beginning, there was hope for complete virus eradication with PI, but at the last World Congress on AIDS in Geneva, Switzerland (1998), this hope seems to have vanished indefinitely We report herein our experience with a select group of patients under PI treatment and the effects of such treatment in terms of hospitalization costs, morbidity, disability, and mortality in Mexican patients with AIDS.

Methods

We reviewed the medical records of all patients with HIV/AIDS actively seen at the Hospital de Infectología in 1997. From among these, we selected for further review those who met the following inclusion criteria: (1) patients treated with PI; (2) patients who had received reverse transcriptase inhibitors during the year prior to PI therapy, and (3) patients with complete information on the following data: number and days of hospitalizations/year, causes for admission, record of drugs prescribed; laboratory tests and radiographic studies performed; number of consultations and surgeries performed (major and minor), and number of disability days. Cases with incomplete or missing information were not included in the study. In addition, at time zero (at initiation of PI treatment), the patients were also followed prospectively for 1 year to collect the parameters mentioned previously.

The behavior of $CD4^+$ cells (flow cytometry) and viral load (NASBA-Organon-Teckmica, sensitivity limit: 400 copies/mL, 2 4 $\log_{10}$ copies/mL) was also examined to assess the host's immunologic status and therapeutic response.

Results

A total of 581 patients with HIV/AIDS were actively seen at our hospital in 1997. From among these we selected 210 patients (36%) classified as clinical stage C3 who received PI. Of these, only 38 (18%) patients met inclusion criteria. Thirty-four patients were males (89.2%) and four were females (10.8%), with a 10:1 male/female ratio. Patient mean age was 36 years (16–46 years). One hundred seventy-two cases (82%) were not included in the analysis due to missing medical record information.

Sexual transmission was the mechanism of HIV infection in 34 patients (89.4%), followed by transfusion in two (5.3%), and perinatal transmission in another two (5.3%). Among patients with HIV sexual transmission, 18 were homosexual (52.94%) and 16 were heterosexual (47.06%).

In the year prior to use of PI, 27 patients were hospitalized once (45.7%), five patients twice (16.9%), three patients three times (15.2%), two patients on four occasions (13.5%), and one patient on five occasions (8.4%), for a total of 59 hospitalizations: the number of admissions was 1.55 per patient. Once patients were on PI, only seven admissions were registered during the follow-up year with 0.18 admissions per patient ($p < 0.001$) (Table 1).

Crude hospitalization costs while on PI treatment decreased 84.6%; however, when PI costs were added to the total number of patients studied ($n = 38$), the cost reduction fell to 35% (Table 2).

The total number of hospitalization days/year decreased from 481 to 100 after the use of PI, although the number of days/hospitalization/patient (14 days) (1–20) was not statis-

Introduction

Since the surge of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) in humans, there has been constant concern for offering better and more opportune treatment alternatives that include antiretrovirals, as well as drugs, to treat the complications generated by the disease itself (e g., opportunistic infections, neoplasms). Unfortunately, the prescription of more potent antiretrovirals and combinations of the latter has led to greater expense in the treatment of patients. In this context, it is mandatory to determine cost-benefit and cost-effectiveness in short-term and long-term studies in developing countries for prescribing these drugs on a rational basis.

Initially, treatment for patients with HIV/AIDS was eminently in-hospital care and included mostly patients with AIDS-related complex diseases (e.g., *P. carinii* pneumonia, Kaposi's sarcoma, wasting syndrome), with little or nothing to be done concerning the disease's prognosis and the patient's quality of life

The majority of the studies on treatment costs for patients with HIV/AIDS are carried out in developed countries. In the U.S., costs of ambulatory care for patients with HIV/AIDS is around $1,500 U.S. dollars (USD) monthly per patient, with costs ranging between $20,000 and $46,000 USD annually when hospitalization costs are added (1). The long-term cost per patient has been estimated to be from $55,000 to $150,000 USD (2,3). In London in 1986, average annual costs per patient were $10.000 USD/£6,800 (pounds Sterling) (4,5).

In Mexico, there have been few studies analyzing the economic impact of HIV/AIDS treatment. In 1992, an evaluation of direct treatment costs was carried out in five public hospitals. Hospital admission costs/patient ranged between $1,430 and $7,350 USD, with an average cost of $2.565 USD (6). In 1998, the annual cost per patient in Mexico ranged between $10,424 and $14,520 USD, and total cost per admission was $3,212 USD (our hospital, unpublished data). These costs are 31–50% lower than those reported in developed countries (1) Nevertheless, the costs are still very high for developing countries such as Mexico and therefore, a cost/effectiveness study must be carried out to investigate direct and indirect costs of AIDS treatment in short-term and long-term studies.

Protease inhibitors (PI) are new drugs introduced recently (June 1997) into the Mexican market. The main goals for prescribing these drugs are disease control and improvement in productivity, quality of life, and increased life expectancy. At the beginning, there was hope for complete virus eradication with PI, but at the last World Congress on AIDS in Geneva, Switzerland (1998), this hope seems to have vanished indefinitely We report herein our experience with a select group of patients under PI treatment and the effects of such treatment in terms of hospitalization costs, morbidity, disability, and mortality in Mexican patients with AIDS.

Methods

We reviewed the medical records of all patients with HIV/AIDS actively seen at the Hospital de Infectología in 1997. From among these, we selected for further review those who met the following inclusion criteria: (1) patients treated with PI; (2) patients who had received reverse transcriptase inhibitors during the year prior to PI therapy, and (3) patients with complete information on the following data: number and days of hospitalizations/year, causes for admission, record of drugs prescribed; laboratory tests and radiographic studies performed; number of consultations and surgeries performed (major and minor), and number of disability days. Cases with incomplete or missing information were not included in the study. In addition, at time zero (at initiation of PI treatment), the patients were also followed prospectively for 1 year to collect the parameters mentioned previously.

The behavior of $CD4^+$ cells (flow cytometry) and viral load (NASBA-Organon-Teckmica, sensitivity limit: 400 copies/mL, 2 4 $\log_{10}$ copies/mL) was also examined to assess the host's immunologic status and therapeutic response.

Results

A total of 581 patients with HIV/AIDS were actively seen at our hospital in 1997. From among these we selected 210 patients (36%) classified as clinical stage C3 who received PI. Of these, only 38 (18%) patients met inclusion criteria. Thirty-four patients were males (89.2%) and four were females (10.8%), with a 10:1 male/female ratio. Patient mean age was 36 years (16–46 years). One hundred seventy-two cases (82%) were not included in the analysis due to missing medical record information.

Sexual transmission was the mechanism of HIV infection in 34 patients (89.4%), followed by transfusion in two (5.3%), and perinatal transmission in another two (5.3%). Among patients with HIV sexual transmission, 18 were homosexual (52.94%) and 16 were heterosexual (47.06%).

In the year prior to use of PI, 27 patients were hospitalized once (45.7%), five patients twice (16.9%), three patients three times (15.2%), two patients on four occasions (13.5%), and one patient on five occasions (8.4%), for a total of 59 hospitalizations: the number of admissions was 1.55 per patient. Once patients were on PI, only seven admissions were registered during the follow-up year with 0.18 admissions per patient ($p < 0.001$) (Table 1).

Crude hospitalization costs while on PI treatment decreased 84.6%; however, when PI costs were added to the total number of patients studied ($n = 38$), the cost reduction fell to 35% (Table 2).

The total number of hospitalization days/year decreased from 481 to 100 after the use of PI, although the number of days/hospitalization/patient (14 days) (1–20) was not statis-

Table 1. Hospital admissions of AIDS patients 1 year prior to and during 1 year on followup of protease inhibitor (PI) therapy

Patient no	Hospital admissions before PI	Admissions/patient/year	Hospital admissions on PI	Admissions/patient/year
38	59[a]	1.55	7[a]	0.18

[a] The difference in the hospitalization rate prior to and on PI was statistically significant ($p < 0.001$)

tically significant between PI-treated and -untreated patients. The number of infections and microorganisms that were the cause for hospital admissions, before and while on PI, decreased significantly with the latter (Table 3).

During the year prior to PI treatment, reasons for hospitalizations were as follows: bacterial infections in 11 patients (28.9%); opportunistic infections in eight (21.1%), including candidiasis, cryptosporidiosis, cryptococcosis, and histoplasmosis); cancer problems (including Hodgkin's and non-Hodgkin's lymphoma and viral infections in four (10.5%); Kaposi's sarcoma in eight (21.1%); major surgery in five (13.5%), and non-AIDS-related events in two patients (5.2%). On the other hand, while patients were under PI treatment, hospitalizations were due only to infectious events.

Disability was assessed in 26 working patients (days/patient/year); a statistically significant decrease in disability days was observed (121.8 ± 107.4 vs. 71.1 ± 96.1; $p < 0.0002$) (Figure 1).

A significant ($p < 0.001$) decline in mortality rate was recorded taking into consideration the total number of patients seen at the hospital in 1997 and 1998 as compared with 1996 (when PI were not available) (Table 4). There were no deaths among the 38 patients studied during the 1-year follow-up; when the observation period was extended 1 additional year, only one patient died (2.63%). Only six (3.48%) of the 172 PI-treated patients with AIDS not included in the study died during the same period. The mortality rate between these two groups was statistically significant ($p < 0.001$) in comparison with the mortality rate of non–PI-treated patients with AIDS (23.2%).

Effectiveness of PI treatment was evaluated by number of $CD4^+$ cells and viral load. The mean amount of $CD4^+$ before PI was 190.56 ± 169.5; after 1 month, a mean of 305.95 ± 255.94 was recorded, at 3 months, the recorded mean was 270.30 ± 251.61, at 6 months, 216.51.51 ± 133.64, and at 12 months, 235 ±112.62 ($p < 0.05$) (Figure 2). Viral loads decreased significantly (from 5 to 2 logs) during the treatment period (Figure 2)

Discussion

AIDS is an entity with worldwide distribution that has caused great economic impact in developing countries. The economic impact for health care institutions is mainly due to the high cost of the drugs used to control the disease process (viral replication), as well as the treatment of opportunistic infections, years of disability, number of hospitalization days, and number of surgical procedures performed. In recent years, new drugs have been introduced into the market, including PI and non-nucleoside analogs. To date, there is no cure for this syndrome. Initiation of antiretroviral therapy represents an expensive, long-term commitment that can become even more expensive if adherence to treatment is poor and if side effects and resistance to antiviral drugs are high. Nevertheless, use of potent and combined therapy has resulted in the decline of morbidity and mortality (7–9). This study was designed to describe the impact of PI in hospitalization costs in a short-term analysis as well as effects on the disability, morbidity, and mortality of patients with AIDS

Table 2. Reduction in hospitalization costs in 38 AIDS patients with protease inhibitor (PI) treatment

Concept	Admissions before PI	Cost before PI (USD)	Admissions on PI	Cost of PI (USD)	Cost reduction (USD)	% reduction
Hospitalization (days)	59	$130,516	7	$21,454	$109,062	83.5
Drugs[a]	59	$16,156	7	$1,634	$14,522	89.8
RTI[b]	38	$15,369	7	$2,830	$12,539	81.5
Laboratory	53	$8,801	39	$740	$8,061	73.9
X-rays, CT scans, MRI	25	$2,287	6	$240	$2,057	89.5
Consultations	53	$3,890	5	$340	$3,550	91.2
Biopsies	14	$7,500	2	$1,000	$6,500	86.5
Surgery	5	$5,122	2	$1,961	$3,161	61.7
Addition		$189,640		$30,199	$159,452	84.6
PI cost				$92,996		
Total[c]	59	$189,640	7	$123,195	$66,445	35.0

[a] Drugs others than antiretroviral therapy, [b] reverse transcriptase inhibitors; [c] total cost ($92,996 USD) of PI therapy for the 38 patients of the study were added to the fifth column

Table 1. Hospital admissions of AIDS patients 1 year prior to and during 1 year on followup of protease inhibitor (PI) therapy

Patient no	Hospital admissions before PI	Admissions/patient/year	Hospital admissions on PI	Admissions/patient/year
38	59[a]	1.55	7[a]	0.18

[a] The difference in the hospitalization rate prior to and on PI was statistically significant ($p < 0.001$)

tically significant between PI-treated and -untreated patients. The number of infections and microorganisms that were the cause for hospital admissions, before and while on PI, decreased significantly with the latter (Table 3).

During the year prior to PI treatment, reasons for hospitalizations were as follows: bacterial infections in 11 patients (28.9%); opportunistic infections in eight (21.1%), including candidiasis, cryptosporidiosis, cryptococcosis, and histoplasmosis); cancer problems (including Hodgkin's and non-Hodgkin's lymphoma and viral infections in four (10.5%); Kaposi's sarcoma in eight (21.1%); major surgery in five (13.5%), and non-AIDS-related events in two patients (5.2%). On the other hand, while patients were under PI treatment, hospitalizations were due only to infectious events.

Disability was assessed in 26 working patients (days/patient/year); a statistically significant decrease in disability days was observed (121.8 ± 107.4 vs. 71.1 ± 96.1; $p < 0.0002$) (Figure 1).

A significant ($p < 0.001$) decline in mortality rate was recorded taking into consideration the total number of patients seen at the hospital in 1997 and 1998 as compared with 1996 (when PI were not available) (Table 4). There were no deaths among the 38 patients studied during the 1-year follow-up; when the observation period was extended 1 additional year, only one patient died (2.63%). Only six (3.48%) of the 172 PI-treated patients with AIDS not included in the study died during the same period. The mortality rate between these two groups was statistically significant ($p < 0.001$) in comparison with the mortality rate of non–PI-treated patients with AIDS (23.2%).

Effectiveness of PI treatment was evaluated by number of $CD4^+$ cells and viral load. The mean amount of $CD4^+$ before PI was 190.56 ± 169.5; after 1 month, a mean of 305.95 ± 255.94 was recorded, at 3 months, the recorded mean was 270.30 ± 251.61, at 6 months, 216.51.51 ± 133.64, and at 12 months, 235 ±112.62 ($p < 0.05$) (Figure 2). Viral loads decreased significantly (from 5 to 2 logs) during the treatment period (Figure 2)

Discussion

AIDS is an entity with worldwide distribution that has caused great economic impact in developing countries. The economic impact for health care institutions is mainly due to the high cost of the drugs used to control the disease process (viral replication), as well as the treatment of opportunistic infections, years of disability, number of hospitalization days, and number of surgical procedures performed. In recent years, new drugs have been introduced into the market, including PI and non-nucleoside analogs. To date, there is no cure for this syndrome. Initiation of antiretroviral therapy represents an expensive, long-term commitment that can become even more expensive if adherence to treatment is poor and if side effects and resistance to antiviral drugs are high. Nevertheless, use of potent and combined therapy has resulted in the decline of morbidity and mortality (7–9). This study was designed to describe the impact of PI in hospitalization costs in a short-term analysis as well as effects on the disability, morbidity, and mortality of patients with AIDS

Table 2. Reduction in hospitalization costs in 38 AIDS patients with protease inhibitor (PI) treatment

Concept	Admissions before PI	Cost before PI (USD)	Admissions on PI	Cost of PI (USD)	Cost reduction (USD)	% reduction
Hospitalization (days)	59	$130,516	7	$21,454	$109,062	83.5
Drugs[a]	59	$16,156	7	$1,634	$14,522	89.8
RTI[b]	38	$15,369	7	$2,830	$12,539	81.5
Laboratory	53	$8,801	39	$740	$8,061	73.9
X-rays, CT scans, MRI	25	$2,287	6	$240	$2,057	89.5
Consultations	53	$3,890	5	$340	$3,550	91.2
Biopsies	14	$7,500	2	$1,000	$6,500	86.5
Surgery	5	$5,122	2	$1,961	$3,161	61.7
Addition		$189,640		$30,199	$159,452	84.6
PI cost				$92,996		
Total[c]	59	$189,640	7	$123,195	$66,445	35.0

[a] Drugs others than antiretroviral therapy, [b] reverse transcriptase inhibitors; [c] total cost ($92,996 USD) of PI therapy for the 38 patients of the study were added to the fifth column

Table 3. Infectious events detected during hospitalization

Infectious agent	Number of infections before PI[a]	%	Number of infections on PI[b]	%
Virus	5	20 83		
Fungi	6	25 00	1	20 00
Bacteria	6	25.00	4	80 00
Parasites	7	29 16		
Total	24	100 00	5	100.00

[a] Eight patients with 24 infectious events, [b]seven patients with five infectious events

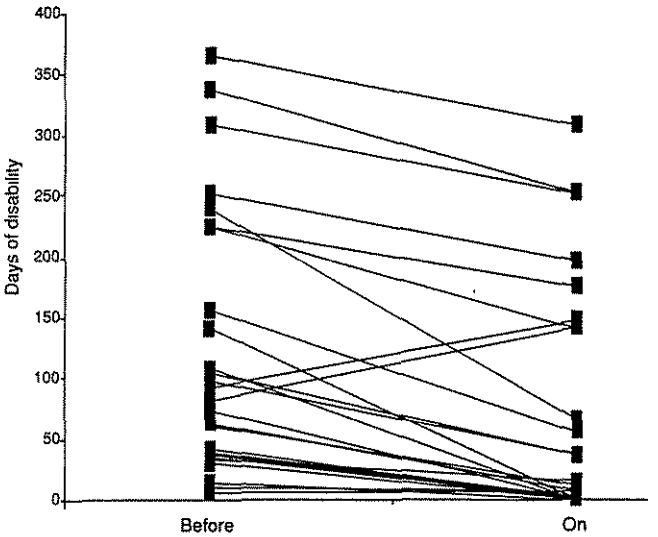

Figure 1. Decline in disability in 26 working patients from 121 8–71 1 days/patients/years (p <0 0002)

In the present study, the average number of hospitalizations for the 38 patients included before PI was 1.55, which is within the lower limit of what has been published in the international literature (1.6–3.2 times a year) (1). This is indirect proof that at our hospital patients with AIDS respond to standard treatment with reverse transcriptase inhibitors, as in developed countries.

The number of hospitalizations/patient/year decreased to 0.18 with the use of PI. This reduction provided a 66% annual savings in hospitalization costs. When PI treatment for the 38 patients was considered, savings decreased to 35%. This reduction is still significant when other benefits such as decrease in disability and mortality are taken into account. Several reports have emphasized that patients who undergo PI therapy decreased the number of opportunistic infections in terms of AIDS-defining events (6–8). In this study, there was a dramatic decrease in viral, parasite, and fungal infections with a consequent cost reduction in drugs other than antiretrovirals.

Use of potent therapy has resulted in the decline of morbidity and mortality (7–9) In a recent report, Palella et al. (7) reported a decline in mortality of their 1,255 patients, from 29.4 per 100 person-years in 1995 to 8.8 per 100 person-years in the second quarter of 1997. These findings are similar to those reported in this paper: mortality declined from 23% in 1996 to 6.5% in 1998.

To avoid bias by selecting only patients with better outcomes, the overall influence of mortality of the 210 patients with AIDS treated with PI was analyzed in the context of the total universe of patients with AIDS treated at the hospital for a period of 3 years. The results of overall mortality were a 23% mortality rate in 1996, 13.2% in 1997 (when PI began to be available at mid-year), and 6.5% in 1998 There were no deaths in the 38 patients of the study during the 1-year follow-up period. When the observation period was extended 1 additional year, only one patient died (2.63%). Only six of the 172 (3.48%) PI-treated patients with AIDS (cases not included in the study due to missing data) died during the same observation period. When overall mortality is compared with the mortality rate of patients treated with PI, the difference is statistically significant (from 23–3%, p <0.001).

Furthermore, before PI were available, hospital beds were 100% occupied, principally by patients with AIDS; once patients with AIDS initiated treatment with PI, monthly hospital occupancy decreased to 50%, and patients were and are at present actually seen at the out-patient clinic (data not shown). The increase in $CD4^+$ cells (p <0.05) in patients studied was substantial enough to decrease the number of infections (from 24 to 5) per year. The incidence of any of three major opportunistic infections (*Pneumocystis carinii, Mycobacterium avium* complex disease, and *cytomegalovirus retinitis*) declined in a failure-rate model from 21.9 per 100 person-years in 1994 to 3.7 per 100 person-years by mid-1997; the inclusion of PI in combined regimens conferred additional benefits (7). On the other hand, viral loads decreased almost continuously during the 12 months of the study, with a total decline of 3.0 $\log_{10}$/copies/

Table 4. Decline in mortality in AIDS patients treated with protease inhibitors[a]

Groups	No of patients	Death at 1 year of follow-up	Death at 2 years of follow-up
All patients before PI	481	116 (23 27%)	[b]
Patients on PI not included in the study	172	None	6 (3.48%)
Patients on PI included in the study	38	None[c]	1 (2 6%)

[a] Inclusion of protease inhibitors began in June 1997, [b]at the time, most patients were on PI and comparison between groups was no longer valid; [c]the difference in mortality rate prior to and on PI was statistically significant (p <0 001).

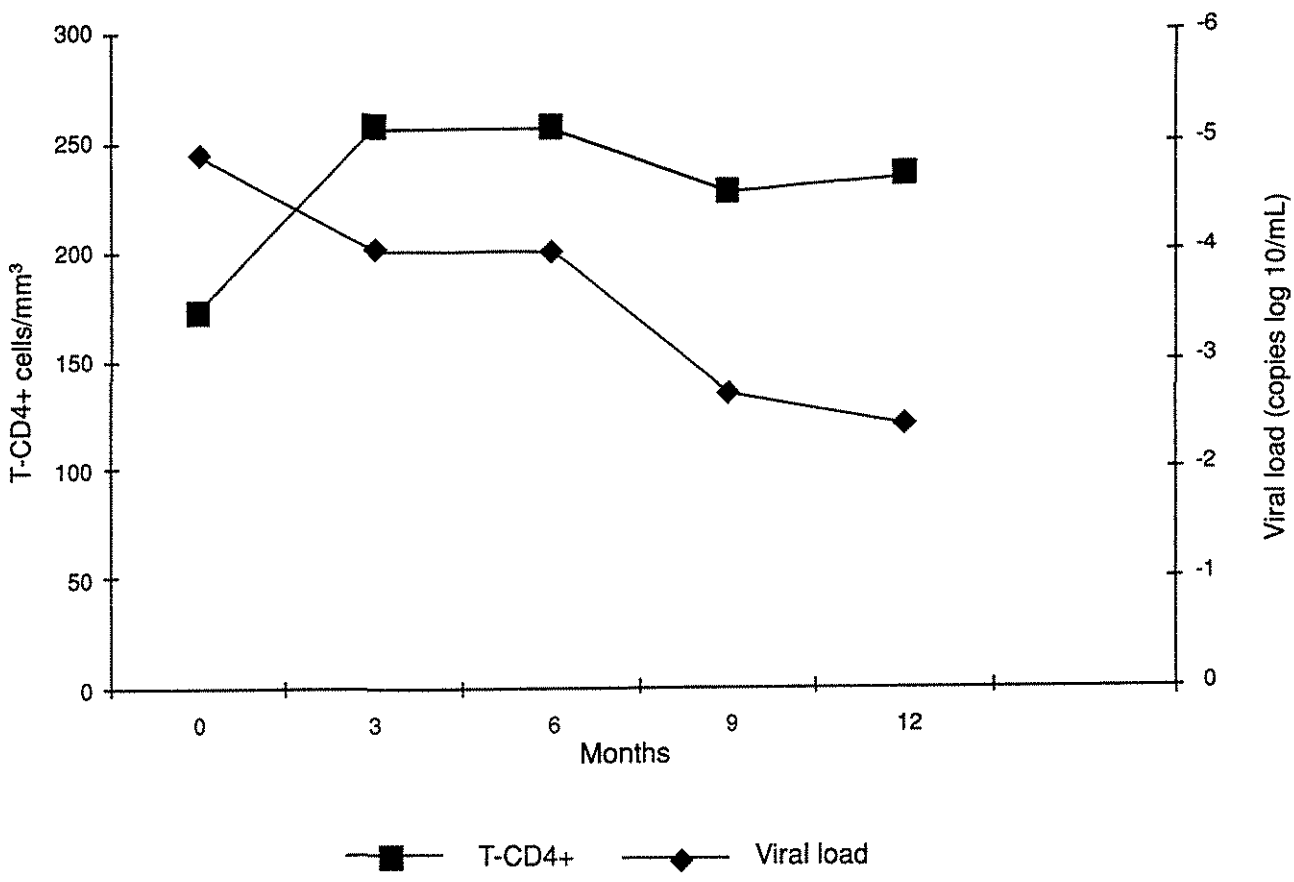

Figure 2. An increase in the amount of $CD4^+$ cells after the first month of PI ($p = <0.05$) Also, viral loads decreased from 5 to 2 logs during the treatment period

mL, a result that is highly significant. These $CD4^+$ and viral load results are in agreement with the decline in mortality and morbidity rates, clinical well-being, and decreased disability of patients, parameters also indirectly observed in reduction of hospitalization costs.

In summary, PI are potent antiretrovirals that have changed the prognosis of patients with AIDS from a rapidly progressing syndrome to one tending toward chronicity. The high cost of these drugs is compensated by a reduction in hospitalization costs and by the return of patients to a productive life. The reduction of 35% in hospitalization costs by PI in the short-term analysis is a benefit that must be evaluated in terms of the long-term commitment for prescribing PI.

References

1 Bozzete SA, Berry SH, Duan N, Frankel MR, Leibowitz AA, Lefkowitz D, et al. The care of HIV-infected adults in the United States N Engl J Med 1998,339(26) 1897

2. Andrulis DP, Beers VS, Bentley JD, Gage LS. The provision and financing of medical care for AIDS patients in US public and private teaching hospitals JAMA 1987,258 1343

3 Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs J Acquir Immune Defic Syndr Hum Retrovirol 1996,12 413

4 Seage GR, Landers S, Barry AM. Medical care cost of AIDS in Massachusetts. JAMA 1986,256·3107.

5 Bozzette SA Specific considerations for cost-effectiveness studies in AIDS. J Acquir Immune Deficit Syndr Hum Retrovirol 1995,10(Suppl 4) S23

6 Tapia-Conyer R, Sepúlveda-Amor J, de la Rosa-Montaño BM, Revuelta-Herrera A. Los costos directos del tratamiento del SIDA en México. Salud Publica Mex 1992;34:371.

7 *Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J,* Statten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection N Engl J Med 1998,338·853

8 Hoogs RS, O'Shaughnessey MV, Gataric N, Yip B, Craib K, Schechter MT, et al. Decline in deaths from AIDS due to new antiretrovirals. Lancet 1997,349:1294.

9 Chiassen MA, Berenson L, Li W, Schwartz S, Singh T, Forlenza S, et al. Accelerating decline in New York City AIDS mortality. In: Program and abstracts of the 5th Conference on retroviruses and opportunistic infections February 1-5, 1998; Chicago, IL, USA (Abstract 9b). JAMA 1998,279·450

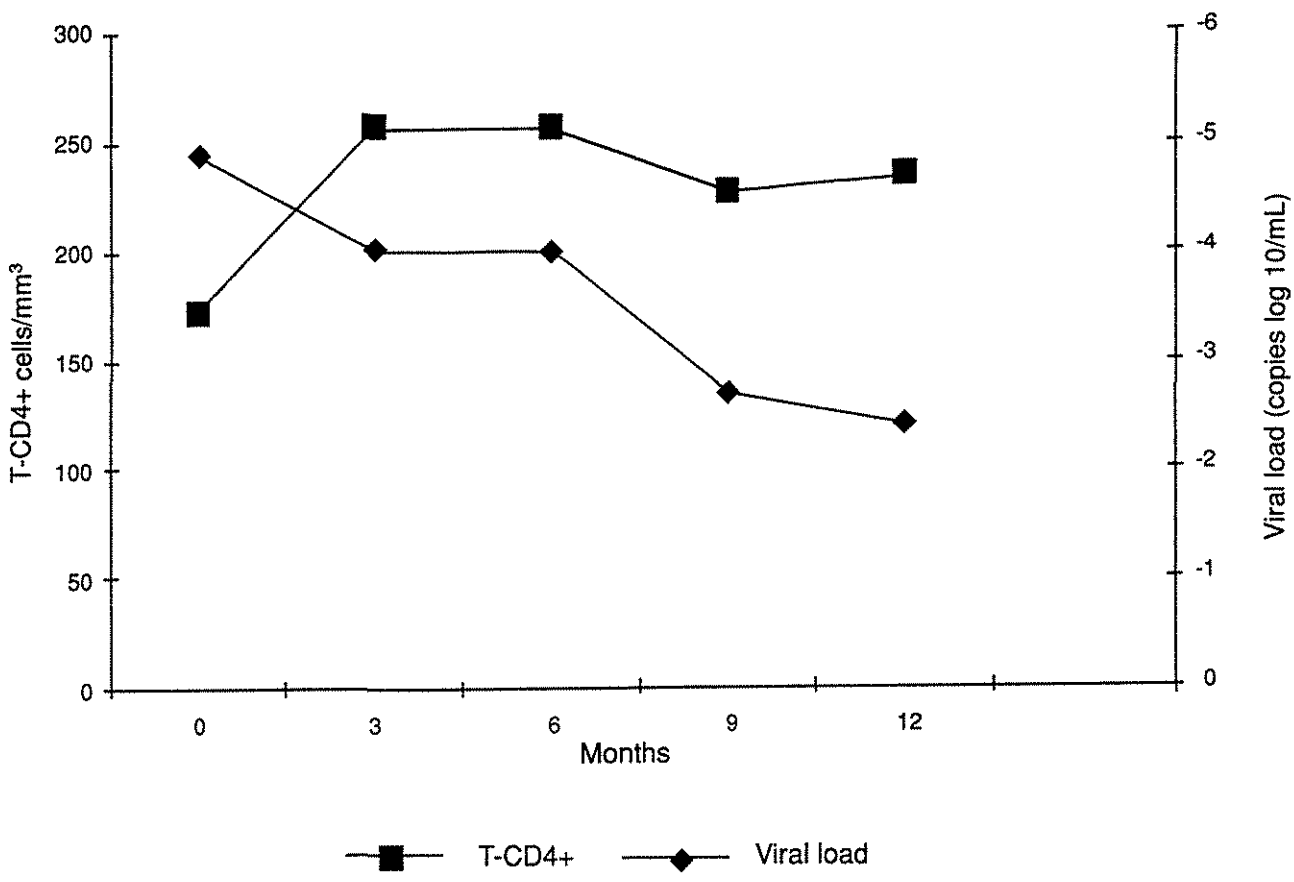

Figure 2. An increase in the amount of $CD4^+$ cells after the first month of PI ($p = <0.05$) Also, viral loads decreased from 5 to 2 logs during the treatment period

mL, a result that is highly significant. These $CD4^+$ and viral load results are in agreement with the decline in mortality and morbidity rates, clinical well-being, and decreased disability of patients, parameters also indirectly observed in reduction of hospitalization costs.

In summary, PI are potent antiretrovirals that have changed the prognosis of patients with AIDS from a rapidly progressing syndrome to one tending toward chronicity. The high cost of these drugs is compensated by a reduction in hospitalization costs and by the return of patients to a productive life. The reduction of 35% in hospitalization costs by PI in the short-term analysis is a benefit that must be evaluated in terms of the long-term commitment for prescribing PI.

References

1 Bozzete SA, Berry SH, Duan N, Frankel MR, Leibowitz AA, Lefkowitz D, et al. The care of HIV-infected adults in the United States N Engl J Med 1998,339(26) 1897

2. Andrulis DP, Beers VS, Bentley JD, Gage LS. The provision and financing of medical care for AIDS patients in US public and private teaching hospitals JAMA 1987,258 1343

3 Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs J Acquir Immune Defic Syndr Hum Retrovirol 1996,12 413

4 Seage GR, Landers S, Barry AM. Medical care cost of AIDS in Massachusetts. JAMA 1986,256·3107.

5 Bozzette SA Specific considerations for cost-effectiveness studies in AIDS. J Acquir Immune Deficit Syndr Hum Retrovirol 1995,10(Suppl 4) S23

6 Tapia-Conyer R, Sepúlveda-Amor J, de la Rosa-Montaño BM, Revuelta-Herrera A. Los costos directos del tratamiento del SIDA en México. Salud Publica Mex 1992;34:371.

7 *Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J,* Statten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection N Engl J Med 1998,338·853

8 Hoogs RS, O'Shaughnessey MV, Gataric N, Yip B, Craib K, Schechter MT, et al. Decline in deaths from AIDS due to new antiretrovirals. Lancet 1997,349:1294.

9 Chiassen MA, Berenson L, Li W, Schwartz S, Singh T, Forlenza S, et al. Accelerating decline in New York City AIDS mortality. In: Program and abstracts of the 5th Conference on retroviruses and opportunistic infections February 1-5, 1998; Chicago, IL, USA (Abstract 9b). JAMA 1998,279·450