Originales

Analysis of the implementation of GESIDA quality indicators in the HIV+ cohort PSITAR

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SUMMARY

Objective: To determine the compliance of quality care indicators (GESIDA) for adult patients living with HIV infection in PSITAR cohort.

Methods: Multi-center, prospective observational study. All adult naive patients, that began treatment during 2011 belonging to the PSITAR cohort, were selected. We recorded demographic data, virological parameters at baseline and 48 weeks of treatment and pharmacotherapy variables. The selected indicators were: The compliance of initial antiretroviral therapy with the Spanish national treatment guidelines (GESIDA) for treatment-naive HIV-infected patient (95%), undetectable viral load at 48 weeks (80%), treatment initiation with Abacavir without screening for HLA-B*5701 (0%), treatment modifications within the first year (<30%), adherence treatment measure (95%), study of resistance in the virologic failure (90%) and average expenditure per patient in the first treatment (GESIDA median).

Results: In total 108 HIV+ naive patients were included, 83.3% men. The median age was 40.5 years (21-75). The most frequent combination was tenofovir-emtricitabine-efavirenz with 61.0%. 28 patients (29.7%) modified their treatment during the first year. Focusing on indicators compliance, starting of treatment with a recommended regimen had 95.4% of compliance, undetectable viral load indicator 74.1%, treatment initiation without Abacavir test 0%, treatment modifications within the first year 25.9%, adherence treatment measure 86.3%, study of resistance in the virologic failure 80% and average expenditure per patient was 8,846 euros.

Conclusion: Quality care follow up indicators were fulfilled in their vast majority. The worst accomplished indicators such as undetectable viral load at 48 weeks, evaluation of adherence and study of resistance must be study to examine the possible improvement points.

Key Words: **HIV, quality indicators, health care, drug therapy.**

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Análisis del cumplimiento de los indicadores de calidad de GESIDA en la cohorte de pacientes VIH+ PSITAR

RESUMEN

Objetivos: Determinar el cumplimiento de los indicadores de calidad de la actividad asistencial GESIDA en la cohorte de pacientes VIH+ PSITAR.

Método: Estudio multicéntrico prospectivo. Se seleccionaron aquellos pacientes VIH naive adulto que iniciaron tratamiento en 2011. Se recogieron variables demográficas, analíticas y farmacoterapéuticas. Los indicadores seleccionados fueron: adecuación de las pautas iniciales de TAR a las guías españolas (95%), carga viral indetectable al año de tratamiento (80%), tratamiento con abacavir sin HLA-B*5701 previo (0%), cambios de tratamiento durante el primer año (<30%), registro de la adherencia al tratamiento (95%), estudio de resistencias en el fracaso virológico (90%) y gasto medio por paciente en primer tratamiento (mediana GESIDA).

Resultados: Se incluyeron 108 pacientes, de ellos el 83,3% hombres. La mediana de edad fue de 40,5 años (21-75). La combinación de inicio más frecuente fue emtricitabina-tenofovir-efavirenz (61%). El 95,4% de los pacientes iniciaron con un tratamiento considerado preferente. El 74,1% presentó carga viral plasmática indetectable a las 48 semanas. Ningún paciente inicio tratamiento con abacavir sin la determinación del HLA-B*5701. El 25,9% discontinuó el TAR en el primer año, registrándose una valoración de la adherencia en el 86,3% de los casos. El estudio de las resistencias en fallo virológico se realizó en el 80,0% de los pacientes y el gasto medio fue de 8.846 euros.

Conclusiones: Los indicadores de calidad de la actividad asistencial se cumplen ampliamente. La carga viral plasmática indetectable, la valoración de la adherencia y el estudio de resistencia requieren de un mayor estudio para detectar puntos de mejora.

Palabras clave: **VIH, indicadores de calidad asistencial sanitaria, tratamiento farmacológico.**

INTRODUCTION

Highly activity antiretroviral therapy (HAART) has substantially reduced morbidity and mortality in patients infected with human immunodeficiency virus (HIV) since its introduction in 1996. This has changed the natural history of disease[1,2]. Over the past few years, drug development has evolved to achieve, in most cases, a partial restoration of the immune system[3] and an approach to the life expectancy of the general population[4].

Both treatment and monitoring of HIV-infected patients are gradually becoming more complex. This and the fact that, HIV disease is considered as a chronic disease, leads to an increased demand for standardize the care for these patients[5]. In order to determine the quality of clinical practice and to implement the appropriate improvements, in 2010, GESIDA (Spanish Study Group on AIDS) quality care indicators for adult patients living with HIV infection were published[6].

Of these, drug therapy management indicators play a key role, as evidenced by the fact that four of these indicators are included among the most relevant indicators and eight among indicators of basic accreditation.

In addition, pharmacotherapy follow-up is a basic pillar of achieving the goals of pharmacotherapy patients. On the other hand, in general, hospital pharmacist role has changed in our working frame. Simple concept of pharmacist as "drugs dispenser" has been replaced by more active and dynamic role. Pharmacist has become co-responsible, with the other members of the multidisciplinary team, for clinical outcomes of drug prescribed to each patient. All this shows the importance of pharmacist dedicated to VIH patient's health care and they are a key element of therapy management and rational drug use.

In order to facilitate pharmacotherapy follow-up and to obtain useful outcomes indicators such as drug effectiveness and safety, PSITAR cohort was developed with its specific registry tool.

PSITAR is a prospective HIV naive patient's cohort. This cohort collects information from patients over 18 years of age belonging to seven hospitals in Andalusia. Patients were included in PSITAR cohort from 2011 to the present.

This new tool is meant to solve one of the main problems faced by health professionals: dispensing heterogeneous software and they are not geared towards drug pharmacotherapy management patients.

This online platform allows easily introducing and exploiting demographic, analytical and pharmacological parameters of patients at baseline and it allows monitoring their development over time.

The aim of this study is to assess the compliance of quality care indicators (GESIDA) for adult patients living with HIV infection in PSITAR cohort.

METHODS

We performed a multi-center, prospective observational study. All adult naive patients, that began treatment during 2011 and were treated in outpatient pharmacy hospitals belonging to the PSITAR cohort, were selected. Also, they must complete a full year of follow-up. Patients participating in clinical trials or expanded access to antiretroviral drugs were excluded.

We recorded demographic data: Age at treatment initiation and sex; Virological parameters at baseline and 48 weeks of treatment as CD4 cells (Cel/mL) count and viral load (copies/mL) and pharmacotherapy variables: First HAART regimen, primary antiretroviral resistance (before treatment initiation), discontinuation in the first 48 weeks of treatment and their causes based on Swiss HIV Cohort[7]. The main reason for treatment modification was classified as treatment failure, intolerance and/or toxic effects, the patient's choice, the physician's decision, and other reasons.

Finally, treatment adherence was recorded by SMAQ questionnaire and recording drug dispensations.

The costs of each regimen were calculated from the laboratory sales price plus 4%. The costs of each HAART were calculated from drug price they include. In case there are combinations, the price would be based on price of the combo. Prices were obtained from consensus GESIDA/National AIDS Plan 2011[8].

Quality care indicators (GESIDA) for adult patients living with HIV infection are described in the document, with the same name, published in 2011[6].

In the final document, 66 indicators were included as follows: Structural conditions, diagnosis and evaluation, follow-up and preventive interventions, follow-up of patients under treatment, specific aspects in women, comorbidities, hospitalization, mortality rates, training and research.

The indicators which were chosen belong to follow-up of patients under treatment section. The following indicators were selected:

The compliance of initial antiretroviral therapy (ART) with the Spanish national treatment guidelines (GESIDA Guidelines) for treatment-naive HIV-infected patient. The guidelines' recommendations for initiating antiretroviral treatment are shown in table 1. Undetectable viral load was defined as a viral load of <50 HIV-1 RNA copies/ml at 48 treatment weeks, treatment initiation with Abacavir without screening for HLA-B*5701, treatment modifications within the first year, adherence treatment measure, study of resistance in the virologic failure and average expenditure per patient in the first treatment. Features of each indicator are shown in table 2.

Statistical analysis

The main variables are taken from the data collection platform PSITAR. The data have been introduced by the heads of each hospital centre through review of dispensations in the outpatient program and review of medical history. The quantitative variables are expressed as median and interquartile range and the qualitative values as percentages. All statistical analyses were performed using SPSS v.20.0.

RESULTS

Baseline characteristics

In total 108 HIV+ naive patients from seven hospitals were included in the study, 83.3% of them were men. The median age was 40.5 years. At the time of initiation of therapy, few patients, 24.1% had an advanced immune deficiency (CD4 cells below 200/ml). The rest of baseline socio-demographic and clinical characteristics are listed in table 3.

Pharmacotherapeutic treatment

Regarding the initial therapy, the most frequent combination in naive patients was tenofovir-emtricitabine with efavirenz with 61.0% of the patients, followed by tenofovir-emtricitabine with atazanavir/ritonavir 15.8%, tenofovir-emtricitabine with darunavir/ritonavir 12.0% and another combinations 11.2%.

Information on primary resistance was available in 73 patients; including three patients had primary drug resistance: one patient developed resistance to protease-inhibitor (PI) and two patients to Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs).

Of 108 individuals starting ART, 28 (29.7%) modified their treatment during the first year. The most frequent reasons for treatment modification were toxic effects (60.7%), followed by a physician's decision (14.3%), treatment failure (17.8%) and other reasons (7.2%).

Finally, in relation to adherence to antiretroviral therapy, 22.2% of the patients were non-adherent to one year after treatment initiation.

Table 1
Guidelines' recommendations for initiating anti-retroviral treatment, GESIDA 2011

3rd Drug	Regimen	Clinical randomized trials
Preferred		
NNRTIs	TDF/FTC/EFV	ECHO, THRIVE, STARTMRK,2NN,ACTG 5202, ASSERT, 934, MERIT,ACTG 5142
	ABC/3TC + EFV*	ACTG 5202, ASSERT, CNA30024
	TDF/FTC + NVP*	ARTEN, OCTANE II
PI/r	ABC/3TC + ATV/r*	ACTG 5202
	ABC/3TC + LPV/r *	KLEAN, HEAT
	TDF/FTC/ATV/r	CASTLE, ACTG 5202, ARTEN
	TDF/FTC/DRV/r	ARTEMIS
	TDF/FTC + LPV/r*	ARTEMS, 730, CASTLE, GEMINI, OCTANE II, HEAT, ACTG 5142
NRTIs	TDF/FTC + RAL	STARMRK
Alternative		
NRTIs	ddI+3TC+EFV	GESIDA 3903
	AZT/3TC+ EFV	934, CNA30024
PI/r	ABC/3TC + FPV/r	KLEAN
	TDF/FTC + SAQ/r	GEMINI

Documento de consenso de Gesida/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana (Actualización enero 2011).

Table 2
Indicators description

Quality care indicators (GESIDA) for adult patients living with HIV infection				
Pharmacotherapeutic follow-up indicators				
Indicators	**Dimension**	**Formula**	**Population**	**Standard**
Compliance of initial antiretroviral therapy with the Spanish national treatment guidelines for treatment-naive HIV-infected patient	EFFECTIVENESS	Number of adult naive patient that began ART with preferred regimens x 100 / Number of adult naive patient that began ART	All adult naive patients that began treatment. No clinical trial patients	95%
Undetectable viral load (<50 copies/ml) at 48 treatment weeks	EFFECTIVENESS	Number of patient that began ART and reached undetectable viral load at 48 week x 100 / Number of patient that began ART	All adult naive patients that began treatment	80%
Treatment initiation with Abacavir without screening for HLA-B*5701	SECURITY	Treatment initiation with Abacavir without screening for HLA-B*5701 x 100 / Number of patient that began ART	All patient that began ART with Abacavir. Not included if they had taken it before	0%
Treatment modifications within the first year	EFFECTIVENESS	Number of patient that made treatment modifications within the first year x 100 / Number of patient that began ART	All adult naive patients that began treatment. Not included loss follow-up, clinical trial and pregnancy	<30%
Adherence treatment measure	FOLLOW-UP	Number of patient with adherence measure x 100 / Number of patient that began ART	All adult naive patients that began treatment	95%
Study of resistance in the virologic failure	EFFECTIVENESS	Number of patient with virologic failure and study of resistance 100/ Number of patient with virologic failure	Patient with virologic failure. Not included patients with viral load greater than 1000 cop/mL	90%
Average expenditure per patient in the first treatment	EFICIENCY	Total annual expenditure in that began ART during 12-24 months before / Number of patient that began ART and reached undetectable viral load at 48 week	All adult naive patients that began treatment in 12-24 months before	GESIDA median

Indicadores de calidad asistencial GESIDA para la atención de personas infectadas por el VIH/sida. Enferm Infecc Microbiol Clin. 2010.28(Supl5);6-88.

Quality care indicators

The most accomplished quality indicators were treatment initiation with Abacavir without screening for HLA-B*5701 with 100% compliance (no patient) and the start of treatment with a recommended regimen as GESIDA guidelines with 95.4% compliance. Antiretroviral therapy discontinuation in the first 12 months was above the reference value with 25.9% of cases.

At the opposite end, quality indicators with poorer outcomes were study of resistance in the virologic failure with 80.0% compliance, not exceeding the minimum value, as well as undetectable viral load indicator with 74.1%. Adherence recording didn't reach the reference value with 86.3% either.

Finally, focusing on cost, mean health expenditure per patient per year was 8,846.0 euros (11,796$). This figure is below the median of rates published in 2011 by GESIDA, with a value of 9,403.8 euros (12,540$).

DISCUSSION

Our study shows that the compliance of drug therapy management indicators (GESIDA) for adult patients living with HIV infection in PSITAR cohort was elevated.

Currently, there are no studies examining the compliance of quality care indicators (GESIDA) for adult patients since its publication in 2010. There are studies that scan the adherence to guidelines and one paper studies these quality indicators in pediatric population. In this

Table 3
Baseline characteristic of study population

Total n	108
Male Gender (%)	90 (83)
Age at enrolment (years) [median (IQR)]	40 (21-75)
Age at enrolment 10-31 31-40 41-50 >50	 24 (22) 30 (28) 27 (25) 27 (25)
CD4 count at enrolment (cells/ l) [median (IQR)] <200 200-350 >350	 26 (24) 36 (33) 46 (43)
Viral load at enrolment copies/mL [median (IQR)]	66.328 (19-4.858.589)

Values are n (%) unless otherwise stated; QR: interquartile rang.

study, quality indicators were adapted to pediatrics patients[9]. All indicators in the follow-up section exceeded standards values less undetectable viral load. In spite of having this document, it is necessary to use the consensus GESIDA/National AIDS Plan 2011[8] to analyze our results.

Among the indicators with better compliance profile are the following: treatment initiation with Abacavir without screening for HLA-B*5701, treatment initiation with a recommended regimen as GESIDA guidelines and antiretroviral therapy discontinuation in the first 12 months indicator. The cost per patient per year of treatment is less than the value proposed in the indicator description.

By contrast, the worst accomplished quality indicators are the percentage of patients with undetectable viral load, study of resistance in the virologic failure and adherence assessment.

In relation to HLA-B*5701 determination, this procedure is routinely done and has been incorporated into daily clinical practice since 2002, when an association between a diagnosis of hypersensitivity reaction to abacavir and carriage of the major histocompatibility complex class I allele HLA-B*5701 was reported independently by two research group[10,11].

In reference to the compliance with clinical practice guidelines for antiretroviral treatment indicator, we knew that most combinations of current drugs achieve undetectable viral load in 70.0% of cases at 48 weeks[12]. Drugs combinations supported by the largest number of clinical trials with optimal efficiency and durability, acceptable tolerance and ease of use are considered "Preferred regimens"[5].

We found that the choice of initial antiretroviral regimen was appropriate in most cases: 95.4% of patients started treatment that was considered recommended by GESIDA guidelines. This is consistent with a study in the Spanish Asociación Médica Vach de Estudios Multicéntricos (VACH) cohort in the years 2004-2006, which found that initial treatment regimens were compliant with the guidelines in 95% of cases[13].

Suarez-Garcia *et al.* study[14], carried out in Spanish cohort CORIS, shows a lower adequacy with 91.5% compliance including preferred and alternative regimens. This data may be because in this study patients have been included since 2004. Since then, knowledge about different antiretroviral treatments has strongly developed and most complete guidelines have been elaborated and have been used by many health professionals.

Studies from the USA have found lower percentages of compliance[15-17]. For example, the Wandeler *et al.* study which compared initial antiretroviral regimens with American clinical practice guidelines, showed a compliance rate of 73.0[18]. These differences across studies can partly be attributed to different populations and health care systems, use of different guidelines and general differences in the experience of caring for HIV-infected patients.

At last, several studies have focused on the analysis of discontinuations of antiretroviral therapy. Initial ART can be maintained over many years. Discontinuation of ART during first year due to its toxicity can have a negative impact on adherence or virological response. Elzi *et al.*[7] in their study collected all treatment modifications in Swiss cohort of HIV patients between 2005 and 2008 with a percentage of discontinuations during the first year of 41.5%.

The broad availability of new drugs with the possibility of once-daily regimens may have triggered treatment modification, as suggested by the high proportion of patients switched to another antiretroviral regimen in this study[19-21].

Recently, a work has been published by The Antiretroviral Therapy Cohort Collaboration (ART-CC)[22] where the percentage of treatment discontinuation and its causes has been analyzed in 18 European and American cohorts between 2002 and 2009. Their results were discontinuation percentages close to 50% supporting this idea.

Cost per patient per year of treatment value was below the median cost of the preferred GESIDA regimens[8] and at the lower limit of data obtained in the Blasco A *et al.* study which has been evaluated the costs and the cost effectiveness of initiating treatment following GESIDA guidelines in different situations in 2011[23].

Among indicators with poorer outcomes, undetectable viral load seems the most important. The aim of ART is to suppress viral replication rapidly and durably to get a figure lower than 50 copies/ml. This goal has been shown to prevent the mutation selection[21,22] and to increase virological response[23].

In our study 74.1% of patients had undetectable viral load. Such a low number can be explained because recent infections or breakthrough viral load was not specified.

The relationship between resistance mutations and virologic failure has been evidenced with the monitoring of the viral load.

Current treatments have dramatically reduced the frequency of treatment failure and virological failure rates in first-line treatment were between 20-40%[24,25].

Prospective randomized studies have shown that the use of genotypic resistances tests in patients with virological failure was associated with a better virological control at three and six months and a better vital prognosis[26].

In our study, patients with virological failure was low (limited) and a percentage value may not be indicative of global relevance.

Therapeutic compliance is one of the variables that best predicts virological response. Non-adherence increases the risk of acquiring resistances and morbidity and mortality associated with HIV infection[5].

Treatment adherence should be assessed regularly because this allows estimated the patient's ability to get involved in their own health care and in their disease.

Our study has several limitations. Firstly, we have work in a follow up cohort from a limited geographical area, Andalusia. We think that this cohort was representative because in this area, the national guidelines were followed. Secondly, all pharmacotherapeutic monitoring indicators have not been selected. Some aspects such as the establishment of the first treatment or first medical visit go beyond the pharmaceutical field.

Our new lines of research will focus on determining persistence of therapy in this cohort and on the analysis of time series data.

In conclusion, in our multicentre cohort, quality care follow up indicators (GESIDA) for adult patients living with HIV infection were fulfilled in their vast majority. The worst accomplished indicators such as undetectable viral load at 48 weeks, evaluation of adherence and study of resistance in the virologic failure must be study to examine the possible improvement points.

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