Cost analysis of HIV treatment and drug-related adverse events when fixed-dose combinations of antiretrovirals (FDCAs) were stopped, versus continuation with FDCAs

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Background

- The anti-HIV-1 therapy has evolved to a single daily pill, with 2 or more antiretroviral agents combined in a fixed-dose.
- This simplification of the regimens has the potential to increase the compliance to the therapy, improving virologic efficacy and clinical outcomes[1].
- In a costs-containment situation, the launch in Spain of a generic form of lamivudine (g3TC), included in several fixed-dose combinations of antiretrovirals (FDCAs), has led to consider switching from lamivudine and emtricitabine containing FDCAs, to separate components including the less expensive g3TC.

Objectives

To determine the cost differences of antiretroviral treatments and drug-related adverse events management between patients where FDCAs were stopped to provide the separate components and those who maintained their FDCAs containing treatment.

Methods

An independent retrospective cost analysis was carried out at Son Llàtzer Hospital to estimate the impact that would produce the FCDAs interruption due to g3TC entry.

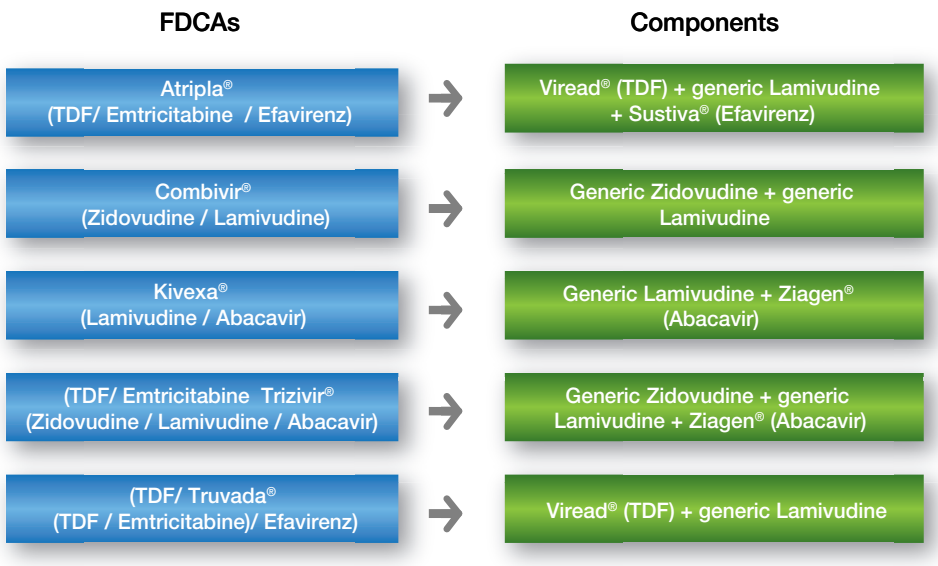
1. Perspective

- The study was carried out from the hospital perspective during the period of June 2010 to July 2011.

2. Patient profile

- A total of 75 patients (exposed group) underwent the substitution of their FDCAs to single agents (Figure 1).
- At the same time, 150 patients (control group) who did not broke their FDCAs were randomly selected.

Figure 1. Disruption scheme: FDCAs to separate components



3. Study design

- For both groups of patients, resource utilization related to adverse drug events management and drugs administered were collected.
- The study period assumed for costs calculations was the mean days that patients stayed with broken FDCAs (120 days).
- An alternative analysis was carried out considering the extra-appointment required to monitor those patients who switched their FDCAs to separate components. The resources considered for the cost analysis due to the extra-appointment were a medical visit, a biochemistry test, a blood count and a coagulation analysis, urine analysis, an analysis of lymphocyte populations and a determination of viral load.
- Unit costs (€, 2011) were obtained from Spanish database[2,3] and are detailed in Table 1.

Table 1: Healthcare resource cost

Resource	Unit cost (€)
Visits	
Day center for mental health	49.36
Visit to infectious disease specialist	114.82
Visit to nurse	15.69
Visit to emergency room	160.14
Admissions	
Internal medicine admission	526.28
Neurology unit admission	410.23
Intensive Care unit	1,797.37
Diagnostic procedures	
Liver biopsy	389.73
Colonoscopy	200.80
Abdominal ultrasound	82.61
Breast ultrasound	47.04
Electroencephalogram	77.94
Lumbar puncture	269.90
MRI brain	232.38
Chest X-ray	20.94
Computer tomography	109.12
Clinical analyses	
Urin test	12.07
Blood test	26.38
Viral load test	119.52
Study of lymphocyte subpopulations	60.97
Coagulation profile study	10.95
Liver profile study	4.69
Serology	26.39
Erythrocyte sedimentation rate study	1.12

Results

- The demographics and baseline characteristics of the patients, which were well matched between the treatment groups, were summarized in Table 2.

Table 2. Demographics and Baseline Characteristics

	Exposed Group (n = 75)	Control Group (n = 150)
Female sex, n (%)	18 (24%)	38 (25%)
Median age	44	46
Transmission mechanism		
Homosexual	18 (25%)	37 (25%)
Addicted to parenteral drugs	29 (39%)	52 (35%)
Heterosexual	19 (25%)	48 (32%)
Unknown	7 (9%)	12 (8%)
Concomitant diseases		
AIDS	18 (24%)	46 (30%)
Chronic hepatitis B	31 (40%)	56 (39%)
Psyquiatric history	17 (23%)	27 (18%)
Methadone consumption	5 (6%)	22 (14%)
Psychotropics use	14 (19%)	19 (13%)
Background Antiretroviral therapy		
Atripla®	36 (48%)	72 (48%)
Truvada®	24 (32%)	48 (32%)
Kivexa®	7 (9%)	16 (11%)
Combivir®	6 (8%)	14 (9%)
Trizivir®	2 (3%)	0 (0%)
NNRTIs	15 (20%)	28 (19%)
Protease inhibitor	22 (29%)	54 (36%)
Integrase	0 (0%)	3 (2%)
HIV-1 RNA > 50 copies /ml, baseline visit	10 of 74 (14%)	10 of 146 (7%)
Median baseline CD4+ cell count, (range) cells/µl	573 (41-1527)	542 (92-1481)

- The number of drug-related adverse events (Table 3) was higher for the exposed group (14) compared to the control group (2).
- The lower costs of the individual components with respect to FDCAs lead to a lower spending in drug antiretroviral treatment in the exposed group, but lead to an increase in the total healthcare costs.
- Considering the antiretroviral treatments and drug-related adverse events management costs, the administration of the components separately increases the total cost in €0.72 per day and per patient compared with FDCAs strategy (Table 4).

Table 3. Drug-related adverse events, severity and incidence

Drug-related adverse events	Severity (grade)	Incidence (number of events)
Control group (n=150)		
Dizziness	1	1
Neuropsychiatric	1	1
Exposed group (n=75)		
Neuropsychiatric	1	2
Neuropsychiatric	2	5
Neuropsychiatric	3	1
Neuropsychiatric	4	1
Diarrhea	2	2
Vomiting	2	1
Hepatotoxicity	3	1
Hepatotoxicity	4	1

- When the cost of the extra-appointment is considered (alternative scenario), the total cost increases by €3.61 per day and per patient during the study period.

Table 4. Cost analysis results

	Control group	Exposed group	Difference
Base case			
ART cost in study period*	3,017.50	2,873.58	143.92
ADE cost in study period*	0,00	230.26	-230.26
Mean total cost in study period*	3,017.50	3,103.84	-86.34
Total cost per day	25.22	25.94	-0.72
Alternative scenario			
ART cost in study period*	3,017.50	2,873.58	143.92
ADE cost in study period*	0,00	230.26	-230.26
Extra-appointment cost in study period*	0,00	345.83	-345.83
Mean total cost in study period*	3,017.50	3,449.67	-432.17
Total cost per day	25.22	28.83	-3.61

ART: Antiretroviral therapy; ADE: Adverse drug events
*Study period: 120 days

Limitations

- As a study based on clinical practice, all patients were aware of FDCAs disruption, and probably did not agree with this change. Hence, it can not be excluded the subjective nature of the adverse drug events, especially the milder ones. However, this does not detract from its impact on clinical practice.
- The cost analysis is based on a single-center study. However, data collected for the study reflects routine clinical practice.

Conclusions

- **Unlike the desired objective of cost-saving, FDCAs disruption led to an increase of healthcare expenditure due to the higher rate of adverse drug events observed in the exposed group compared to those observed in the control group.**
- **The approval in certain centers of interrupt the FDCAs to provide the separate components, means for these patients the access to a highly complex treatment that can lead to a difficult compliance, despite having a common National Health System.**

References

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