INNSZ

INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN

06/09/12

MÉXICO, D.F., A 04 DE SEPTIEMBRE DE 2012.

DR. JUAN SIERRA MADERO
INVESTIGADOR PRINCIPAL
DEPTO. DE INFECTOLOGÍA
P R E S E N T E

Por este medio, me permito informarle que, la Comisión de Ética en Investigación, del Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, **ha revisado y aprobado** el Protocolo de Investigación clínica, titulado:

"Estudio piloto para evaluar el síndrome inflamatorio de reconstitución inmune cardiaco en pacientes VIH positivos que inician un primer esquema de tratamiento antirretroviral"

REF. 659

La vigencia de la aprobación termina el día 04 de septiembre de 2013. Si la duración del estudio es mayor tendrá que solicitar la re-aprobación anual del mismo, informando sobre los avances y resultados parciales de su investigación e incluyendo todos los datos sobresalientes y conclusiones.

Sin más por el momento quedo de usted.

INCMNSZ
= 4 SEP 2012
COMISIÓN DE ÉTICA EN INVESTIGACIÓN

ATENTAMENTE,

DR. CARLOS A. AGUILAR SALINAS
COORDINADOR
COMISIÓN DE ÉTICA EN INVESTIGACIÓN

Investigación
Tradición Servicio
Asistencia Docencia

c.c.p. Dr. Rubén Lisker Y,. Director de Investigación.
C.P. Martha Arredondo Urzúa, Jefe del Depto. C.F.E.I.

CAAS/mrg

20007700

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• Delegación Tlalpan
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INSTITUTO NACIONAL DE
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Y NUTRICIÓN
SALVADOR ZUBIRÁN

MÉXICO, D.F., A 06 DE SEPTIEMBRE DE 2013.

DR. JUAN G. SIERRA MADERO
INVESTIGADOR PRINCIPAL
DEPARTAMENTO DE INFECTOLOGÍA
PRESENTE

ESTIMADO DR. SIERRA:

Le informamos que con relación al Protocolo de Investigación clínica, titulado:

"Estudio Piloto Para Evaluar El Síndrome Inflamatorio De Reconstitución Inmune Cardiaco En Pacientes VIH Positivos Que Inician Un Primer Esquema Antirretroviral"
Ref. 659

Estos Comités toman conocimiento del estado actual del estudio de fecha 23 de agosto de 2013, así mismo se **autoriza** la re-aprobación anual **con vigencia hasta el 06 de septiembre de 2014.**

Sin otro particular, reciba un cordial saludo.

ATENTAMENTE,

INCMNSZ
06 SEP 2013
COMISIÓN DE ÉTICA EN INVESTIGACIÓN

DR. CARLOS A. AGUILAR SALINAS
PRESIDENTE
COMITÉ DE INVESTIGACIÓN

DR. ARTURO GALINDO FRAGA
PRESIDENTE
COMITÉ DE ÉTICA DE INVESTIGACIÓN

Recibí original

Raúl Ortega Pedro

17/09/13

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INSTITUTO NACIONAL DE
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SALVADOR ZUBIRÁN

ACUSE

MÉXICO, D.F., A 30 DE OCTUBRE DE 2013.

DR. JUAN G. SIERRA MADERO
INVESTIGADOR PRINCIPAL
DEPARTAMENTO DE INFECTOLOGÍA
P R E S E N T E

ESTIMADO DR. SIERRA:

Le informo que con relación al Protocolo de Investigación clínica, titulado:

"Estudio Piloto Para Evaluar El Síndrome Inflamatorio De Reconstitución Inmune Cardiaco En Pacientes VIH Positivos Que Inician Un Primer Esquema Antirretroviral"
Ref. 659

Este Comité ha recibido y revisado el informe del estado actual del estudio y el formato de conflicto de intereses, con fecha 22 de octubre de 2013. Así mismo le informo que el proyecto cuenta con la re-aprobación anual con **vigencia hasta el 06 de septiembre de 2014.**

Sin más por el momento, quedo de usted.

INCMNSZ
30 OCT 2013
COMISIÓN DE ETICA EN INVESTIGACIÓN

ATENTAMENTE,

DR. ARTURO GALINDO FRAGA
PRESIDENTE
COMITÉ DE ÉTICA DE INVESTIGACIÓN

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INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN

ACUSE

MÉXICO, D.F., A 27 DE JULIO DE 2015

DR. JUAN G. SIERRA MADERO
INVESTIGADOR PRINCIPAL
DEPARTAMENTO DE INFECTOLOGÍA
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN, "SALVADOR ZUBIRÁN"
AV. VASCO DE QUIROGA NO. 15,
COL. BELISARIO DOMÍNGUEZ SECCIÓN XVI,
DEL. TLALPAN, C.P. 14080, MÉXICO, D.F.
PRESENTE

Por medio de la presente le informamos que se **ha revisado y aprobado** la siguiente documentación correspondiente al Protocolo de Investigación clínica, titulado:

"Estudio Piloto Para Evaluar El Síndrome Inflamatorio De Reconstitución Inmune Cardiaco En Pacientes VIH Positivos Que Inician Un Primer Esquema Antirretroviral"
Ref. 659

1. Enmienda No. 3 del protocolo, V2.3, del 23-Julio-2015.
2. Enmienda No. 2 del Consentimiento Informado, V2.2, del 23-Julio-2015.

Se toma conocimiento del estado actual del estudio detallado en su informe de fecha 23 de julio de 2015, así mismo se **autoriza** la re-aprobación anual **con vigencia hasta el 27 de julio de 2016.**

Sin otro particular, reciba un cordial saludo.

INS. NACIONAL DE CIENCIAS MEDICAS Y NUTRICIÓN "SALVADOR ZUBIRÁN"
27 JUL 2015
COMITÉ DE ÉTICA EN INVESTIGACIÓN

ATENTAMENTE,

DR. CARLOS A. AGUILAR SALINAS
PRESIDENTE
COMITÉ DE INVESTIGACIÓN

DR. ARTURO GALINDO FRAGA
PRESIDENTE
COMITÉ DE ÉTICA DE INVESTIGACIÓN

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30-JULIO-2015

INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN

ACUSE

CIUDAD DE MÉXICO, A 1° DE JULIO DE 2016

DR. JUAN G. SIERRA MADERO
INVESTIGADOR PRINCIPAL
DEPARTAMENTO DE INFECTOLOGÍA
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN, "SALVADOR ZUBIRÁN"
AV. VASCO DE QUIROGA NO. 15
COL. BELISARIO DOMÍNGUEZ SECCIÓN XVI
DEL. TLALPAN, C.P. 14080, CD. DE MÉXICO
PRESENTE

Le informamos que con relación al Protocolo de Investigación clínica, titulado:

"Estudio Piloto Para Evaluar El Síndrome Inflamatorio De Reconstitución Inmune Cardiaco En Pacientes VIH Positivos Que Inician Un Primer Esquema Antirretroviral"
Ref. 659

Se ha recibido y revisado el informe de **cierre** del estudio, con fecha 29-Junio-2016.

Sin otro particular, reciba un cordial saludo.

ATENTAMENTE,

DR. CARLOS A. AGUILAR SALINAS
PRESIDENTE
COMITÉ DE INVESTIGACIÓN

DR. ARTURO GALINDO FRAGA
PRESIDENTE
COMITÉ DE ÉTICA DE INVESTIGACIÓN

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CARLOS MAGRIGAL 15JUL2016

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Instituto Nacional de Ciencias Médicas y Nutrición
Salvador Zubirán

INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN

SALVADOR ZUBIRAN

Dirección de Investigación

FORMA ÚNICA PARA REGISTRO DE PROYECTOS

11 JUN 2012

DIRECCIÓN DE INVESTIGACIÓN
DEPTO. DE CONTROL DE FONDOS ESPECIALES PARA LA INVESTIGACIÓN

FECHA DE RECEPCIÓN: 31/05/2012 CLAVE: INF-659-12/13-1

TÍTULO: Estudio piloto para evaluar el síndrome inflamatorio de reconstitución inmune cardiaco en pacientes VIH positivos que inician un primer esquema de tratamiento antirretroviral

INVESTIGADOR RESPONSABLE: Sierra Madero Juan Gerardo

DEPARTAMENTO O SERVICIO: DEPARTAMENTO DE INFECTOLOGÍA

TIPO DE INVESTIGACIÓN: Investigación Clínica

PATROCINADORES:

Patrocinador Cantidad

VIGENCIA DEL PROYECTO: Del 01/08/2012 al 30/06/2013

Trimestre 1 Trimestre 2 Trimestre 3 Trimestre 4

COSTO TOTALES DE LA INVESTIGACIÓN	
Personal	$ 0.00
(sueldos y sobresueldos al personal)	
Equipos	$ 0.00
(de laboratorio, cómputo, transporte, etc.)	
Materiales	$ 0.00
(reactivos, consumibles, desechables, etc.)	
Animales	$ 0.00
(adquisición, cuidado, procedimientos, etc.)	
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FIRMAS

Investigador responsable	Jefe de Departamento
Comité de Investigación en Humanos	Comité de Investigación en Animales
Director de Investigación	Director General

Fecha de resolución

06-SEP-2012

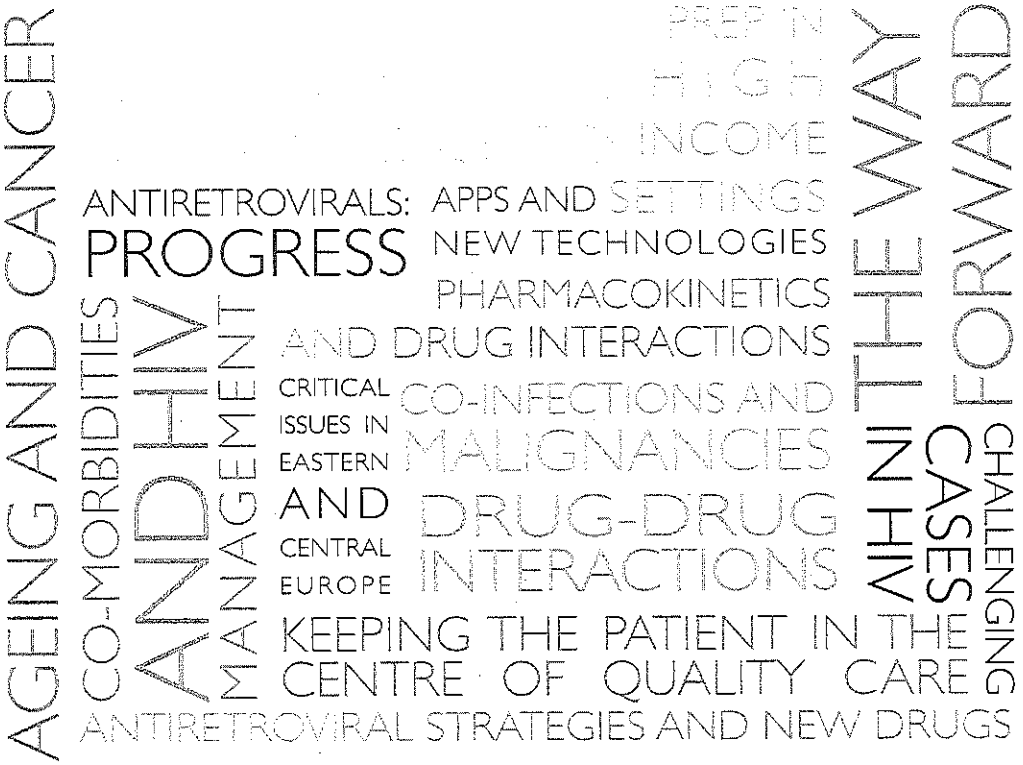
JIAS Journal of the International AIDS Society

HIV 2016

Abstract supplement

International Congress of Drug Therapy in HIV Infection

23-26 October 2016, Glasgow, UK



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Volume 19, Supplement 7
October 2016

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Abstract P184–Table 1. Agreement between D:A:D and other CVD calculation tools (high, non-high risk)

	Framingham CVD	Framingham Hard CHD	Score	PROCAM	QRISK2	CUORE
D:A:D						
K	0.729	0.191	0.434	0.595	0.266	0.206
95% CI	0.475, 0.982	−0.104, 0.485	0.092, 0.775	0.278, 0.912	−0.070, 0.602	−0.137, 0.548
p-value	<0.001	0.047	<0.001	<0.001	0.004	0.002

University of Athens, Greece. [2]Infectious Diseases Department, Evangelismos General Hospital, Athens, Greece

Introduction: ART has led to improvements in life expectancy but chronic diseases, including cardiovascular disease (CVD), have emerged as a major factor of morbidity and mortality among the HIV infected. Traditional CVD risk prediction tools have questionable accuracy in this population. Only the D:A:D algorithm has been specifically developed for HIV patients. This study aims: a) to describe the prevalence of CVD risk factors in an HIV-infected population using various CVD risk prediction tools; b) to compare the results calculated by standard CVD risk assessment tools with those of the D:A:D risk equation.

Materials and methods: A cross-sectional study was conducted in Evangelismos General Hospital in Athens, Greece. Patients attending the outpatient HIV clinic during the period of 1 to 31 March 2016 were included. A total of 120 patients were included and their data were analyzed. Electronic medical records were used to collect data. Seven cardiovascular risk assessment tools were used (Framingham CVD, Framingham Hard CHD, SCORE, PROCAM Health Check, CUORE, QRISK2 and D:A:D Risk Score). Agreement among results was assessed using Cohen's weighted kappa coefficient.

Results: 81.5% (95% CI 73.6–87.5) of participants were male and 76.3% (95% CI 67.8–83.0) were born in Greece. The mean age was 41.9 (SD 10.47) and transmission mode was sexual in 62.2% (95% CI 53.2–70.4) and intravenous drug use in 30.3% (95% CI 22.7–39) of cases; 67.8% were current smokers. D:A:D risk equation classified 8.9% as of low (L), 83% as of medium (M) and 8% as of high risk (H) for CVD. Respectively, other equations' estimated results were: Framingham CVD (L:72% – M:20.6% – H:7.5%), Framingham Hard CHD (L:73.7% – M:18.4% – H:7.9%), CUORE (L:61.5% – M:37.4% – H:1.1%), SCORE (L:65.8% – M:30.8% – H:3.4%), PROCAM (L:90.4% – M:6.1% – H:3.5%) and QRISK2 (L:90.4% – M:4.4% – H:5.3%). Calculating weighted Cohen's kappa using three categories, "low-risk," "medium-risk" and "high-risk," coefficient values were very low (<0.2), indicating poor agreement between different tools. However, when categories "low-risk" and "medium-risk" were merged into one ("non-high risk"), Cohen's kappa resulted in significantly better agreement between the results of the various algorithms (in some cases $\kappa \sim 0.7$) (Table 1).

Conclusions: General population CVD risk assessment tools underestimate CVD risk of HIV patients, especially in the "medium-risk" strata. D:A:D risk equation might be the tool of choice for this population [1,2]. Smoking prevalence is high in the present cohort and efforts should focus on assisting patients to quit smoking.

References

1. Nery MW, Martelli CMT, Aparecida Silveira E, Sousa CA, de, Falco M, de O, Castro A, de C, et al. Cardiovascular risk assessment: a comparison of the Framingham, PROCAM, and DAD equations in HIV-infected persons. . Sci World J. 2013;2013:969281.
2. Pirš M, Jug B, Eržen B, Šabović M, Karner P, Poljak M, et al. Cardiovascular risk assessment in HIV-infected male patients: a comparison of Framingham, SCORE, PROCAM and DAD risk equations. Acta Dermatovenerol Alp Pannonica Adriat. 2014;23:43–7.

P185

Myocardial inflammatory changes before and after ART in HIV-infected patients with advanced disease

Alicia Piñeirua Menendez[1]; Rommel Flores Miranda[2]; Dulce Adoración Sánchez Nava[2]; Raúl Ortega Pérez[2]; Francisco Belaunzaran Zamudio[2]; Santiago Pérez Patrigeon[2]; Aylin Cardenas Ochoa[2]; Jorge Oseguera Moguel[3]; Jaime Galindo Uribe[3]; Consuelo Orihuela Sandoval[3]; Zuilma Yurith Vásquez Ortiz[3]; Jorge Vásquez Lamadrid[4]; Martha Morelos Guzmán[4]; Sandra Rosales Uvera[4]; Brenda Crabtree Ramírez[2] and Juan Sierra Madero[2]
[1]Infectious Diseases Department, Clínica Especializada Condesa/Iztapalapa, Mexico City, Mexico. [2]Infectious Diseases Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico. [3]Cardiology Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico. [4]Radiology Department, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

Introduction: The effect of immune restoration with ART on HIV-related cardiac inflammation is unknown. We investigated the presence of myocarditis before and after ART initiation in patients with HIV advanced disease.

Materials and methods: Myocardial inflammatory changes were studied with MRI, using Lake Louise Consensus Criteria [1] in ART-naïve, HIV-infected adults with CD4+ T cell counts <200 cells/μL, at ART initiation and 6 weeks later. Myocardial function was assessed with transthoracic echocardiogram. Troponin I, proBNP (heart-injury biomarkers) and serum antibodies and plasma PCR for cardiotropic pathogens were measured. Immune activation and lymphocyte differentiation were analyzed by flow cytometry.

Results: Seventeen patients were enroled, 15 (88%) were men. At baseline, median age was 34 years and CD4 count 46 cells/μL. No patients had cardiovascular-related symptoms at enrolment. We summarized in Table 1 the frequency of myocardial inflammation, myocardial dysfunction and pulmonary hypertension, and the presence of HHV-6, HHV-8 and parvovirus B19 at baseline and 6 weeks after ART in all subjects. Among those with baseline myocardial inflammation (n = 6), three (50%) had systolic dysfunction and one had diastolic dysfunction. None had cardiovascular-related symptoms. Among the five (29%) patients with myocardial inflammation at week 6, two (40%) had systolic dysfunction, two (40%) diastolic and one more had both. One patient progressed to symptomatic heart failure after ART initiation. He had the most severe baseline systolic dysfunction (LVEF 41%), which resolved with medical treatment after 1 year of follow-up (LVEF 61%). No myocardial inflammation at baseline and at 6 weeks was observed in eight (47%) subjects; four (23%) had baseline inflammation that spontaneously resolved after 6 weeks; inflammation persisted after 6 weeks of ART in 2/6 patients, and three more developed new inflammation after ART. Baseline and 6-week IgG for *T. gondii*, CMV

Abstract P185–Table 1. Frequency of abnormal findings in heart assessment, cardiotropic pathogens and CD4+ counts and HIV RNA measurements at baseline and 6 weeks after ART initiation in 17 patients starting treatment with advanced HIV disease (<200 CD4+ cells/mm^3)

Variable	Basal n (%)	6 weeks n (%)
Myocardial inflammation	6 (35)	5 (29)
Systolic dysfunction (LVEF <60%)	5	3
Diastolic dysfunction (slow relaxation pattern)	2	3
Systolic + diastolic dysfunction	1	0
Pulmonary hypertension (TTE)	1	1
Plasma PCR for HHV6	0	1
Plasma PCR for HHV8	1	2
Plasma PCR for parvovirus B19	2	0
CD4+ cells/mm^3	46 (18–81)	208 (90.5–205)
CD4+/CD8+ ratio	0.063 (0.048–0.092)	0.25 (0.131–0.326)
HIV RNA copies/mm^3	449,967 (227,367–740,959)	143 (87–502)

and EBV were frequent and not associated with myocardial inflammation. No evidence of past or present *T. cruzi* or Coxsackie virus was found. No association was found between myocardial inflammation and HPVB19, HHV-6 or -8, or with immune activation markers.

Conclusions: Subclinical myocarditis was common in this group of patients with HIV-associated advanced disease; and resolved spontaneously after ART initiation in most patients. Three patients developed myocarditis after ART initiation with no apparent associated infectious cause, suggesting a possible role of immune restoration disease. In one of them, myocardial inflammation caused heart failure requiring clinical management for 1 year. Awareness of this condition may improve management of those patients.

Reference

1. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, et al. Cardiovascular magnetic resonance in myocarditis: a JACC White Paper. J Am Coll Cardiol. 2009;53:1475–87. doi: http://dx.doi.org/10.1016/j.jacc.2009.02.007

P186

TDF/FTC/RPV + atorvastatin as comorbidity-driven cART

Franco Maggiolo[1]; Elisa Di Filippo[1]; Laura Comi[1]; Annapaola Callegaro[2]; Daniela Valenti[1] and Giampietro Gregis[1]
[1]Infectious Diseases, ASST Papa Giovanni XXIII, Bergamo, Italy.
[2]Laboratory of Microbiology and Virology, ASST Papa Giovanni XXIII, Bergamo, Italy

Introduction: Comorbidities are relevant in the management of HIV infection; however, few studies have considered the choice of ARV regimen based on non-HIV-dependent comorbidities.

Materials and methods: In this uncontrolled pilot study, we enroled patients with cardiovascular disease or diabetes. All were on an effective cART (HIV RNA <50 copies/mL for >6 months). Patients were switched to TDF/FTC/RPV STR and all received a 40 mg dose of atorvastatin. According to the American Heart Association indications [1], the reduction of LDL-cholesterol levels at 3 and 6 months were used as primary goal of the study.

Results: Twenty patients, half diabetics and half with a previous cardiovascular accident (e.g. stroke, MI, stent positioning), were enroled. Nineteen were males, with a mean age of 55 years (range 40–69). One-third were smokers. They had been on cART for a mean of 11 years (range 2–22) and on current cART for 4.8 years (range 0.6–13). At enrolment, all had HIV RNA <50 copies/mL with a mean CD4 count of 693 cells/mcL. Their copharmacy included aspirin and beta-blockers (40% each), antidiabetics, statins (35% each) ramipril, anti-lipid drugs (30% each) and a sartan (20%). Other medications were taken by 35% of subjects. All patients maintained viral suppression over time, a single virologic blip (60 copies/mL) was observed in one patient at 6 months. CD4 counts increased by 57 cells/mcL. Total cholesterol decreased from 206 (SD 33) to 144 mg/dL (SD 35), HDL from 46 (SD 19) to 39 mg/dL (SD 14) and LDL from 123 (SD 19) to 79 mg/dL (SD 24) (for all $p<0.001$); HDL/LDL ratio was normalized in all patients. D-dimer levels were studied to explore the anti-inflammatory, non-lipidic lowering effects of atorvastatin. They varied from 391 ng/mL (SD 263) at baseline to 311 ng/mL (SD 260) ($p=0.010$) at 3 months, to 319 ng/mL (SD 251) after 6 months ($p=0.012$). Therapy was well tolerated and CPK levels did not modify.

Conclusions: The management of comorbidities is paramount in HIV patients. Cardiovascular diseases are recognized as a major contributor to morbidity and mortality in HIV-infected subjects. TDF/FTC/RPV has a neutral lipid effect and no interactions with statins allowing for the use of these drugs at full dose. We demonstrated that the concomitant use of TDF/FTC/RPV and atorvastatin reduces the cardiovascular risk of HIV patients by significantly lowering both LDL and d-dimer blood levels while maintaining virologic suppression.

Reference

1. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic heart association task force on practice guidelines cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. [cited 2013 Nov 12]. Available from http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a.citation. doi: http://dx.doi.org/10.1161/01.cir.0000437738.63853.7a

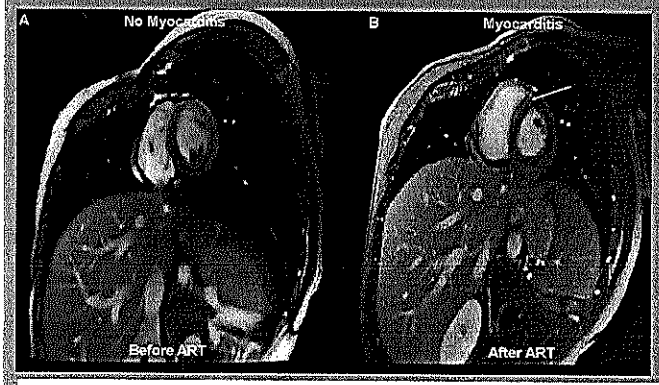
P187

Lipid profile in HIV patients with long-term ART: darunavir versus raltegravir versus rilpivirine

Bianca Branco Ascenção; Isabel Casella; Catarina Gonçalves; Nuno Luís; Ana Teresa Goes; Joana Sá; Ana Paula Brito and José Poças

Myocardial Inflammatory Changes Before and After Antiretroviral Therapy (ART) in HIV Infected Patients with Advanced Disease

PIÑEIRUA-MENENDEZ A. MD[1], FLORES-MIRANDA R. MD[2], SÁNCHEZ-NAVA D. MD[2], ORTEGA-PÉREZ R. MD[2], BELAUNZARAN-ZAMUDIO F. MD[2], PÉREZ-PATRIGEON S. MD[2], CÁRDENAS-OCHOA A. MSC[2], OSEGUERA-MOGUEL J. MD[2], GALINDO-URIBE J. MD[2], ORIHUELA-SANDOVAL C. MD[3], VÁZQUEZ-ORTIZ Z. MD[4], VÁZQUEZ-LAMADRID MD[4], MORELOS-GUZMÁN M. MD[1], ROSALES-UVERA S. MD[1], CRABTREE-RAMÍREZ B. MD[2], SIERRA-MADERO J. MD[2].



Conclusions

Subclinical myocarditis was common in patients with HIV-associated advanced disease (CD4+ T lymphocytes <200 cells/μL); and resolved spontaneously after ART initiation in most patients. Three patients developed myocarditis after ART initiation with no apparent associated infectious cause, suggesting a possible role of immune restoration disease. In one of them, myocardial inflammation caused heart failure requiring clinical management for one year. Awareness of this condition may improve management of patients with advanced HIV infection. More research is needed to determine the role of HIV infection in the development of subclinical myocarditis.

Figure 1. We show two images obtained by cardiac magnetic resonance belonging to the same patient. A) No images suggestive of myocarditis before the start of ART were observed. B) After the sixth week of antiretroviral therapy, late enhancement seen in the interventricular septum suggestive of myocardial inflammation were observed.

Introduction

The effect of immune restoration with ART on HIV-related cardiac inflammation is unknown. We looked for the presence of myocarditis before and after ART initiation in patients with HIV-advanced disease.

Methods

Myocardial inflammatory changes were studied with MRI, using Lake – Louis Consensus Criteria for myocarditis in ART-naïve HIV-infected adults with CD4+ T cells counts <200 cells/μL at ART initiation and 6 weeks later. Myocardial function was assessed with transthoracic echocardiogram (TTE) (*Figure 2*).

Troponin I, pro-BNP (heart injury biomarkers), serum antibodies for *Toxoplasma gondii*, *Trypanosoma cruzi*, *Epstein-Barr* virus, *Cytomegalovirus*, and plasma PCR for cardiotropic viruses (HHV-6, HHV8 and Human Parvovirus B19) were measured. Immune activation and lymphocyte differentiation were analysed by flow cytometry.

Results

17 patients were enrolled, 15(88%) were men. At baseline, a median age was 34 yo and CD4+ count 46 cells/μL. No patients had cardiovascular-related symptoms at enrollment (*Table 1*).

Among those with baseline myocardial inflammation (n=6), 3(50%) had systolic dysfunction and 1 had diastolic dysfunction. None had cardiovascular-related symptoms. Among the five patients with myocardial inflammation at week six, 2(40%) had systolic dysfunction, 2 (40%) diastolic dysfunction and one more had both. One patient progressed to symptomatic heart failure after ART initiation. He had the most severe baseline systolic dysfunction with a left ventricle ejection fraction (LVEF) of 41%, which resolved with medical treatment after 1 year of follow-up (LVEF 61%).

Table 1. Cardiac Imaging Evaluation

	Before ART					After ART				
#	Myocarditis	LVEF	PASP	DD	PE	Myocarditis	LVEF	PASP	DD	PE
1	-	64	5	-	-	+	60	22	-	-
2	+	55	35	-	-	-	65	29	-	-
3	-	58	30	-	-	+	64	35	-	-
4	-	69	34	-	-	-	72	5	-	-
5	-	68	30	-	-	+	71	20	-	-
6	-	72	3	-	-	-	65	31	-	-
7	+	41	20	-	-	+	50	33	SRP	-
8	-	68	26	SRP	-	-	73	30	-	-
9	-	56	28	SRP	-	-	78	39	SRP	-
10	+	72	24	-	-	-	74	29	-	-
11	-	65	20	-	-	-	73	33	SRP	-
12	+	70	8	-	-	+	70	7	-	-
13	-	71	30	-	-	-	65	43	-	-
14	-	62	31	-	+	-	65	34	-	-
15	+	56	33	-	-	-	70	23	-	-
16	-	67	30	-	+	-	54	20	-	-
17	+	65	48	-	+	-	56	33	-	-
6	6	65	30	2	3	5	65	30	3	0

DD: Diastolic dysfunction. PASP: Pulmonary artery systolic pressure (mmHg). PE: Pericardial effusion. SRP: Slow relaxation pattern (TDE 240 ms, E/A <1, E'/A' <1).[2]

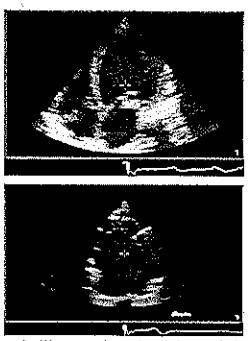


Figure 2. We use advanced techniques of doppler echocardiography to determine the diastolic function.

No myocardial inflammation at baseline and at 6 weeks was observed in 8 (47%) subjects. 4(23%) had baseline inflammation that spontaneously resolved after 6 weeks; inflammation persisted after 6 weeks of ART in 2 of 6 patients, and 3 more developed new inflammation after ART. Baseline and 6 week IgG for *T. gondii*, CMV and EBV were frequent and not associated to myocardial inflammation.

No evidence of past or present *T. cruzi* or Coxsackie virus was found. No association was found between myocardial inflammation and HPVB19, HHV-6 or 8. Through the gating strategy shown in *Figure 3* we determine cell differentiation and activation of T lymphocytes CD4 + and CD8 + which was unrelated to the presence of myocarditis at any moment.

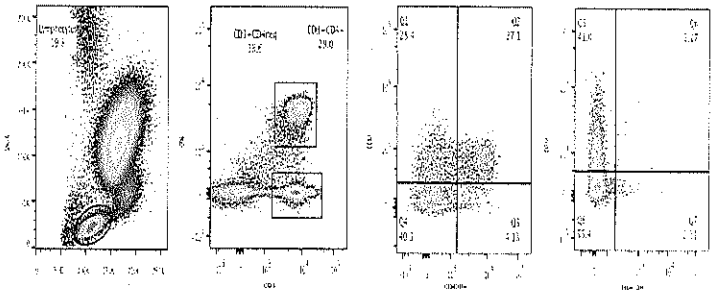


Figure 3. Gating strategy for flow cytometry analysis.

We summarized in *Table 2* the frequency of myocardial inflammation, myocardial dysfunction, pulmonary hypertension and the presence of HHV6, HH-8, and Parvovirus B19 at baseline and six weeks after ART initiation in all subjects.

Table 2. Summary of results

Variable	Baseline n(%)	6 weeks n(%)
Myocardial inflammation	6 (35)	5 (29)
Systolic dysfunction (LEVF <60%)	5	3
Diastolic dysfunction	2	3
Systolic – diastolic dysfunction	1	0
Pulmonary hypertension (TTE)	1	1
HHV6 PCR in Plasma	0	1
HHV8 PCR in Plasma	1	2
Parvovirus B19 PCR in Plasma	2	0
CD4+ cells/μL.	46 (18 – 81)	208 (90.5 – 205)
CD4+/CD8+ ratio	0.063 (0.048 - 0.092)	0.25 (0.131 – 0.326)
HIV – RNA copies/mm³	449967 (227367 – 740959)	143 (87 – 502)

1) Friedrich MG, Sechetem U, Schulz-Menger J. et al. Cardiovascular magnetic resonance in myocarditis: A JACC White Paper. J Am Coll Cardiol. 2009;53:1475 – 1487.
2) Vasan RS, Levy, D. "Defining diastolic heart failure: a call for standardized diagnostic criteria. Circulation. 2000; 101:2118 - 2121.

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