

Influenza dell'attività fisica sul valore ematico dei lipidi in una piccola coorte di pazienti che vivono con infezione da HIV, soppressi e dislipidemicici, dopo lo switch da un regime contenente tenofovir alafenamide a dolutegravir/rilpivirina.

Influence of physical activity level on serum lipid values in a small cohort of suppressed dyslipidemic people living with HIV after switching from a tenofovir alafenamide regimen to dolutegravir/rilpivirine.

Andrea Delama¹, Massimiliano Lanzafame¹, Emanuela Lattuada¹, Giovanni Mori¹, Sandro Vento²

¹ Unit of Infectious Diseases, Ospedale Santa Chiara, Azienda Provinciale per i Servizi Sanitari (APSS), Trento, Italy

² Faculty of Medicine, University of Puthisastra, Phnom Penh, Cambodia

Corresponding Author:

Massimiliano Lanzafame
Via Strada Romana 11,
San Bonifacio (VR), 37047, Italy

lanzafame.massimiliano@gmail.com

Keywords:
HIV, Physical Activity,
Dyslipidemia, Dolutegravir/
Rilpivirine, Diet

Conflict of interest:
none

JHA 2024; 9(2): 25-28

DOI: 10.19198/JHA31573

Riassunto

In una piccola coorte di 41 persone dislipidemiche affette da HIV, regolarmente seguite presso la nostra Unità, abbiamo valutato retrospettivamente le variazioni dell'indice di massa corporea (BMI), dei livelli sierici dei lipidi e dell'uso di agenti ipolipemizzanti un anno dopo il passaggio da un trattamento contenente tenofovir alafenamide a una combinazione "metabolicamente favorevole" di dolutegravir e rilpivirina. Abbiamo anche valutato l'impatto dell'attività fisica su questi parametri. Dopo un anno dal passaggio, il numero di pazienti trattati con agenti ipolipemizzanti è aumentato e il BMI non è cambiato. Solo un paziente ha avuto un ritorno a valori normali di lipidi sierici a causa della sua elevata attività fisica, sottolineando come l'attività fisica debba essere la priorità di persone anziane che vivono con l'infezione da HIV.

Abstract

In a small cohort of 41 dyslipidemic people living with HIV, regularly followed at our Unit, we have evaluated retrospectively changes in Body Mass Index (BMI), serum lipid levels and lipid-lowering agents use one year after a switch from a tenofovir alafenamide containing regimen to a "metabolic friendly" combination of dolutegravir and rilpivirine. We have also assessed the impact of physical activity on these parameters.

After one year post the switch, the number of patients on lipid-lowering agents increased and BMI did not change. Only one patient had a return to normal values of serum lipids due to his high physical activity, remarking how physical activity must be the priority of aging people living with HIV infection.

Introduction

Life expectancy of people living with HIV (PLWH) has improved because of antiretroviral therapy (1). However, PLWH developed more comorbidities (e.g., dyslipidemia, diabetes, cardiovascular diseases) and at a younger age than people without HIV (2). To prevent or at least reduce their incidence, pharmacological (e.g., switch of antiretroviral regimen such as stopping tenofovir disoproxil fumarate in presence of a mild kidney hypofunction) and nonpharmacological interventions (diet and physical exercise) are adopted. Diet and physical activity, in particular, have been associated to a reduction of visceral adipose tissue in PLWH (3,4), even though less adopted than in the general population (5,6).

In the SWORD 1 and 2 trials, a switch to dolutegravir/rilpivirine regimen, compared to a control arm, has not been associated to a statistically significant improvement in the lipid profile (7); this has been confirmed in real-life studies (8,9).

In a small cohort of PLWH, regularly followed at our Unit, we have evaluated retrospectively changes in Body Mass Index (BMI), serum lipid levels and lipid-lowering agents use one year after a switch from a tenofovir alafenamide containing regimen to a “metabolic friendly” combination of dolutegravir and rilpivirine. We have also assessed the impact of physical activity on these parameters.

Material and methods

At our Outpatient Clinic in “Santa Chiara” Hospital, Trento, Northern Italy, 603 PLWH are regularly followed. At the time of our retrospective analysis, performed in December 2023, 88 of them were on a dual dolutegravir/rilpivirine single tablet regimen. Forty-one of these 88 patients had been switched to dolutegravir/rilpivirine because of dyslipidemia. We asked all people whether they had changed their lifestyle, practiced physical activity or consulted a nutritionist/dietologist during the first year after the switch. Physical activity level was retrospectively assessed through a telephone interview and measured using the International Physical Activity Questionnaire (IPAQ) (10).

Results

All 41 (29 males, 12 females; mean age 54.2 years, range 37-79) individuals were, before the switch, on a tenofovir alafenamide antiretroviral regimen;

36 were on tenofovir alafenamide/ emtricitabine/ rilpivirine, 4 on tenofovir alafenamide /emtricitabine/darunavir/cobicistat, and one on tenofovir alafenamide/emtricitabine plus dolutegravir. The people had lived with HIV for a mean of 19.02 years (range 4-33). The mean length of antiretroviral therapy was 16.5 years (range 4-32 years) and they were all HIV-RNA negative (<20 copies/ml).

Table 1 reports the following data at the time of the switch and 12 months later: BMI at the time of switch and after one year, serum total cholesterol, HDL and LDL cholesterol levels, use of lipid-lowering agents, and physical activity level. At the time of the switch, the mean BMI was 23.97 (range 21-35); 20 people had a normal weight, 18 were overweight and 3 were obese. Nine individuals were on lipid-lowering agents, even though 27 other people had serum total cholesterol levels above the desired threshold (<190 mg/dL). Physical activity was absent in 20 individuals and minimal in another 20; only one person was highly active. Only one patient consulted a nutritionist/dietologist and started an intermittent diet to lose weight. The statistical difference in serum lipids was calculated by Student t-test (with $p < 0.005$ as significant).

The mean total cholesterol at the time of the switch was 218.98 mg/dL and 12 months later was 201.12 mg/dL ($p = 0.0004$). The mean LDL cholesterol level decreased from 134.88 mg/dL to 121.63 ($p = 0.002$), while the mean HDL cholesterol level did not change (55.07 mg/dL at the time of the switch versus 55.76 mg/dL 12 months later ($p = 0.67$)).

The mean BMI was 24.51 (range 19-35) 12 months after the switch. The number of people with a normal weight decreased from 20 to 19, whereas the number of overweight individuals increased from 18 to 19 and the number of obese people did not change.

The number of people on lipid-lowering agents increased from 9 to 12 (the three newly treated individuals being all inactive).

The only person (number 34 in table 1) whose serum lipids returned to a normal value without the introduction of a lipid-lowering agent, was highly active; his BMI decreased by one point, and he remained in the normal weight category. The BMI of the only person who started a diet, but not increased physical activity, decreased from 22 to 19 (number 21).

PATIENT	Body Mass Index at antiretroviral therapy switch	TOTAL CHOLESTEROL (desiderable value<190 mg/dl) at antiretroviral therapy switch	LDL-CHOLESTEROL (desiderable value<115 mg/dl) at antiretroviral therapy switch	HDL-CHOLESTEROL (desiderable value>40 mg/dl) at antiretroviral therapy switch	Body Mass Index after 12 months post switch	TOTAL CHOLESTEROL (desiderable value<190 mg/dl) after 12 months post switch	LDL-CHOLESTEROL (desiderable value<115 mg/dl) after 12 months post switch	HDL-CHOLESTEROL (desiderable value>40 mg/dl) after 12 months post switch	Use of lipid lowering drugs at antiretroviral therapy switch	Use of lipid lowering drugs after 12 months post switch	Physical activity level (measured using the International Physical Activity Questionnaire)
1	24	226	157	33	24	215	148	35	NO	NO	INACTIVE
2	30	190	122	39	30	200	142	45	NO	NO	INACTIVE
3	27	234	147	64	27	252	152	51	NO	NO	INACTIVE
4	25	217	148	50	25	199	132	48	NO	NO	MINIMALLY ACTIVE
5	23	189	106	49	23	163	93	50	SI	SI	INACTIVE
6	23	184	112	60	23	174	106	61	SI	SI	INACTIVE
7	26	223	134	35	26	194	143	34	SI	SI	INACTIVE
8	27	219	147	37	27	199	139	42	NO	NO	MINIMALLY ACTIVE
9	25	238	147	76	25	267	173	77	NO	NO	INACTIVE
10	25	217	133	48	25	191	122	43	NO	NO	INACTIVE
11	23	197	114	69	23	173	85	74	SI	SI	MINIMALLY ACTIVE
12	21	212	152	49	23	169	90	55	NO	SI	MINIMALLY ACTIVE
13	22	236	148	36	22	168	106	38	SI	SI	INACTIVE
14	27	245	147	59	26	210	122	53	NO	NO	INACTIVE
15	22	195	138	50	23	213	137	54	NO	NO	INACTIVE
16	27	205	125	59	27	250	173	62	NO	NO	INACTIVE
17	26	198	132	48	26	207	139	46	NO	NO	MINIMALLY ACTIVE
18	23	242	99	73	23	204	71	63	SI	SI	INACTIVE
19	35	291	147	55	35	253	148	52	NO	NO	INACTIVE
20	29	223	146	52	29	231	157	52	NO	NO	MINIMALLY ACTIVE
21	22	221	139	46	19	235	139	94	NO	NO	INACTIVE
22	22	220	144	41	22	166	105	33	NO	NO	MINIMALLY ACTIVE
23	21	233	149	60	21	153	75	61	SI	SI	MINIMALLY ACTIVE
24	27	213	125	51	27	221	127	70	NO	NO	INACTIVE
25	27	250	172	56	27	174	110	49	NO	NO	MINIMALLY ACTIVE
26	23	186	117	37	23	159	94	30	NO	NO	MINIMALLY ACTIVE
27	25	217	146	54	25	191	117	51	SI	SI	MINIMALLY ACTIVE
28	22	241	141	83	22	233	134	72	NO	NO	INACTIVE
29	24	216	126	66	25	231	167	55	NO	NO	INACTIVE
30	23	215	129	68	23	219	127	69	NO	NO	MINIMALLY ACTIVE
31	30	226	128	61	30	221	125	63	NO	NO	INACTIVE
32	29	213	134	53	29	172	100	49	NO	SI	INACTIVE
33	28	206	122	54	28	195	123	56	NO	NO	MINIMALLY ACTIVE
34	22	244	167	63	22	190	106	63	NO	NO	HEPA ACTIVE
35	28	217	147	52	29	176	110	40	NO	NO	MINIMALLY ACTIVE
36	28	197	117	55	28	189	101	54	NO	NO	MINIMALLY ACTIVE
37	26	164	98	46	26	165	100	47	SI	SI	MINIMALLY ACTIVE
38	22	245	107	67	22	166	62	76	NO	SI	MINIMALLY ACTIVE
39	21	218	139	54	21	211	146	66	NO	NO	MINIMALLY ACTIVE
40	21	263	158	89	21	250	124	99	NO	NO	MINIMALLY ACTIVE
41	24	192	124	61	24	197	117	54	NO	NO	MINIMALLY ACTIVE

Table 1. Body Mass Index, Serum lipid levels [total cholesterol, HDL (High density lipoprotein)-cholesterol and LDL(Low density lipoprotein)-cholesterol], use of lipid-lowering drugs at baseline and 12 months after the switch and physical activity level in the same period.

Discussion

We observed in our cohort an underutilization of lipid-lowering drugs in PLWH, confirming data reported in the literature (11-13). More efforts must be made to increase the number of PLWH treated with lipid-lowering drugs, considering the recent results of the REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV) study that showed a reduction in atherosclerotic cardiovascular disease for people living with HIV at low to moderate predicted risk, taking pitavastatin (14).

Current guidelines recommend a switch to two drug regimens (such as dolutegravir/rilpivirine combination) to decrease toxicity and side-effects in PLWH. In the SWORD trial, a dolutegravir/rilpivirine combination showed a neutral effect on serum lipid levels (7). However, real life studies indicated that a switch from a tenofovir alafenamide-containing antiretroviral regimen to dolutegravir/rilpivirine combination was associated with a reduction of serum total cholesterol and LDL cholesterol levels (even though without a return to normal values or a reduction in the use of lipid-lowering agents) (15). In our cohort, a switch to a dolutegravir/rilpivirine combination was not associated with a decreased use of lipid-lowering drugs; on the contrary, the number of individuals on lipid-lowering drugs increased. The only person who had a return to normal serum lipid values had modified considerably his lifestyle.

Notwithstanding its limitations (retrospectivity, and small number of individuals), our study confirms that PLWH have low physical activity (16,17) and shows that without an important increase in it, serum lipid values are not modified by a switch in antiretroviral therapy. ■

Notwithstanding its limitations (retrospectivity, and small number of individuals), our study confirms that PLWH have low physical activity (16,17) and shows that without an important increase in it, serum lipid values are not modified by a switch in antiretroviral therapy. ■

REFERENCES

1. Collaboration ATC. *Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies.* *Lancet HIV.* 2017; 4: e349–56.
2. Guaraldi G, Orlando G, Zona S, et al. *Premature age-related comorbidities among HIV-infected persons compared with the general population.* *Clin Infect Dis.* 2011; 53: 1120–6.
3. Reeds DN, Pietka TA, Yarasheski KE, et al. *HIV infection does not prevent the metabolic benefits of diet-induced weight loss in women with obesity.* *Obesity (Silver Spring)* 2017; 25: 682–8.
4. Roubenoff R, Weiss L, McDermott A, et al. *A pilot study of exercise training to reduce trunk fat in adults with HIV-associated fat redistribution.* *AIDS* 1999; 13: 1373–5.
5. Schafer J, Young J, Calmy A, et al. *High prevalence of physical inactivity among patients from the Swiss HIV Cohort Study.* *AIDS care.* 2017; 29: 1056–61.
6. Schuelter-Trevisol F, Wolff FH, Alencastro PR, et al. *Physical activity: do patients infected with HIV practice? How much? A systematic review.* *Current HIV research.* 2012; 10: 487–97.
7. Ribera E. *New Dual Combination of Dolutegravir-Rilpivirine for Switching to Maintenance Antiretroviral Therapy.* *AIDS Rev.* 2018; 20: 179–86.
8. Palacios R, Gómez-Ayerbe C, Casado JL, et al. *Efficacy and safety of dolutegravir/rilpivirine in real-world clinical practice.* *GeSIDA study* 1119. *HIV Med.* 2023; 24: 933–7.
9. Palacios R, Mayorga M, González-Domenech CM, et al. *Safety and Efficacy of Dolutegravir Plus Rilpivirine in Treatment-Experienced HIV-Infected Patients: The DORIVIR Study.* *J Int Assoc Provid AIDS Care.* 2018; 17: 2325958218760847.
10. *Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ)- Short Form.* 2004.
11. Clement ME, Park LP, Navar AM, et al. *Statin utilization and recommendations among HIV- and HCV-infected veterans: a cohort study.* *Clin Infect Dis* 2016; 63: 407e13.
12. Gallegos Aragon K, Ray G, et al. *Underprescribing of statin therapy in people with HIV at risk for atherosclerotic cardiovascular disease.* *Am J Health Syst Pharm* 2022; 79: 2026e31.
13. Coburn SB, Lang R, Zhang J, et al. *Statins utilization in adults with HIV: the treatment gap and predictors of statin initiation.* *J Acquir Immune Defic Syndr* 2022; 9: 469e78.
14. Lu MT, Ribaudo H, Foldyna B, et al; REPRIEVE Trial Writing Group. *Effects of Pitavastatin on Coronary Artery Disease and Inflammatory Biomarkers in HIV: Mechanistic Substudy of the REPRIEVE Randomized Clinical Trial.* *JAMA Cardiol.* 2024; 9: 323–34.
15. Bendala-Estrada AD, Diaz-Almiron M, Busca C, et al. *Change in metabolic parameters after switching from triple regimens with tenofovir alafenamide to dolutegravir-based dual therapy. Bi-lipid study.* *HIV Med.* 2023; 24: 558–67.
16. Bernard C, Dabis F, de Rekeneire N. *Physical function, grip strength and frailty in people living with HIV in sub-Saharan Africa: systematic review.* *Trop Med Int Health.* 2017; 22: 516–25.
17. Shephard RJ. *Physical impairment in HIV infections and AIDS: responses to resistance and aerobic training.* *The Journal of sports medicine and physical fitness.* 2015; 55: 1013–28.