19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE CENTRO CONGRESSI EUROPA
RESEARCH and CARE: FROM BENCH, TO BEDSIDE, TO COMMUNITY
Promosso da SIMIT
16° CONGRESSO NAZIONALE ICAR Italian Conference on AIDS and Antiviral Research
P 178
POSTER 4 YOU ICAR 2024

Evaluating tolerance and safety profiles of Pre-Exposure Prophylaxis (PrEP) for HIV: insights from renal and hepatic function monitoring

G. Cuomo, M. Menozzi, M. Albertini, V. Todisco, L. Gozzi, E. Martini, D. Lusetti, G. Guaraldi, C. Mussini.
Azienda Ospedaliero-Universitaria di Modena – Università degli Studi di Modena e Reggio Emilia

Introduction

- The availability of HIV Pre-Exposure Prophylaxis (PrEP) is expanding globally, providing an important tool in the prevention of HIV transmission. PrEP typically involves the use of antiretroviral medications, with the combination of tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) being one of the most common regimens. However, TDF/FTC exposure has been associated with an increased incidence of adverse effects, particularly impacting renal and hepatic functions. Understanding the safety and tolerability of PrEP is crucial to its broader implementation and adherence.
- Our study aims to assess the safety and tolerability of PrEP among recipients in Modena, with a specific focus on monitoring hepatic and renal function.

Methods

- This is a retrospective study from April 2018 to February 2024; all subjects >18 years old referred to our PrEP service who had a follow-up period of at least 30 days (two visits) and had taken at least one 2:1:1 (On-Demand) course of TDF/FTC or taken it for 7 consecutive days were enrolled.
- Nephrotoxicity was defined as 50% rise or more than baseline creatinine by 2 mg/dL, ALT elevation value > 40 U/L. Users underwent quarterly monitoring of serum creatinine and ALT alongside routine PrEP screening. Adherence was defined as having taken TDF/FTC at least 80% of doses in the daily regimen and 100% in the 2:1:1 regimen.
- Univariate analyses were performed, using chi-square and t-student to compare variables, and a Kaplan-Meier curve was performed to identify the renal failure events.

Results (1)

- We observed 182 subjects. We excluded 26 individuals didn't met inclusion criteria (156 subjects studied). 98.7% were male, 89.7% were of Italian origin, mostly men who have sex with men (MSM). The main reason for starting PrEP was risky sexual encounters, followed by previous STIs. 62.8% of users chose the 2:1:1 regimen. The adherence criterion was met in 94.9% of people. Discontinuation rate was 25%, mainly due to loss to follow-up, with only one interruption due to side effects. Toxicity was found in 23.1% of subjects, with gastrointestinal disorders (nausea or diarrhoea) occurring in 13.5% of cases, ALT elevation in 5.8%, headache in 2.6%, and one case (0.6%) of renal toxicity, the only leading to PrEP discontinuation (Table 1).

Results (2)

- Analysis of serum creatinine at baseline and follow-up showed a statistically significant mean increase between the two measurements (p<0.01, Table 2), which did not occur for ALT.
- Kaplan-Meier analysis revealed an increasing trend over time in cases with creatinine >1.4 mg/dL (Figure 1).
- Univariate analysis between people who experienced side effects and who did not showed a significantly longer follow-up period (p=0.002) and a greater % increase in creatinine (p=0.041) in the first group. No differences were observed regarding regimen type, adherence or comorbidities (Table 3).

Total=156		Count	Column N %	Minimum	Maximum	Median
Gender	M	154	98.7%			
	MTF	2	1.3%			
Country of Origin	Italy	139	89.1%			
	Other	17	10.9%			
Age				18	62	38
MSM	N	8	5.1%			
	Y	124	79.5%			
	Unknown	24	15.4%			
Reasons for PrEP	Risky sexual Intercourses	125	80.1%			
	Partner HIV+	1	0.6%			
	Previous STI	17	10.9%			
	Previous PEP	5	3.2%			
	Chemsex	3	1.9%			
	Multiple	5	3.2%			
Regimen	2.1.1	98	62.8%			
	Daily	58	37.2%			
Adherence	N	8	5.1%			
	Y	148	94.9%			
PrEP interruption	N	117	75.0%			
	Y	39	25.0%			
Condom Use	Never	59	37.8%			
	Always	26	16.7%			
	Discontinuous	71	45.5%			
Cause of Interruption	No	117	75.0%			
	Stable Partner	4	2.6%			
	Lost FU	28	17.9%			
	Side Effect	1	0.6%			
	Other	1	0.6%			
	COVID-19	5	3.2%			
Side Effects	N	120	76.9%			
	Y	36	23.1%			
Side Effects	N	120	76.9%			
	GI	21	13.5%			
	Kidney	1	0.6%			
	ALT elevation	9	5.8%			
	Headache	4	2.6%			
	Other	1	0.6%			
Comorbidities	N	108	69.2%			
	Y	48	30.8%			
Comorbidities	N	108	69.2%			
	CNS	11	7.1%			
	CV	20	12.8%			
	Thyroids	4	2.6%			
	Liver	2	1.3%			
	GI	2	1.3%			
	Other	6	3.8%			
	Prostate	3	1.9%			
Days of Follow-Up				35	2452	453

Table 1: General Characteristics of the study population

2A

	Mean	Median	95.0% Lower CL for Median	95.0% Upper CL for Median
Basal Creatinine	.93	.91	.88	.94
FU Creatinine	.97	.95	.93	.99
delta_crea	.18	.03	.02	.06
Basal ALT	26.00	23.00	22.00	25.00
FU ALT	32.26	25.00	22.00	28.00
delta_ALT	6.31	1.00	.00	4.00

2B

	Paired Differences (T-Test)					t	Significance
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper		Two-Sided p
FU Creatinine – Basal Creatinine	.04270	.11655	.01038	.02215	.06325	4.112	<.001
FU ALT – Basal ALT	6.31200	41.23779	3.68842	-.98842	13.61242	1.711	.090

Table 2: Median creatine and ALT at baseline and follow-up (2A), and comparison by T-test of values in the two periods (2B).

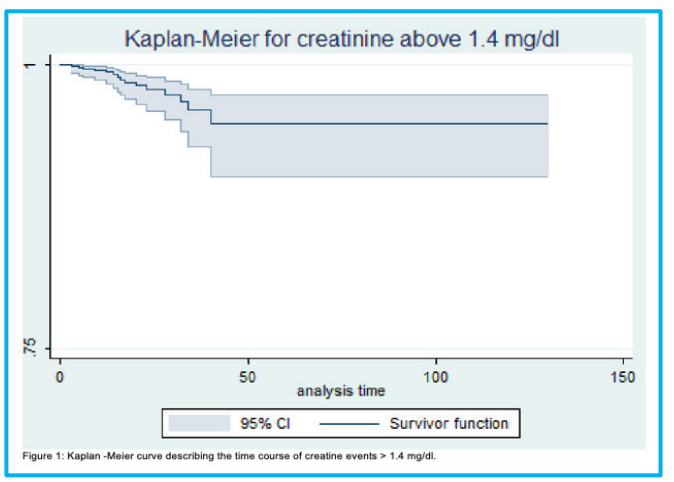

Figure 1: Kaplan -Meier curve describing the time course of creatine events > 1.4 mg/dl.

		NO SIDE EFFECTS (n= 120) Count	Column N %	Mean	Median	95.0% Lower CL for Median	95.0% Upper CL for Median	YES SIDE EFFECTS (n=36) Count	Column N %	Mean	Median	95.0% Lower CL for Median	95.0% Upper CL for Median	Sign. p
Gender	M	119	99.2%					35	97.2%					.363
	MTF	1	0.8%					1	2.8%					
Country of Origin	Italy	108	90.0%					31	86.1%					.511
	Other	12	10.0%					5	13.9%					
Age					38	36	42				40	34	43	.301
MSM	N	7	5.8%					1	2.8%					.281
	Y	92	76.7%					32	88.9%					
	Unknown	21	17.5%					3	8.3%					
Reasons for PrEP	Risky sexual Intercourses	100	83.3%					25	69.4%					.266
	Partner HIV+	0	0.0%					1	2.8%					
	Previous STI	11	9.2%					6	16.7%					
	Previous PEP	3	2.5%					2	5.6%					
	Chemsex	2	1.7%					1	2.8%					
	Multiple	4	3.3%					1	2.8%					
Regimen	2.1.1	73	60.8%					25	69.4%					.348
	Daily	47	39.2%					11	30.6%					
Adherence	N	7	5.8%					1	2.8%					.466
	Y	113	94.2%					35	97.2%					
PrEP interruption	N	87	72.5%					30	83.3%					.188
	Y	33	27.5%					6	16.7%					
Cause of Interruption	No	87	72.5%					30	83.3%					.236
	Stable Partner	3	2.5%					1	2.8%					
	Lost FU	24	20.0%					4	11.1%					
	Side Effect	0	0.0%					1	2.8%					
	Other	1	0.8%					0	0.0%					
	COVID-19	5	4.2%					0	0.0%					
Comorbidities	N	84	70.0%					24	66.7%					.144
	Y	36	30.0%					12	33.3%					
Days of follow-up				560	424	329	523			869	749	444	951	.002
Basal Creatinine				.92	.91	.88	.94			.96	.91	.85	.96	.09
Basal ALT				23.35	22.00	20.00	25.00			28.10	28.00	23.00	35.00	.158
Delta_Creatinine				.21	.03	.01	.06			.08	.06	.02	.12	.339
Delta_ALT				6.64	.00	-1.00	3.00			5.27	2.50	-1.00	7.00	.437
%Variation Creatinine				3.78	2.90	.92	6.06			8.44	6.80	2.17	13.33	.041
%Variation ALT				23.43	.00	-4.76	17.65			21.25	13.14	-4.17	40.91	.442

Table 3: Univariate analysis of different characteristics between patients who developed side effects and those who did not.

		NO COMORBIDITIES (N= 108) Count	Column N %	Mean	Median	95.0% Lower CL for Median	95.0% Upper CL for Median	YES COMORBIDITIES (N=48) Count	Column N %	Mean	Median	95.0% Lower CL for Median	95.0% Upper CL for Median	Sign. p
Gender	M	106	98.1%					48	100.0%					.343
	MTF	2	1.9%					0	0.0%					
Country of Origin	Italy	94	87.0%					45	93.8%					.214
	Other	14	13.0%					3	6.3%					
Age					35	32	38				45	41	51	<.001
MSM	N	4	3.7%					4	8.3%					.282
	Y	85	78.7%					39	81.3%					
	Unknown	19	17.6%					5	10.4%					
Reasons for PrEP	Risky sexual Intercourses	86	79.6%					39	81.3%					.937
	Partner HIV+	1	0.9%					0	0.0%					
	Previous STI	13	12.0%					4	8.3%					
	Previous PEP	3	2.8%					2	4.2%					
	Chemsex	2	1.9%					1	2.1%					
	Multiple	3	2.8%					2	4.2%					
Regimen	2.1.1	72	66.7%					26	54.2%					.136
	Daily	36	33.3%					22	45.8%					
Adherence	N	7	6.5%					1	2.1%					.250
	Y	101	93.5%					47	97.9%					
Side Effects	N	84	77.8%					36	75.0%					.704
	Y	24	22.2%					12	25.0%					
Side Effects	N	84	77.8%					36	75.0%					.333
	GI	16	14.8%					5	10.4%					
	Kidney	0	0.0%					1	2.1%					
	ALT elevation	6	5.6%					3	6.3%					
	Headache	2	1.9%					2	4.2%					
	Other	0	0.0%					1	2.1%					
PrEP interruption	N	75	69.4%					42	87.5%					.016
	Y	33	30.6%					6	12.5%					
Cause of Interruption	No	75	69.4%					42	87.5%					0.82
	Stable Partner	3	2.8%					1	2.1%					
	Lost FU	25	23.1%					3	6.3%					
	Side Effect	0	0.0%					1	2.1%					
	Other	1	0.9%					0	0.0%					
	COVID-19	4	3.7%					1	2.1%					
Days of follow-up				598	429	289	523			707	654	385	837	.132
Basal Creatinine				.91	.89	.87	.94			.95	.92	.88	.97	.094
Basal ALT				25.45	24.00	22.00	27.00			27.07	22.00	20.00	28.00	.256
Delta_Creatinine				.04	.03	.00	.06			.06	.05	.01	.09	.267
Delta_ALT				1.84	.50	-2.00	3.00			14.84	2.00	.00	14.00	.047
%Variation Creatinine				4.28	3.53	.00	6.32			6.07	5.38	1.28	9.28	.229
%Variation ALT				16.57	2.17	-5.26	16.00			34.98	10.00	-2.70	25.00	.065

Table 4: Univariate analysis of different characteristics between patients who had co-morbidities and those who did not.

Results (3)

- Univariate analysis comparing subjects with and without comorbidities revealed that users with comorbidities were significantly older (p < 0.001) and had fewer therapeutic interruptions for any reason (p = 0.016), suggesting higher consistency in their PrEP regimen adherence. Additionally, they exhibited a greater change in ALT levels (ALT delta) between follow-up measurements, indicating an increase in ALT during therapy (p = 0.047) (Table 4).

Conclusion

- PrEP is generally well-tolerated among our users, resulting in minimal side effects and only one discontinuation (0.6%) attributed to adverse effects. However, during therapy, we observed a statistically significant increase in serum creatinine levels and notable changes in ALT among patients with comorbidities. These findings underscore the importance of ongoing clinical and laboratory monitoring for all PrEP users to promptly identify and manage potential health issues.

References

1. Huang X, et al. Efficacy and Safety of Oral TDF-Based Pre-exposure Prophylaxis for Men Who Have Sex With Men: A Systematic Review and Meta-Analysis. Front Pharmacol. 2018 Sep 4;9:799.
2. Petruccelli KCS, et al. Kidney function and daily emtricitabine/tenofovir disoproxil fumarate pre-exposure prophylaxis against HIV: results from the real-life multicentric demonstrative project PrEP Brazil. AIDS Res Ther. 2022 Feb 24;19(1):12.