



A descriptive analysis of serum creatinine variation in users assuming TDF-PrEP: a possible role of age and comedication

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Introduction

Pre-exposure prophylaxis (PrEP), based on the association of tenofovir disoproxil (TDF)/emtricitabine (FTC), is an efficacious strategy to prevent HIV infection in seronegative people. TDF may be associated with increase of serum creatinine as a proxy of kidney toxicity.

This study aims to describe the population of PrEP users from our centre, focusing on serum creatinine levels trends and the differences between the population aged over and under 50 years old (yo).

Study Design and Methods

We conducted a retrospective observational study reviewing data from the University Hospital of Modena, collected from January 2019 to March 2023.

- Every 3 months clinical assessment and serum creatinine levels were collected.
- Nephrotoxicity was defined as at least 20% increase in serum creatinine between basal and last follow-up value.
- We divided the population by age group at PrEP initiation (<50 yo, > 50 yo); a secondary analysis was performed including users aged >50 yo only, focusing on nephrotoxicity prevalence in that population.

A descriptive analysis was performed using mean (standard deviations) and number (frequency) for continuous and categorical variables respectively. Comparisons were done with Mann-Whitney U test, ANOVA and Chi-square test according to variable distribution and type.

Results

We collected data of 111 PrEP subjects. Table 1 describes cohort characteristics, PrEP regimens, reasons for PrEP begin and interruption and side effects.

Tab. 1 PrEP users characteristics

	<50 years n (%)	>50 years n (%)	tot n (%)	p-value
Sex				0.30
M	87 (98.9)	22 (95.7)	109 (98.2)	
MTF	1 (1.1)	1 (4.4)	2 (1.8)	
Nationality				0.58
Italy	74 (84.1)	22 (95.7)	96 (86.5)	
South America	4 (4.6)	1 (4.4)	5 (4.5)	
Africa	5 (5.7)	0 (0)	5 (4.5)	
Asia	3 (3.4)	0 (0)	3 (2.7)	
East Europe	2 (2.3)	0 (0)	2 (1.8)	
MSM				0.71
No	4 (4.6)	1 (4.4)	5 (4.5)	
Yes	72 (81.8)	18 (78.3)	90 (81.1)	
Not known	12 (13.6)	4 (17.3)	16 (14.4)	
Regimen				0.87
On-demand	53 (63.1)	14 (60.9)	67 (62.6)	
Daily	20 (23.8)	5 (21.7)	25 (23.4)	
Both	11 (13.1)	4 (17.4)	15 (14.0)	
Reason of begin				0.86
Risk sexual intercourse	55 (68.8)	13 (68.4)	68 (68.7)	
Previous STIs	12 (15)	3 (15.8)	15 (15.2)	
Previous PEP	2 (2.5)	1 (5.3)	3 (3.0)	
Chemsex	2 (2.5)	1 (5.3)	3 (3.0)	
Self-safety	9 (11.3)	1 (5.3)	10 (10.1)	
Not known	8 (9.1)	4 (17.4)	12 (10.0)	
Interruption reason				0.19
Stable partner	3 (11.5)	0 (0)	3 (9.7)	
Lost to follow-up	18 (69.2)	3 (60)	21 (67.7)	
Toxicity	1 (3.8)	0 (0)	1 (3.2)	
Lockdown	0 (0)	1 (20)	1 (3.2)	
Parenthood	0 (0)	0 (0)	0 (0)	
Not known	4 (15.4)	1 (20)	5 (16.1)	
Side effects				0.76
None	52 (71.2)	17 (77.3)	69 (72.6)	
Gastrointestinal disturbs	10 (13.7)	4 (18.2)	14 (14.7)	
Nephrotoxicity	1 (1.4)	0 (0)	1 (1.0)	
Hepatic toxicity	9 (12.3)	1 (4.6)	10 (10.5)	
Other	1 (1.4)	0 (0)	1 (1.1)	
Not known	0 (0)	0 (0)	0 (0)	
Condom use				0.41
Never	7 (10.6)	1 (4.8)	8 (9.2)	
Always	19 (28.8)	4 (19.1)	23 (26.4)	
Intermittent	40 (60.6)	16 (76.2)	56 (64.4)	

NEPHROTOXICITY

Focusing on renal function, data were available for 95 users.

Twelve (13,3%) subjects presented nephrotoxicity (tab 2).

The maximum increase was of 0,75 ml/min (from 1,36 ml/min to 2,11 ml/min) in a man undergoing lisinopril comedication, leading to PrEP interruption.

Tab. 2 Population with nephrotoxicity

	Basal creatinine level (mg/dl)	Last creatinine level (mg/dl)	Difference (mg/dl)	Age (years)	PrEP regimen	Nephrotoxic drugs
User 1	0.88	1.07	0.19	39	On demand	proteins
User 2	1.01	1.23	0.22	47	Daily	ramipril, allopurinol
User 3	0.77	2.24	0.23	39	Daily	proteins
User 4	0.88	1.07	0.19	28	Both	
User 5	0.71	0.86	0.15	44	On demand	
User 6	1.36	2.11	0.75	49	On demand	lisinopril
User 7	0.71	0.88	0.17	41	Daily	gabapentin
User 8	0.65	0.8	0.15	56	Daily	
User 9	1.09	1.32	0.23	64	On demand	olmesartan, rosuvastatin
User 10	0.74	0.96	0.22	62	Daily	losartan
User 11	0.81	0.98	0.17	63	Daily	zofenopril, rosuvastatin
User 12	0.68	0.86	0.18	51	Daily	

NEPHROTOXICITY IN POPULATION OVER 50 YEARS OLD

In the secondary analysis among the population over 50 yo including 23 subjects, 5 (21,7%) developed nephrotoxicity (tab 3). None of them experienced an increase in creatinine value that required PrEP interruption. Our analysis did not show any statistically significant difference between the two age groups.

Tab. 3 Population over 50 years old

	Basal creatinine level (mg/dl)	Last creatinine level (mg/dl)	Difference (mg/dl)	PrEP regimen	Nephrotoxic drugs
User 1	0,65	0,80	0,15	Daily	
User 2	1,09	1,32	0,23	On demand	olmesartan, rosuvastatin
User 3	0,74	0,96	0,22	Daily	losartan
User 4	0,81	0,98	0,17	Daily	zofenopril, rosuvastatin
User 5	0,68	0,86	0,18	Daily	
User 6	0,85	0,90	0,05	On demand	
User 7	0,78	0,90	0,12	On demand	allopurinol
User 8	0,88	0,93	0,05	On demand	avanafil
User 9	1,19	1,19	0	On demand	ramipril
User 10	0,77	0,89	0,12	On demand	
User 11	1,11	1,01	-0,10	On demand	
User 12	1,14	1,08	-0,06	On demand	
User 13	0,98	0,77	-0,21	On demand	
User 14	0,81	0,76	-0,05	Both	
User 15	1,06	missing		On demand	
User 16	0,88	0,81	-0,07	On demand	ramipril, rosuvastatin
User 17	1,15	1,30	0,15	On demand	
User 18	0,88	0,94	0,06	On demand	
User 19	0,91	0,85	-0,06	On demand	
User 20	0,73	0,80	0,07	Both	ramipril, mirtazapine
User 21	1,02	1,16	0,14	On demand	
User 22	0,92	0,89	-0,03	On demand	rosuvastatin
User 23	0,93	0,85	-0,08	Daily	

Conclusion

Our data confirm safety of TDF as a PrEP medication, with low interruption rates even in older users. Nevertheless, it remains fundamental to consider concomitant comedications which may increase the risk of renal toxicity and larger cohorts.

In this perspective the advent of newer prevention strategies alternative to oral TDF may be considered in some special categories of PrEP users.

References

- US Public Health Service: Preexposure prophylaxis for the prevention of hiv infection in the unitedstates–2021 update, a clinical practice guideline
- Drak et al «Renal impairment in a large-scale HIV preexposure prophylaxis implementation cohort»
- Gandhi et al., «Age, baseline kidney function, and medication exposure are associated with declines in creatininclearance on PrEP
- R. Schaefer et al "Kidney function in tenofovir disoproxil fumarate-based oral pre-exposure prophylaxis users: a systematic review and meta-analysis of published literature and a multi-country meta-analysis of individual participant data"

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