


Post-exposure prophylaxis for HIV infection in sexual assault victims*

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Objectives

Sexual assault (SA) is recognized as a public health problem of epidemic proportions. Guidelines recommend the administration of post-exposure prophylaxis (PEP) after an SA. However, few data are available about the feasibility of this strategy, and this study was conducted to assess this.

Methods

We conducted a retrospective, longitudinal, observational study in SA victims attending the Hospital Clinic in Barcelona from 2006 to 2015. A total of 1695 SA victims attended the emergency room (ER), of whom 883 met the PEP criteria. Five follow-up visits were scheduled at days 1, 10, 28, 90 and 180 in the out-patient clinic. The primary endpoint was PEP completion rate at day 28. Secondary endpoints were loss to follow-up, treatment discontinuation, occurrence of adverse events (AEs) and rate of seroconversion.

Results

The median age of participants was 25 years [interquartile range (IQR) 21–33 years] and 93% were female. The median interval between exposure and presentation at the ER was 13 h (IQR 6–24 h). The level of risk was appreciable in 47% ($n = 466$) of individuals. Of 883 patients receiving PEP, 631 lived in Catalonia. In this group, the PEP completion rate at day 28 was 29% ($n = 183$). The follow-up rate was 63% ($n = 400$) and 38% ($n = 241$) at days 1 and 28, respectively. Treatment discontinuation was present in 58 (15%) of 400 patients who attended at least the day 1 visit, the main reason being AEs ($n = 35$; 60%). AEs were reported in 226 (56%) patients, and were mainly gastrointestinal ($n = 196$; 49%). Only 211 (33%) patients returned for HIV testing at day 90. A single seroconversion was observed in a men who have sex with men (MSM) patient at day 120.

Conclusions

Follow-up and compliance rates in SA victims were poor. In addition, > 50% of the patients experienced AEs, which were the main reason for PEP interruption. Strategies to increase follow-up testing and new better tolerated drug regimens must be investigated to address these issues.

Keywords: female, follow-up studies, HIV infections, patient compliance, post-exposure prophylaxis, sexual assault

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Introduction

Sexual assault (SA) is a broad term that encompasses non-consented sexual acts, the definition of which includes touching, rubbing and physical coactions as well as rape (penetration with any object without the consent of the victim). There are no accurate data on the prevalence of SA, partly as a consequence of variation in the operational definition applied. Many victims do not identify their experience as rape [1,2]. In spite of this, the World Health

Organization (WHO) reports that one in six women are victims of rape during their lifetime and 35% of women experience some degree of physical or sexual violence [3,4]. This has huge physical, psychological and social repercussions [5–7]. Although SA occurs throughout the world, little information is available in most countries. In Spain, at least 1000 rapes are reported annually, 91% by female victims [8]. There is an important association between SA and the use of alcohol and submission drugs, as has been shown in prospective studies [9]. The most common drug in Barcelona is alcohol (48.8%) [10].

SA victims are vulnerable to a large number of sexually transmitted diseases; the prevalence in cohort studies varies from 8% to 32% [11–15]. In places where there is a high HIV prevalence, 4% of new HIV cases are related to a rape episode. Nevertheless, there are few documented cases of HIV transmission [16–20]. The transmission rate varies depending on the modality of sexual contact; receptive anal exposure carries the highest risk (0.8–3%), followed by receptive vaginal exposure (0.1–0.5%) and oral sex (0.0001–0.01%) [21–23]. Furthermore, any sexual exposure is considered to carry a risk when a condom is not used or is broken. The risk of HIV acquisition increases exponentially in the presence of factors such as genital trauma, genital ulcers, sexually transmitted infections (STIs), high viral load, blood exposure, ejaculation and rape by multiple assailants [24,25]. In cases where the victim of an SA had known the assailant for > 24 h, it was found that the perception of risk was lower and the victim tended to consider the use of PEP unnecessary [26].

The evidence of the efficacy of PEP to prevent HIV infection is based on case–control studies in health care workers, studies of the prevention of perinatal infection in pregnant woman, and animal studies in macaques [27–29]. In populations with a high prevalence of STIs, the use of PEP is recommended as soon as possible in the first 72 h [30–32]. There is a higher rate of completion in nonoccupational consented exposures than in situations of SA, in which completion, follow-up and diagnostic testing rates are low [33,34]. In a meta-analysis of 24 cohort studies, the median adherence to PEP in SA was approximately 40.3% [35]. Factors associated with PEP noncompletion are stigmatization of HIV infection, psychological trauma after rape, adverse events related to medication, limited knowledge about PEP indications, absence of proper multidisciplinary health care support in most Hospitals, and lack of psychological support [36–38].

Currently, there are few studies in Europe that have investigated the rate of treatment discontinuation, the rate of and factors associated with PEP noncompletion, adverse events and the number of seroconversions in SA victims. The purpose of this study was to describe follow-up in a cohort of sexually assaulted victims in the out-patient

clinic at the Hospital Clinic in Barcelona, a reference centre in Catalonia.

Methods

We performed an observational, descriptive, longitudinal study. A review was performed of all medical records codified in the emergency room (ER) at the Hospital Clinic from January 2006 until December 2015 as SA, sexual aggression, rape or suspected victim of sexual assault with a potential exposure to HIV.

The assistance circuit for SA victims was standardized and the quality of care was monitored by the committee against gender violence of the hospital. The initial care of the attacked person was multidisciplinary, with the participation of social workers, nurses, gynaecologists, surgeons, traumatologists and forensic specialist psychiatrists, as well as the infectious disease specialists. In this scenario, anamnesis, a physical examination, biological sampling (of blood, urine and genital secretions), and toxicological screening using mass spectrometry (for alcohol, amphetamines, benzodiazepines, cannabis, cocaine, methadone, opiates, gamma hydroxybutyrate and ketamine) were performed together with prophylaxis for STIs (hepatitis B, chlamydial and gonococcal infections, syphilis and *Trichomonas vaginalis* infection). PEP recommendation and prophylactic measures for STIs other than HIV infection were performed according to international guidelines [2006 Centers for Disease Control and Prevention (CDC) PEP guidelines, and 2012 and 2015 updated versions] and national guidelines from Study group for AIDS published in 2015 (Supporting Information Figure S1) [30–32].

A 7-day PEP prescription was given and PEP was initiated immediately in the ER (day 0). HIV testing in the ER was not performed, according to the hospital protocols, and therefore HIV-negative status could not be confirmed before starting PEP. The follow-up procedure was also explained to patients and they were provided with counselling about antiretroviral therapy (ART). Five follow-up visits were scheduled for days 1, 7, 28, 90 and 180 after the ER visit. The primary endpoint was PEP noncompletion at day 28, which was considered to occur when the patient was lost to follow-up before this day or the treatment was discontinued or switched for any reason, including death. Secondary endpoints were loss to follow-up at subsequent visits, discontinuation rate, the number of adverse events and the rate of seroconversion.

The first visit was scheduled with an infectious disease specialist within 72 h of starting PEP (day 1). Demographics, social background, past medical history, characteristics of the assault, risk stratification for HIV acquisition, physical examination, time between SA and first intake of PEP

and blood toxicology screen were recorded and recompiled from ER charts. As part of the risk assessment, information was gathered about the HIV serostatus of the assailant when possible. At day 7, test results from the day 1 visit and possible adverse events were evaluated. Laboratory monitoring and sexual risk exposure counselling were performed and repeated on days 28, 90 and 180. Adverse events were assessed at every scheduled visit.

The hospital's research ethics committee and the competent Spanish authorities approved the protocol describing the project proposed by the researcher (approval number HCB/2014/0346). The ethics committee waived the requirement for written informed consent as all information that directly or indirectly identified patients was removed from the data files, guaranteeing strict anonymity and total confidentiality. The processing, reporting and transfer of personal data for all participating subjects complied with the provisions in Organic Act 15/1999 of 13 December (Spanish Royal Decree 1720/2007 of 21 December), on personal data protection.

Statistical analysis

For data collection, variables were extracted from electronic health records in the SAP 740 Hospital Information System® (Societas Europaea, Walldorf, Alemania, Germany) and the out-patient clinic database. The results obtained were included in a database created with the program MICROSOFT EXCEL® for later analysis with the statistical package SPSS v18.0® (IBM corporation, Armonk, New York, USA). The primary endpoint of the study, PEP noncompletion, was analysed using Fisher's exact test. Categorical variables were compared between groups using the χ^2 test or Fisher's exact test. A multivariate logistic regression model was used to assess the independent factors associated with PEP noncompletion at day 28. The inferential analysis of continuous variables, such as laboratory values, was performed using parametric tests (Student's *t*-test).

Results

Demographics of the population

From January 2006 to January 2015, a total of 2015 SA victims attending the ER for potential exposure to HIV and meeting PEP criteria were included in the registry. Figure 1 shows the study flow chart. There were 320 erroneous entries. A total of 1695 medical charts were reviewed. The median age of the population was 25 years [interquartile range (IQR) 21–33 years] and 93% ($n = 1583$) were female. Ethnicity groups were as follows: 72% ($n = 1223$) were European, mostly Spanish 52% ($n = 887$); non-Europeans were mainly

from Latin America (17%; $n = 290$), followed by North America (6%; $n = 93$) and Africa (3%; $n = 47$). In 76% ($n = 1291$) of cases, the victim's residency was in Catalonia.

Past medical history was available in 1150 cases. Eleven per cent of these patients ($n = 126$) had previously experienced an SA and 29% ($n = 336$) had an active psychiatric disorder, the most frequent of which were depression (33%; $n = 110$) and anxiety (15%; $n = 50$). Substance abuse disorder was present in 8% ($n = 92$) of cases. Disabled persons and sex workers were a minority of the study population: 4% ($n = 41$) and 2% ($n = 24$), respectively. The demographic characteristics of the sexually assaulted patients are shown in Table 1.

Characteristics of the assault

The time of day of the SA was reported for 546 people; for 382 of them (70%), this was from 12 pm to 7 am. The assailant was known only in 21% ($n = 241$) of cases; the assailant was an intimate partner in 37% of these cases ($n = 89$), had an unnamed known relationship with the victim in 54% ($n = 130$) and was a neighbour, family member or work partner in the remainder (9%; $n = 22$). SA with multiple perpetrators was reported in 16% ($n = 164$) of cases, with a median of 3 (IQR 2–6) perpetrators per assault.

In physical examinations, physical injuries as a result of the assault were observed in 36% ($n = 419$) of the 1150 individuals. Of these injuries, 11% ($n = 121$) were genital trauma, 21% ($n = 241$) haematomas or ecchymosis, 12% ($n = 140$) lacerations and 0.5% ($n = 6$) life-threatening lesions (pneumothorax, subarachnoid haemorrhage, pulmonary contusion, cervical fractures, cranial fractures and rib fractures).

Loss of consciousness in the context of drug-facilitated sexual assault (DFSA) was present in 54% of cases ($n = 621$ of 1150 registered cases). Assault victims self-referred alcohol intake in 54% of cases ($n = 544$ of 1000 registered cases). In toxicological analysis of 859 samples, alcohol was the most commonly detected substance, being found in 25% ($n = 215$) of cases, followed by cannabinoids (14%; $n = 121$), cocaine (12%; $n = 101$), benzodiazepines (10%; $n = 82$), amphetamines (7%; $n = 56$), 3,4-Methyl enedioxy methamphetamine, commonly known as ecstasy (8%; $n = 69$), morphine (2%; $n = 13$), GHB (0.4%; $n = 3$) and ketamine (0.4%; $n = 3$). The combination of alcohol and other central nervous system active drugs was detected in 11% ($n = 95$) of the samples. The median alcohol levels were 1.39 g/L (IQR 0.87–2.09 g/L) in positive results. The median estimated blood alcohol concentration was 2.5 g/L (IQR 1.9–3.3 g/L) at the time of the incident. Of those with impaired mental status ($n = 528$), 30% ($n = 158$) had

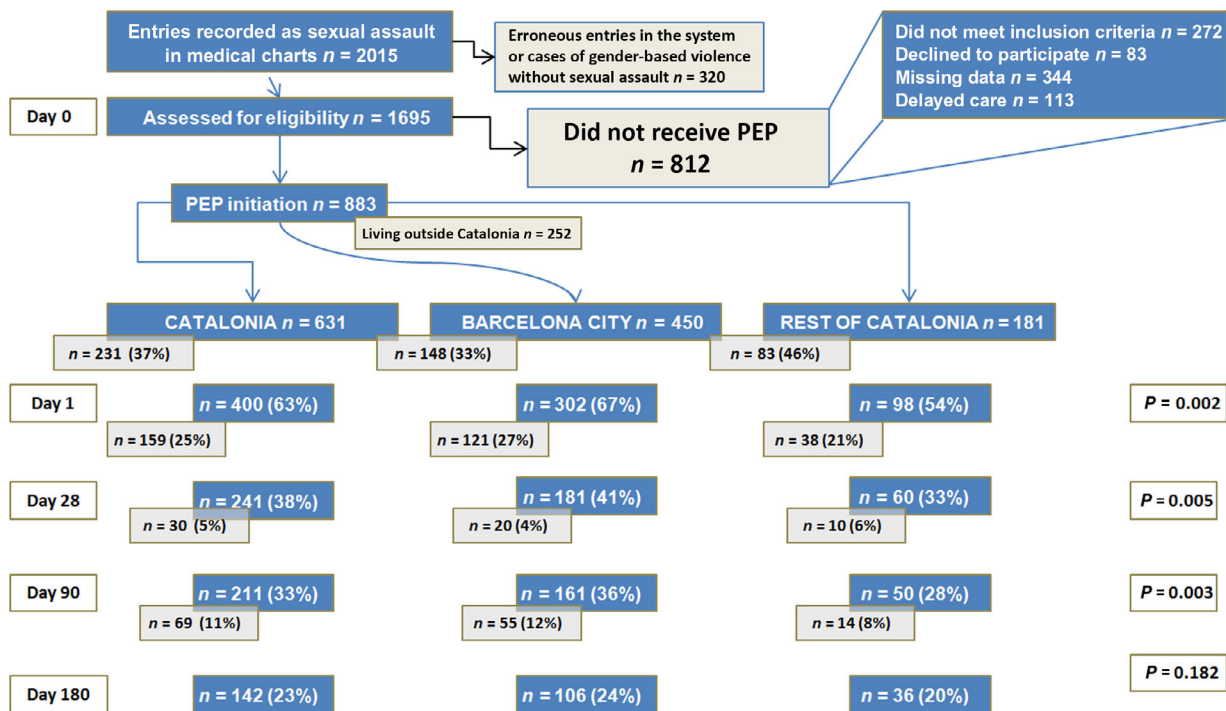


Fig. 1 Study flow chart. On day 0, for patients who met the criteria, treatment was immediately initiated in the emergency room (ER). Blue boxes represent individuals in follow-up according to location; grey boxes represent individuals lost to follow-up according to location. Grey boxes between day 0 and day 1 represent those lost to follow-up before day 1. On day 1, blue boxes represent patients who attended the first follow-up visit scheduled with an infectious disease specialist within the first week; grey boxes represent those subsequently lost to follow-up by day 28. On day 28, blue boxes represent patients who attended the day 28 visit; grey boxes represent those subsequently lost to follow-up by day 90. On day 90, blue boxes represent patients who attended the visit at day 90; grey boxes represent those subsequently lost to follow-up by day 180. On day 180, blue boxes represent patients who attended the visit at day 180 and completed the study. *P*-values are for the comparison between patients living in the metropolitan area and the rest of Catalonia.

positive alcohol blood levels and 67% ($n = 354$) self-referred alcohol intake.

PEP initiation and treatment regimens

Factors associated with PEP initiation were appreciable risk (53% in those receiving PEP versus 29% in those not receiving PEP; $P < 0.0001$), multiple perpetrators (18% versus 12%, respectively; $P = 0.003$), loss of consciousness (60% versus 44%, respectively; $P < 0.0001$), alcohol consumption (58% versus 47%, respectively; $P = 0.003$), substance abuse disorder (9% versus 5%, respectively; $P = 0.01$), psychiatric disorders (31% versus 25%, respectively; $P = 0.01$), unknown assailant (28% versus 17%, respectively; $P < 0.0001$), being European (89% versus 68%, respectively; $P < 0.0001$) and living in Catalonia (80% versus 73%, respectively; $P = 0.003$).

The median time of PEP initiation was 13 h (IQR 6–24 h) and appreciable risk was presented in 47% ($n = 466$) of the 1000 documented cases. Antibiotics were

administered in all the patients receiving PEP, while vaccination coverage was 53% ($n = 610$). Excluding the missing data for PEP candidates who did not start the treatment, 42% ($n = 196$) did not receive it before 72 h or refused it despite it being indicated.

Among the 883 patients receiving ART, 43% ($n = 380$) were treated with a lopinavir/ritonavir (LPV/r)-containing regimen, 34% ($n = 300$) with atazanavir (ATV), 21% ($n = 185$) with raltegravir (RAL) and 2% ($n = 18$) with elvitegravir. The backbone therapy was variable over the years, but all patients received either zidovudine/lamivudine (77%; $n = 680$) or tenofovir/emtricitabine (23%; $n = 203$). For the analysis, these third drugs were categorized as belonging to the ATV, LPV/r or RAL group.

PEP completion rates and loss to follow-up

Among the 631 SA victims with residency in Catalonia, follow-up rates were 63% ($n = 400$) at baseline (day 1) and 38% ($n = 241$) and 33% ($n = 211$) at days 28 and 90,

Table 1 Characteristics of the sexual assault victims in the entire cohort ($n = 1695$) and those who received post-exposure prophylaxis (PEP) ($n = 883$) and who did not receive PEP ($n = 811$)

Variable	Entire cohort	Receiving PEP	Not receiving PEP	<i>P</i> -value
<i>n</i>	1695	883	812	
Age (years) [median (IQR)]	25 (21–33)	25 (21–32)	25 (21–33)	0.800
Female gender [<i>n</i> (%)]	1583 (93)	817 (93)	766 (94)	0.524
European [<i>n</i> (%)]	1223 (72)	597 (68)	726 (89)	0.0001
Catalonia residency [<i>n</i> (%)]	1291 (76)	641 (73)	650 (80)	0.003
Lost consciousness [<i>n</i> (%)]	621 (54) [†]	440 (60)	181 (44)	0.0001
Received antibiotics [<i>n</i> (%)]	1010 (88) [‡]	824 (100)	186 (57)	0.0001
Received HBV vaccination [<i>n</i> (%)]	610 (53) [†]	499 (60)	111(34)	0.0001
Known assailant [<i>n</i> (%)]	241 (21) [†]	125 (17)	116(28)	0.0001
Appreciable risk [<i>n</i> (%)] [‡]	466 (47) [‡]	384 (53)	82 (29)	0.0001
Sex worker [<i>n</i> (%)]	24 (2) [†]	18 (2)	6 (2)	0.217
Disabled [<i>n</i> (%)]	41 (4) [†]	26 (3)	15 (4)	0.577
Previous aggression [<i>n</i> (%)]	126 (11) [†]	79(10)	47 (13)	0.122
Physical trauma [<i>n</i> (%)]	419 (36) [†]	299 (38)	120 (33)	0.082
Multiple perpetrators [<i>n</i> (%)]	164 (16) [‡]	124 (18)	40 (12)	0.003
Substance abuse disorder [<i>n</i> (%)]	92 (8) [†]	73 (9)	19 (5)	0.016
Psychiatric disorder [<i>n</i> (%)]	336 (29) [†]	248 (31)	88 (25)	0.019
Alcohol consumption [<i>n</i> (%)]	544 (54) [‡]	408 (58)	136 (47)	0.003
Alcohol blood level [median (IQR)]	1.3 (0.8–2)	1.5 (0.9–2.1)	1.1 (0.7–1.7)	0.001

IQR, interquartile range; HBV, hepatitis B virus.

*Defined as any sexual exposure excluding low risk. [†]Number of nonmissing values was 1150. [‡]Number of nonmissing values was 1000.

Bold formatting represents significant *P*-values.

respectively. Statistically significant differences in PEP completion rates were observed between individuals living in Barcelona City and the rest of Catalonia at day 1 (67% versus 54%, respectively; $P < 0.002$), day 28 (41% versus 33%, respectively; $P < 0.005$) and day 90 (36% versus 28%, respectively; $P < 0.003$) (Fig. 1).

In a total of 631 individuals living in Catalonia who initiated PEP, the PEP completion rate at day 28 was 29% ($n = 183$). The number of individuals completing PEP was taken to be the number who were still in follow-up at day 28 ($n = 241$), excluding those who did not complete treatment ($n = 58$). Factors associated with PEP noncompletion were analysed in a multivariate logistic

regression model (Table 2). Independent factors associated with higher rates of PEP noncompletion were low risk perception ($P < 0.001$), previous aggression ($P < 0.032$), a known aggressor ($P < 0.006$) and a positive test result for cocaine ($P < 0.026$). PEP treatment group was not associated with PEP noncompletion.

Prevalence and incidence of HIV and other sexually transmitted infections

The prevalence of hepatitis A and B virus protective antibodies was 74% ($n = 296$) and 82% ($n = 328$), respectively, in patients who attended the clinic at least on day

Table 2 Factors associated with post-exposure prophylaxis (PEP) noncompletion at day 28 attributable to any cause or to adverse events

Characteristic	PEP discontinuations attributable to any cause in the entire cohort ($n = 883$) OR (95% CI)*		PEP discontinuations attributable to any cause in patients living in Barcelona City ($n = 631$) OR (95% CI)*	
	Univariate	Multivariate	Univariate	Multivariate
Known aggressor	1.29 (1.17–1.43) $P = 0.001$	2.87 (1.41–5.84) $P = 0.004$	1.28 (1.15–1.42) $P = 0.0001$	2.73 (1.34–5.56), $P = 0.006$
Previous aggression	1.39 (0.94–2), $P = 0.017$	2.73 (1.10–6.78) $P = 0.030$	1.17 (1.04–1.32) $P = 0.021$	2.67 (1.08–6.55), $P = 0.033$
Low risk assessment	2.32 (1.62–3.31), $P = 0.001$	3.14 (1.81–5.44), $P = 0.0001$	2.55 (1.79–3.62), $P = 0.001$	3.05 (1.75–5.29), $P = 0.001$
Substance abuse disorder	0.47 (0.25–0.87), $P = 0.015$		0.59 (0.31–1.12), $P = 0.047$	
Location: residency in Barcelona City	1.45 (1.01–2.08), $P = 0.044$		1.35 (0.93– 1.96), $P = 0.106$	
European ethnicity	1.41 (1–1.98), $P = 0.044$		1.32 (0.92–1.89), $P = 0.120$	
Consumed alcohol	1.97 (1.22–3.18) $P = 0.005$		1.65 (1.13–2.43) $P = 0.007$	
Positive test for cocaine	OR = 0.45 (0.24–0.84), $P = 0.011$	2.57 (1.12–5.92) $P = 0.026$	0.42 (0.21–0.80), $P = 0.008$	2.57 (1.12–5.92) $P = 0.026$
Adverse events			0.83 (0.54–1.27) $P = 0.396$	

*Individuals with an HIV-positive test at baseline were excluded from analysis.

Bold formatting represents significant *P*-values.

CI, confidence interval; OR, odds ratio.

1 ($n = 400$). Chronic hepatitis B virus infection was presented in 4% of cases ($n = 18$), and only one case of active hepatitis at the first consultation was detected. Chronic hepatitis C was presented in 2% ($n = 10$) of the tested patients on day 1 ($n = 400$). HIV prevalence in the whole cohort was 1.1% ($n = 20$; three of these were new diagnoses). A single seroconversion was observed in a male in the men who have sex with men (MSM) category at day 120, with multiple potential exposures after PEP. There were no cases of hepatitis B, hepatitis C or syphilis reported during follow-up at day 90.

Adverse events and treatment discontinuation

Adverse events and treatment discontinuation rates were only collected in patients who attended the clinic at least on day 1 ($n = 400$). Adverse events were reported by 226 (57%) patients and were significantly more common in the LPV/r group compared with the ATV group (65% versus 46%, respectively; $P = 0.0001$). No differences were observed in the proportion of adverse events when the LPV/r and ATV groups were compared with the RAL group ($P = 0.113$ and $P = 0.167$, respectively) (Fig. 2). Gastrointestinal symptoms were the most common adverse events ($n = 196$; 63%), followed by fatigue ($n = 69$; 22%) and neuropsychiatric episodes ($n = 45$; 15%) (Table 3).

Treatment discontinuation was present in 58 of 400 patients (15%), with the main reason being adverse events ($n = 35$; 60%). There were 44 patients with adverse events who had not finished treatment at day 28 ($n = 19$ in the LPV/r group, $n = 12$ in the ATV group, and $n = 3$ in the RAL group). Discontinuation rates were higher in the LPV/r group compared with the RAL group (18% versus 7%, respectively; $P = 0.02$). No differences

were observed when comparing both groups with the ATV group (Fig. 3).

Abnormal laboratory values for exposed individuals

There were no discontinuations related to clinically relevant abnormal laboratory values. Statistically significant changes were observed in total cholesterol level within each treatment group, with increases in mean level at day 28 compared with baseline [+20 mg/dL in the LPV/r group ($P < 0.0001$), +8 mg/dL in the ATV group ($P < 0.0001$) and +7 mg/dL in the RAL group ($P = 0.013$)]. Statistically significant differences were observed in bilirubin levels in the protease inhibitors with a decrease on the mean levels after day 28 when compared to baseline bilirubin levels (-1.05 mg/dL in the ATV group and -0.6 mg/dL in the LPV/r group) (Table 4). There were no statistically significant differences compared with the normal laboratory ranges except for the ATV group for bilirubin levels (Table 4 shows overall values for the entire cohort).

Discussion

Few studies have described PEP completion rates in SA victims, and most of them lack detailed information regarding PEP regimens, follow-up visits, adverse events and rate of seroconversion. We herein report for the first time these rates in a population group from Catalonia over 10 years. In this study, the PEP completion rate was 29%. Factors associated with a significantly higher risk of PEP noncompletion were low-risk perception, a known assailant, previous aggression and a positive cocaine test.

It should be considered that 42% of those who did not receive PEP had an indication for it. The main reasons

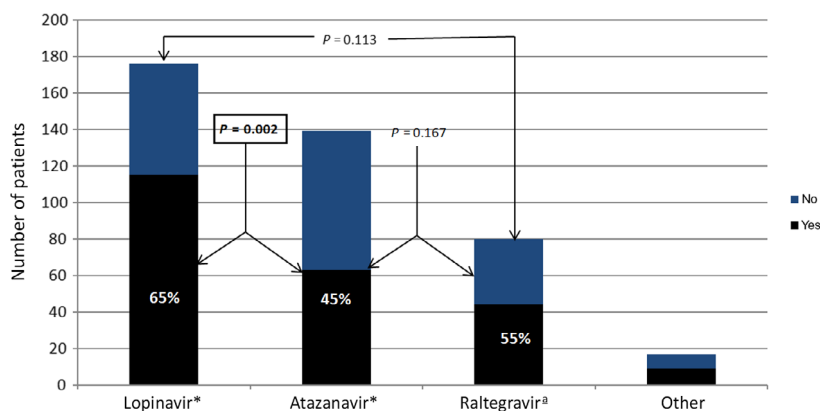


Fig. 2 Adverse effects experienced by sexual assault (SA) victims in the entire cohort coming to at least one follow-up visit ($n = 400$). ^aTenofovir/emtricitabine as backbone. *Lamivudine/zidovudine as backbone.

Table 3 Adverse effects (AEs) experienced by sexual assault victims in the entire cohort coming to at least one follow-up visit for each treatment group (*n* = 400)

	Total	Lopinavir/r*	Atazanavir*	Raltegravir†	Other
Exposed individuals [<i>n</i> (%)]‡	400	172 (43)‡	136 (34)‡	80 (20)‡	12 (3)‡
Individuals with AEs [<i>n</i> (%)]	226 (56)	112 (65)	63 (46)	44 (55)	6 (50)
Type of symptoms [<i>n</i> (%)]					
Gastrointestinal§	196 (63)	100 (63)	54 (61)	38 (66)	4 (57)
Neuropsychiatric¶	45 (15)	22 (14)	15 (17)	7 (12)	1 (14)
Asthaenia	69 (22)	36 (23)	19 (22)	12 (21)	2 (28)

*Lamivudine/zidovudine as backbone. †Tenofovir/emtricitabine as backbone. ‡Overall percentage of the whole cohort. §Such as nausea, vomiting, diarrhoea, abdominal pain and flatulence. ¶Such as headache, insomnia and nightmares.

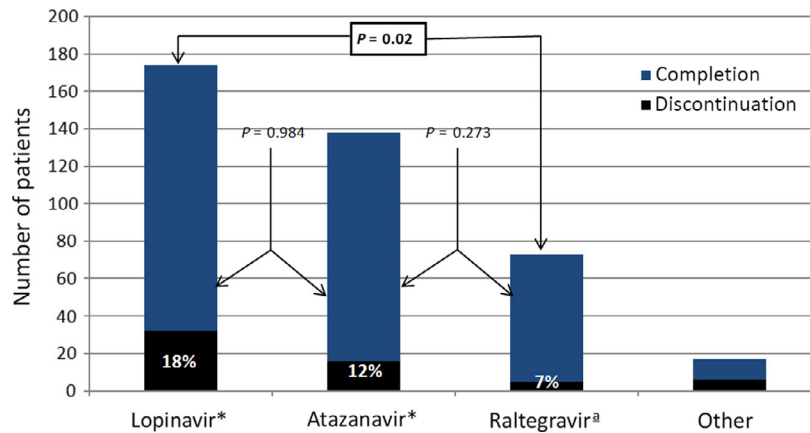


Fig. 3 Discontinuation rates for sexual assault (SA) victims coming to at least one follow-up visit (*n* = 400). †Tenofovir/emtricitabine as backbone. *Lamivudine/zidovudine as backbone.

Table 4 Abnormal laboratory values of exposed individuals in the entire cohort comparing baseline values (day 1) with follow-up values (day 28) for each treatment group (*n* = 400)

Laboratory test	Lopinavir/r*			Atazanavir*			Raltegravir†		
	Day 15 (3–7)	Day 2834 (30–39)	<i>P</i>	Day 15 (3–7)	Day 2831 (27–35)	<i>P</i>	Day 15 (3–7)	Day 2831 (27–35)	<i>P</i>
Total cholesterol (mg/dL) (normal < 200 mg/dL)	166	186	0.0001	161	169	0.0001	155	162	0.013
Triglycerides (mg/dL) (normal < 150 mg/dL)	98	93	0.291	82	77	0.52	74	79	0.43
AST (UI/L) (normal 5.0–40.0 UI/L)	23	23	0.778	21	22	0.32	22	22	0.78
ALT (UI/L) (normal 5.0–40.0 UI/L)	18	22	0.010	18	24	0.001	19	19	0.65
BT (mg/dL) (normal 0.20–1.20 mg/dL)	1.2	0.6	0.0001	2	0.95	0.0001	0.63	0.74	0.11
Leucocytes (cells/μL) [normal 400–1100 cells/μL]	434	635	0.431	460	683	0.0001	481	636	0.0001
Haemoglobin (g/dL) (normal 120–150 g/dL)	131	127	0.0001	130	126	0.001	130	130	0.218
Platelets (× 10 ⁹ cells/L) (normal 130–400 × 10 ⁹ cells/L)	276	263	0.111	299	297	0.789	281	289	0.325
Creatinine (mg/dL) (normal 0.30–1.30 mg/dL)	0.71	0.71	0.444	0.79	0.79	0.789	0.70	0.70	0.497

AST, aspartate aminotransferase; ALT, alanine aminotransferase; BT, total bilirubin.
*Lamivudine/zidovudine as backbone. †Tenofovir/emtricitabine as backbone.
Bold formatting represents significant *P* values.

for not initiating PEP were delayed care, self-refusal and knowing the perpetrator. In this studied cohort, follow-up rates were low: 63% and 38% at baseline and day 28, respectively. These results are similar to those of previous studies on SA with small cohorts in industrialized nations [16,26,33].

In this analysis, follow-up rates were greatly influenced by geographical proximity. Patients living further away from the specialized source of care displayed lower attendance rates than those living nearby. To overcome this issue, health care might be decentralized or be supported by additive interventions such as short message phone

reminders, telephone calls and a full course of PEP, or telemedicine resources could be used to maintain contact with exposed individuals beyond the ER period. The efficacy of these interventions remains unclear [39].

Adverse events were present in 65% of the assault victims in the whole cohort, and were mainly gastrointestinal. Results for PEP discontinuation in SA victims were similar to those in the MSM population, for which there is well-documented scientific evidence from clinical trials and observational studies, while data are scarce in sexually assaulted individuals [40]. The adverse event leads to nonadherence and treatment discontinuation. A recent prospective Belgian cohort study reported that being a sexual assault victim was an independent risk factor for lower adherence [41]. In our study, treatment discontinuation rates were as high as 15%. As RAL discontinuation rates were lower than those of LPV/r and ATV, these results suggest using integrase inhibitors as better-tolerated regimens in this fragile population, as previously demonstrated in the MSM population [40].

This study has a number of limitations. First, it had a retrospective design. Secondly, some of the information collected was incomplete as a consequence of partial amnesia or blackout intervals affecting the victim's recall of the assault at the ER evaluation. Moreover, patients with PEP treatment being lost to follow-up at day 1 (37%) also restricted the recollected information. It is also worth noting that a specific electronic database of sexual contacts was implemented after 2008 with a more detailed medical history. Thirdly, there was no recorded assessment of treatment adherence. Fourthly, the adverse events might also have been related to comedication such as ceftriaxone, azithromycin, metronidazole and progestin contraceptive pills. Finally, the median time between the SA and the arrival of the patient at the ER was 13 h, which is too long an interval for detection of drug use with a standard toxicological test [42].

Conclusions

SA victims displayed low PEP completion rates and poor follow-up rates. Access to a local health care facility at which the necessary resources are available could improve follow-up rates as well as HIV testing rates in these populations. Use of integrase inhibitor regimens might decrease treatment discontinuation rates and the number of adverse events compared with protease inhibitors. The results of this study suggest that it would be beneficial in future studies to further investigate adverse events, discontinuations and tolerance of current regimens in order to improve completion rates and decrease the number of side effects.

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Author contributions

AI, LL, EG, VDB, CL, AL and FG performed clinical assessments. AI and FG designed the study, contributed to data analysis and wrote the first draft of the manuscript. AI, LM and JGP were responsible for data entry. AI, LL, LM, EG, VDB, CL, JGP and FG critically reviewed the manuscript and agreed on its final version.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.