Tolerability and Adherence of Antiretroviral Regimens Containing Long-Acting Fusion Inhibitor Albuvirtide for HIV Post-Exposure Prophylaxis: A Cohort Study in China

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ABSTRACT

Introduction: There have been no prospective clinical studies investigating adherence and tolerability of HIV post-exposure prophylaxis (PEP) in China. Tolerability, adherence, and transmitted drug resistance are concerns, especially when single-tablet regimen (STR) usage is low. The present study aimed to explore the safety, tolerability, and adherence of regimens containing albuvirtide (ABT) compared with recommended non-STR antiretrovirals for HIV PEP.

Methods: This was a prospective, open-label, multicenter cohort study. The subjects were stratified into 3 groups based on their preference: ABT + Dolutegravir (DTG) (Group 1), ABT + Tenofovir disoproxil fumarate (TDF) + Lamivudine (3TC) (Group 2), and DTG + TDF + 3TC (Group 3). All enrolled subjects received PEP within 72 h after exposure and continued for 28 days, and were followed-up for 12 weeks.

Results: A total of 330 participants were enrolled in the three groups. Most participants were male (87.2%). Sexual contact was the most frequent mode of exposure (91.9%). The average time from exposure to treatment was 26.8 ± 19.5 h. There were no statistically significant differences between the three study groups with respect to completion of oral medication at 28 days. The 28-day completion rate was shown to be significantly higher with ABT versus oral (88.9% vs. 64.0%; $p < 0.0001$), and adherence with ABT was 94.4% compared to 75.7% with oral PEP ($p < 0.0001$). Subjects in ABT-containing Group 1 exhibited higher adherence than those in Group 3 (87.3% vs. 72.9%; $p < 0.05$). None of the participants reported serious adverse drug reactions which led to withdrawal from the study. All the drug regimens were found to be safe and well tolerated. No HIV incident case was observed during the study period.

Conclusions: ABT-containing regimens (ABT + DTG or ABT + TDF + 3TC) offer a good option for HIV PEP due to higher completion rates and adherence than the DTG + TDF + 3TC regimen. The overall safety was comparable and acceptable among the three groups.

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Key Summary Points
Why carry out this study?
There have been no prospective clinical studies investigating adherence and safety of HIV post-exposure prophylaxis (PEP) in China.
Tolerability, adherence, and transmitted drug resistance are concerns, especially when single-tablet regimen (STR) usage is low.
The aim of this study was to explore the safety, tolerability, and adherence of co-administration of albuvirtide (ABT) with other non-STR antiretrovirals for HIV PEP.
What was learned from the study?
ABT-containing regimens (ABT + DTG or ABT + TDF + 3TC) offered a good option for HIV PEP.
ABT-containing regimens showed higher completion rates than the DTG + TDF + 3TC regimen.

INTRODUCTION

Global HIV/AIDS statistics estimate that there are approximately 38 million people living with HIV worldwide at the end of 2019, with about 1.7 million new infections and 690,000 deaths occurring in 2019 [1, 2]. In China, AIDS morbidity (1/100,000), mortality (1/100), and HIV new infection rates (1/100,000) increased from 0.235 to 3.990, from 0.057 to 1.034, and from 1.020 to 6.442, respectively, from 2004 to 2016,

despite the country's unremitting efforts [3]. Currently, some of the strategies developed specifically for HIV prevention in China have included treatment as prevention (TasP), active work towards the WHO 90–90–90 targets, pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP), detection and treatment of sexually transmitted infections (STIs), prevention of mother-to-child transmission, promotion of condom use, and safe blood donation [4]. Antiretroviral therapy (ART) is considered the best option for TasP and PEP to prevent HIV transmission and infection [5].

According to recommendations of the International Antiviral Society-USA panel and China AIDS Guidelines (2018 edition), ART should be provided immediately to newly exposed individuals to avoid HIV transmission. Dolutegravir (DTG), lamivudine (3TC), tenofovir disoproxil fumarate (TDF), bictegravir (BIC), and emtricitabine (FTC) are the recommended drugs for HIV PEP by current guidelines [6, 7]. Three-drug regimens, including three-drug single-tablet regimens (STRs), are usually recommended as PEP regimens for high-risk individuals. However, STRs are not widely available in China, and adherence is always a concern when using non-STR three-drug ART for HIV PEP. Additionally, given the importance of PEP and the more than 100,000 new reported HIV infections annually in China, there has been no prospective PEP clinical study conducted in China to date [3], and international studies mentioned below have not included Chinese participants.

The effectiveness of PEP has been demonstrated in several previous overseas studies, but poor adherence and low completion rates were concerning observations in those studies which warrant further improvement [8–10]. There is a demand for PEP regimens that could overcome challenges of poor adherence, severe adverse events, and dosing convenience. Two previous overseas studies using co-formulated STRs (elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine) of HIV PEP found that the majority of participants achieved a higher drug completion rate (> 70%) and favorable drug tolerance [11, 12]. However, these studies did not include Chinese participants or cohorts,

and the real-world usage of these STRs in China was low.

Using parenteral long-acting antiretrovirals may be another strategy for improving adherence, tolerability, and convenience, and thereby have the potential to enhance expected outcomes. Preliminary animal PrEP studies have shown that long-acting cabotegravir can prevent simian/HIV acquisition from rectal, vaginal, and intravenous challenge [13]. Another study has demonstrated that monthly administration of long-acting cabotegravir and rilpivirine was non-inferior to daily oral administration of TDF/FTC for PrEP in mice [14]. In the HPTN083 and HPTN084 studies, cabotegravir showed superiority to oral TDF/FTC for HIV PrEP in males having sex with men and cisgender women [15, 16].

Albuvirtide (ABT) is a long-acting 3-maleim-imidopropionic acid (MPA)-modified peptide that binds to human serum albumin and inhibits HIV fusion. The binding of ABT with serum albumin to form a conjugate is responsible for its extended half-life of 12 days [17, 18], and it reduces the need for frequent intravenous administration [19]. The phase 3 TALENT study indicated that the dual regimen of ABT (weekly infusion) and oral daily ritonavir-boosted lopinavir (LPV/r) was well tolerated and non-inferior to the WHO-recommended second-line three-drug regimen in HIV patients with first-line treatment failure [20]. ABT was approved by the China National Medical Products Administration (NMPA) for marketing in 2018. In real-world practice, it is widely used in patients with HIV-1 infection and has been proven to have good safety and effectiveness. Due to the unique features of ABT, such as long-acting, intravenous administration, not metabolized by CYP450 liver enzymes, and subsequently fewer drug–drug interactions, the real-world clinical application has extended to special populations with high unmet medical needs, such as patients with hepatic impairment or renal impairment, perioperative use for abdominal surgery, hospitalized patients with critical conditions, and treatment-naïve HIV-infected patients with or without AIDS [21–23].

Due to the low usage of STRs in China, there have been concerns about the existing ART options in real-world PEP practice, such as the lower adherence and pill burden of non-STR regimens. Therefore, it is of interest to generate evidence of better options, including the newly approved long-acting injectable fusion inhibitor for PEP. The present study aimed to explore the safety, tolerability, adherence, and effectiveness of co-administration of ABT with other non-STR antiretrovirals for HIV PEP. Subjects were treated with 2 injections (1st and 15th days) of ABT combined with 1 integrase inhibitor or 2 nucleotide/nucleosides (NRTIs). Compared to the traditional three-drug non-STR PEP treatment, we hypothesize that once every 2 weeks ABT-containing regimens may offer a better therapeutic option by reducing pill burden and improving adherence, and the potential benefits of ABT use in PEP may be associated with the fact that it blocks viral fusion and acts early in the viral life cycle, reaches inhibitory drug concentration rapidly in blood via injection, and exhibits a high resistance barrier and long half-life of 12 days.

METHODS

Study Design and Participants

This was a prospective, open-label, multicenter cohort study conducted at three clinical centers in China: Chongqing Public Health Medical Center, Kunming Third People's Hospital, and The First Hospital of Changsha. Randomized design was not considered for the present study due to the potential implementational and analytical complexity involved with using both intravenous and oral drugs in the intervention arms. It was thus decided to conduct an exploratory open-label cohort study as the first study with respect to this specific study area in China. The three treatment options were offered to patients, and participants chose a therapeutic option based on their preference.

The study was registered in Chinese Clinical Trial Registry with registration number (ChiCTR1900022881, http://www.chictr.org.cn/showprojen.aspx?proj=37395), was approved by the Ethics Committees at each of the participating centers, and was conducted in

accordance with the tenets of the 1964 Declaration of Helsinki. All participants provided written informed consent.

Subjects with HIV exposure visiting these clinical centers between May 2019 and December 2019 were enrolled for the study. All subjects were asked to provide their history of exposure. A rapid HIV antibody examination was performed for all the subjects within 72 h of exposure to initiate the first preventive drug use. The inclusion criteria included: (1) persons above 18 years of age; (2) with a history of HIV exposure within 72 h through damaged skin-stabbing or cuts and/or contaminated skin/mucous membrane or unprotected sexual intercourse with a suspected or confirmed HIV-positive person; (3) tested negative for HIV antibody and urine pregnancy testing after exposure; and (4) provided signed informed consent. Urine pregnancy tests were performed only for women. The exclusion criteria were persons living with HIV or co-infected with hepatitis B virus (HBV), those with exposure exceeded 72 h, those who had an allergic reaction history or were intolerant to PEP drugs or excipients, and pregnant or breast-feeding women or women planning a pregnancy.

The subjects were stratified into 3 groups based on their preference: ABT + DTG (Group 1), ABT + TDF + 3TC (Group 2), and DTG + TDF + 3TC (Group 3). Subjects were initially screened, and, if they were found to have renal disease, they were to be allocated to the non-TDF arms of our study. However, we did not have any subjects with renal disease in our cohort. Group 1 and 2 regimens were designed based on the potential benefits of ABT from real-world clinical experience [21–23], while Group 3 was the regimen recommended by the China AIDS Guidelines. All enrolled subjects received PEP within 72 h after exposure and PEP was continued for 28 days,; patients were followed-up for 12 weeks. All the recruited subjects were appropriately educated by attending doctors with respect to the importance of adherence of PEP, and were reminded by the doctors 2–3 days before the next follow-up visit. The primary measurements were the 28-day drug completion rate and adherence,

HIV sero-conversion, and the occurrence of adverse drug reactions (ADR).

Study Procedure

Based on the principle of starting prophylactic medication as early as possible after high-risk HIV exposure, the collection of high-risk exposure history, informed consent, HIV antibody test results, urine pregnancy test results (only for women), vital signs, and physical examinations were completed rapidly, and the first preventive dose of medication was administered within 72 h after exposure.

The drugs utilized in the present study and their respective dosages were as follows: ABT, 320 mg, given intravenously (IV) on day 1 and day 15; DTG, 50 mg, taken orally, once a day for 28 days; TDF, 300 mg, orally once a day, for 28 days; and 3TC, 300 mg, orally, once a day, for 28 days. Post-exposure prophylactic therapy was initiated in all the subjects within 72 h of exposure. Oral study medication was dispensed for 28 days, and subjects were followed up for 12 weeks.

The results of laboratory examinations at the Day 1 visit (blood cell count, biochemistry, urinalysis, HBV markers, hepatitis C antibody, and syphilis markers) were used as baseline data. Follow-up visits were conducted on Day 14 and Day 28, and Week 8 and Week 12 to evaluate blood-testing results and urinalysis, drug adherence, ADR, anti-HIV antibody test, vital signs, and physical examination.

Based on drug distribution records, study doctors calculated the percentage of subjects who completed the 28-day course of ABT and oral prophylaxis drug regimens. The subjects received ABT by the study nurse via IV-infusion at the hospital. The infusion was documented in the hospital database, and these data were included in the calculation of adherence. Oral drug adherence (actual doses/theoretical doses × 100%) was measured by pill counts at each study visit.

The 28-day individual adherence rates to ABT and each of the oral drugs were calculated concurrently, and the adherence rates to each regimen were calculated at the same time. In

the two-drug regimen of Group 1, each drug was weighted as ½ weights, while in the three-drug regimens of Groups 2 and 3, each drug was weighted as 1/3 weights. The effectiveness of prophylaxis was evaluated by calculating the HIV infection rates at 28 days and 12 weeks. Safety evaluation included recording and evaluating the incidence of ADR, physical examination, and the results of laboratory tests, such as hematology, blood biochemistry, and urinalysis.

Outcomes

The primary measurements were the 28-day drug completion rate, adherence, HIV seroconversion, and occurrence of ADRs. The percentage of subjects who had completed 28 days of ABT and oral PEP medications was calculated based on drug distribution records. The 28-day drug adherence rate to ABT and the oral drugs was calculated, and the regimen adherence rate of the three groups was calculated. The formula used to calculate drug adherence (%) was consumed doses/prescribed doses × 100%. Safety endpoints included the recording and evaluation of the occurrence of ADRs. The HIV seroconversion included the HIV infection rate at Day 28 and Week 12.

Statistical analysis

Assuming that the true population drug completion rate of the Group 3 regimen is 70%, a sample size of 100 participants per treatment group is expected to provide approximately 80% power if the ABT regimen has a true drug completion rate 16% higher than the Group 3 regimen, at a nominal two-sided level of 0.05. Similarly, a sample size of 100 participants per treatment group provides approximately 80% power when the ABT regimen has a true drug adherence rate exceeding that of the Group 3 regimen by 0.12 (or 12%), assuming the true standard deviation to be 0.3 for all groups, at a nominal two-sided level of 0.05.

Continuous datasets were described as mean ± standard deviation, and classified datasets as percentage and event frequency. The χ^2 test and Fisher's exact test were performed to compare categorical variables. Continuous variables were compared using the paired t test and the F test (analysis of variance) was used for multiple comparisons with T correction. Statistical significance was set at a p value of 0.05, and CIs at 95%. All statistical analyses were performed using SAS software (v.9.4; SAS Institute, Cary, NC, USA). The Safety Set (SS) included all subjects who received the assigned PEP medications. The Full Analysis Set (FAS) included all subjects except those with negative HIV exposure sources and hepatitis B Infection.

RESULTS

Study participants and baseline characteristics

A total of 330 subjects were enrolled and stratified into three groups: Group 1 (ABT + DTG), Group 2 (ABT + TDF + 3TC), and Group 3 (DTG + TDF + 3TC), with 126, 104, and 100 subjects in each group, respectively. The SS included all 330 participants. The FAS comprised 297 participants, with 99 subjects each per group, after excluding 4 subjects, whose exposure source was confirmed to be negative, and 29 cases, who were confirmed to have hepatitis B infection. Figure 1 illustrates the distribution of subjects in the study.

The participants were mostly men (87.2%), their mean age was 31.58 ± 8.82 years, and 92.2% of them were of the Chinese-Han ethnicity. There were no significant differences in mean height or weight between the study groups. With regards to mode of exposure, sexual exposure was calculated to have highest proportion in all three groups (90.9%, 88.8%, and 95.9%, respectively). Vaginal intercourse was the most prevalent mode of sexual exposure, at proportions of 70.7%, 59.6%, and 56.3%, respectively. The overall average exposure time was 26.8 ± 19.5 h. More than half of the study participants in each of the three groups initiated PEP therapy within 24 h of exposure (51.5%, 58.2%, and 58.5%, respectively) (Table 1).
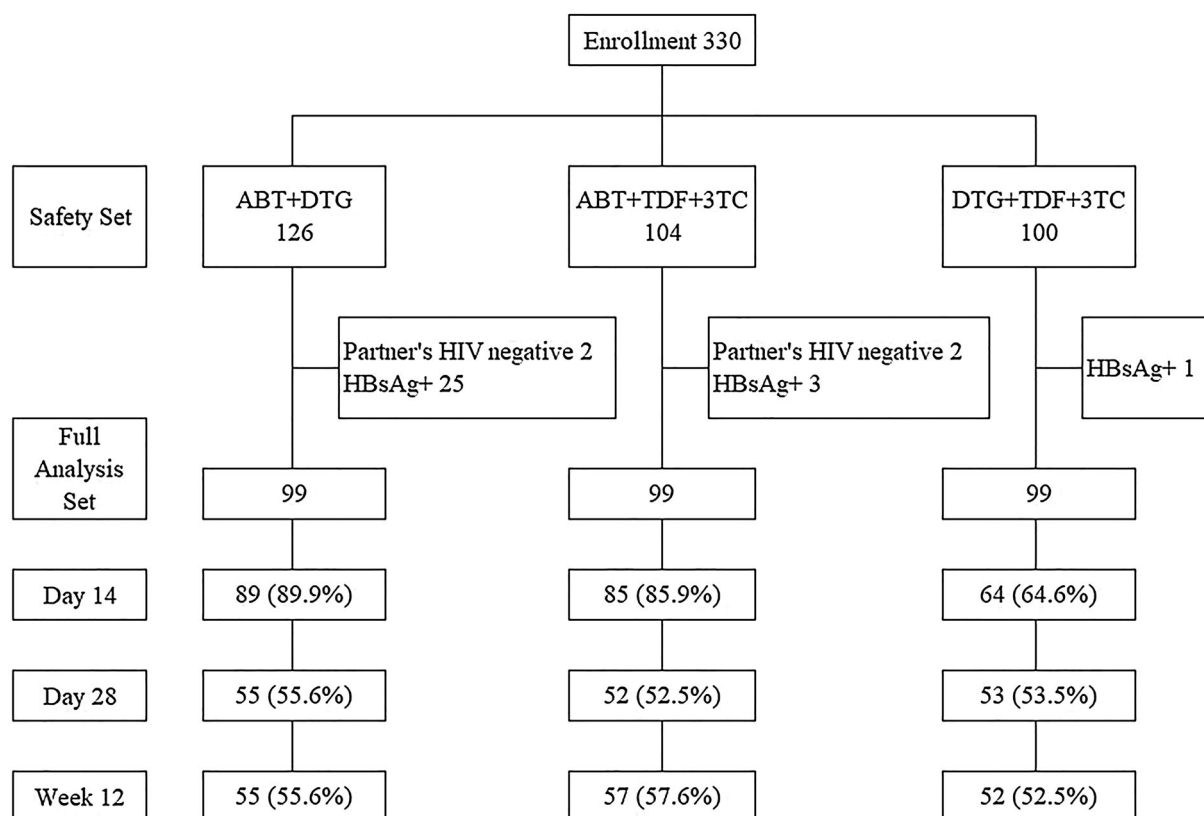
Fig. 1 Distribution of subjects in the study

The percentage of subjects who completed Day 15 visits in the three groups were 89.9%, 85.9%, and 64.6%, respectively. The percentage of subjects who completed Day 28 visits in the three groups were 55.6%, 52.5%, and 53.5%, respectively. Those who completed Week 12 visits were 55.6%, 57.6%, and 52.5% in the three groups, respectively. Compared to the Day 15 visits, there was a decrease in the proportion of subjects who completed Day 28 and Week 12 visits (Fig. 1). This was due to subjects erroneously believing that they had completed all the required treatment and did not need to present themselves for follow-up on Day 28. As the HIV self-test is widely available in China, subjects preferred to do self-testing for HIV after treatment.

Drug completion

Of the total of 297 participants, 91.9% of Group 1 participants and 85.9% of Group 2 participants completed 2 infusions of ABT. The proportions of subjects who completed 14 days of oral drug prophylaxis in each of the three groups were 91.9%, 85.9%, and 80.8%, respectively. Overall, 64.0% (190/297) of the subjects completed 28 days of oral drug prevention with proportions of 63.6%, 64.6%, and 63.6% in each of the three groups, respectively. There was no significant difference in the rates of oral medication completion over 28 days between the three groups. The 14-day and 28-day completion rate of ABT was significantly higher than the oral drug completion rate ($p < 0.0001$) for all subjects (Table 2).

Table 1 Demographic data and baseline characteristics

	Total (n = 297)	Group 1 (ABT + DTG) (n = 99)	Group 2 (ABT + TDF + 3TC) (n = 99)	Group 3 (DTG + TDF + 3TC) (n = 99)	p value
Age, years	31.58 ± 8.82	32.02 ± 8.71	31.66 ± 9.13	31.07 ± 8.67	0.7503
Male	259 (87.2)	85 (85.9)	88 (88.9)	86 (86.9)	0.8096
Ethnicity					0.8266
Chinese-Han	249 (92.2)	91 (92.9)	90 (90.9)	68 (93.2)	
Other	21 (7.8)	7 (7.1)	9 (9.1)	5 (6.8)	
Height (cm)	171.3 ± 6.6	171.6 ± 7	170.8 ± 6.1	171.4 ± 6.8	0.6980
Weight (kg)	67.7 ± 10.7	68.4 ± 10.3	67.8 ± 10.9	66.9 ± 10.9	0.6490
BMI (kg/m^2)	23 ± 3	23.2 ± 2.9	23.2 ± 3.1	22.7 ± 3	0.4893
Hepatitis C Ab (+)	1 (0.4)	1 (1.1)	0 (0.0)	0 (0.0)	0.3225
Treponema pallidum antibodies (+)	6 (2.2)	3 (3.4)	0 (0.0)	3 (3.3)	0.1957
Mode of exposure					0.3333
Occupational exposure	8 (2.7)	2 (2.0)	5 (5.1)	1 (1.0)	
Sexual exposure	270 (91.9)	90 (90.9)	88 (88.8)	92 (95.9)	
Unknown	9 (3.1)	3 (3.0)	1 (1.0)	5 (5.2)	
Anal sex	55 (18.7)	9 (9.1)	16 (16.2)	30 (31.3)	
Vaginal intercourse	183 (62.2)	70 (70.7)	59 (59.6)	54 (56.3)	
Oral sex	23 (7.8)	8 (8.1)	12 (12.1)	3 (3.1)	
Blood/body fluid exposure	16 (5.4)	7 (7.1)	6 (6.1)	3 (3.1)	
Exposure time					
Average exposure time (h)	26.8 ± 19.5	28.0 ± 19.1	26.0 ± 19.7	26.5 ± 19.9	0.7690
≤ 24 h (, %)	163 (56.0)	51 (51.5)	57 (58.2)	55 (58.5)	
24–48 h	80 (27.5)	30 (30.3)	27 (27.6)	23 (24.5)	
48–72 h	44 (15.1)	17 (17.2)	14 (14.3)	13 (13.8)	
> 72 h	4 (1.4)	1 (1.0)	0 (0.0)	3 (3.2)	

Data are *n* (%) or mean ± SD

Drug adherence

The 28-day drug adherence rates to ABT, oral medication, and combination therapy were 94.4% ± 15.8%, 75.7% ± 36.0%, and 80.5% ± 31.4%, respectively. A significantly higher adherence rate to ABT than to oral drugs was observed in all subjects ($p < 0.0001$) and in

Table 2 Preventive drug completion rates

Completion rate n (%)	Total (n = 297)	Group 1 (ABT + DTG) (n = 99)	Group 2 (ABT + TDF + 3TC) (n = 99)	Group 3 (TDF + 3TC + DTG) (n = 99)
1st infusion of ABT	198 (100.0)	99 (100.0)	99 (100.0)	–
2nd infusions of ABT	176 (88.9)*	91 (91.9)*	85 (85.9)*	–
Oral medication for 14 days	256 (86.2)	91 (91.9)**	85 (85.9)	80 (80.8)
Oral medication for 28 days	190 (64.0)	63 (63.6)	64 (64.6)	63 (63.6)

*$p < 0.0001$ (vs. oral medication); **$p < 0.05$ (vs. Group 3)

Table 3 Preventive drug adherence

Adherence Mean ± SD (%)	Total (n = 297)	Group 1 (ABT + DTG) (n = 99)	Group 2 (ABT + TDF + 3TC) (n = 99)	Group 3 (TDF + 3TC + DTG) (n = 99)
ABT	94.4 ± 15.8*	96.0 ± 13.7*	92.9 ± 17.5*	–
Oral medication	75.7 ± 36.0	78.6 ± 32.1	75.5 ± 36.5	72.9 ± 39.2
Combination	80.5 ± 31.4**	87.3 ± 21.5**	81.3 ± 29.4	72.9 ± 39.2

*$p < 0.0001$ (vs. oral medication); **$p < 0.01$ (vs. all 3 groups or vs. Group 3)

subjects of Group 1 and 2. For the oral medication, the adherence rates in Group 1 and 2 were slightly higher than in Group 3, but without a statistically significant difference. Group 1 and Group 2 participants exhibited higher adherence to their respective therapeutic regimens compared to Group 3 participants, with a statistically significant difference between Group 1 and 3 ($p < 0.01$) (Table 3).

HIV infection rate

Among the 297 participants, 73.1% (217/297) underwent HIV antibody testing during the period between Day 15 and Week 12 after the administration of the first prophylactic drug, but none of the participants was found to be positive.

Adverse drug reactions

None of the participants reported ADR that would have led to withdrawal from the study. In Group 1 (ABT + DTG), 26.2% of subjects had 49 ADR of severity grade 1–2, common ADRs being dizziness (7.1%), diarrhea (5.6%), and asthenia (4.8%). In Group 2 (ABT + TDF + 3TC), 46 ADRs of severity grade 1–2 were observed in 32.7% of subjects, and common ADRs were dizziness (6.7%), abnormal liver functions (4.8%), asthenia (3.9%), and diarrhea (3.9%). In Group 3 (DTG + TDF + 3TC), 26% of subjects had 40 ADRs of severity grade 1–2, with common ADRs being elevated triglycerides (7.0%), dizziness (7.0%), and asthenia (5.0%) (Table 4).

DISCUSSION

To the best of our knowledge, our study is the first prospective study in China aiming at providing clinical evidence of

Table 4 Adverse drug reactions occurring in ≥ 1% of subjects (*n*, %)

	Total *n* = 330	Group 1 *n* = 126	Group 2 *n* = 104	Group 3 *n* = 100
Number of subjects with ADR	93 (28.2)	33 (26.2)	34 (32.7)	26 (26.0)
Number of grade 1–2 ADR	135	49	46	40
Nervous system disorder				
Dizziness	23 (7.0)	9 (7.1)	7 (6.7)	7 (7.0)
Somnolence	4 (1.2)	0 (0.0)	2 (1.9)	2 (2.0)
Gastrointestinal disorders				
Diarrhea	13 (3.9)	7 (5.6)	4 (3.9)	2 (2.0)
Nausea	9 (2.7)	3 (2.4)	2 (1.9)	4 (4.0)
General disorders and administration site conditions				
Asthenia	15 (4.6)	6 (4.8)	4 (3.9)	5 (5.0)
Pyrexia	5 (1.5)	2 (1.6)	2 (1.9)	1 (1.0)
Feeling hot	4 (1.2)	1 (0.8)	2 (1.9)	1 (1.0)
Laboratory examinations				
Blood triglycerides increased	14 (4.2)	5 (4.0)	2 (1.9)	7 (7.0)
Blood uric acid increased	5 (1.5)	2 (1.6)	1 (1.0)	2 (2.0)
Gamma-glutamyltransferase increased	2 (0.6)	1 (0.8)	0 (0.0)	1 (1.0)
Alanine aminotransferase increased	1 (0.3)	0 (0.0)	0 (0.0)	1 (1.0)
Hepatobiliary disorders				
Hepatic function abnormal	6 (1.8)	1 (0.8)	5 (4.8)	0 (0.0)
Respiratory, thoracic and mediastinal disorders				
Oropharyngeal pain	5 (1.5)	4 (3.2)	1 (1.0)	0 (0.0)
Metabolism and nutrition disorders				
Decreased appetite	5 (1.5)	2 (1.6)	3 (2.9)	0 (0.0)
Skin and subcutaneous tissue disorders				
Rash	4 (1.2)	1 (0.8)	2 (1.9)	1 (1.0)
Musculoskeletal and connective tissue disorders				
Arthralgia	3 (0.9)	0 (0.0)	2 (1.9)	1 (1.0)

Data are *n* (%)

injectable antiretroviral-containing PEP regimens. The results of our study revealed that the 28-day completion rate and the drug adherence rate of ABT were significantly higher than those of the oral drugs, that no subjects tested seropositive for HIV at the termination of the study, and that co-administration of ABT with oral drugs was found to be safe, effective, and well tolerated.

In our cohort, sexual contact was the predominant mode of exposure, while occupational exposure accounted for only 2.7%. Among those with sexual exposure, vaginal intercourse was the most prevalent sexual method of exposure in our study. This observation differs from that of a prospective study conducted in Paris, in which the primary mode of sexual exposure was anal sex in 65% of patients, while vaginal intercourse accounted for only 26% of cases [12]. However, an observational, cross-sectional study of 678 patients in Spain found vaginal intercourse (99.2%) to be the commonest sexual method of HIV exposure [24].

Our study showed that the 14-day and 28-day completion rates of ABT were significantly higher than the oral drug completion rate for all subjects. The adherence rates to prescribed regimens in Groups 1 and 2 were higher than that in Group 3, with a statistically significant difference. A significant increase in adherence rates to ABT than to oral drugs was noticed in all subjects. Comparing the adherence of all subjects to ABT and oral drugs, we found that the adherence rate to ABT was higher, with a statistically significant difference. This is an expected outcome that replacing 2 NRTIs with an injectable (ABT) may facilitate the PEP drug completion rate. The above findings also suggest that biweekly administration of ABT was well accepted by most of the participants, and could significantly improve drug completion rates. In addition, a significant reduction in the proportion of subjects who completed the oral medication for 14 days was observed in Group 3 as compared to Group 1, indicating that the higher pill burden contributed to the lower completion rate in Group 3.

A similar study conducted in Barcelona, Spain, in which 157 patients had potential sexual exposure to HIV, reported a higher non-completion rate using LPV/r (47%) versus elvitegravir/cobicistat (33%). Significantly poor adherence to PEP and more adverse events were reported in the LPV/r group versus the elvitegravir/cobicistat group (47% vs. 9%, $p = 0.0001$ and 90% vs. 49%, $p = 0.0001$, respectively) [10]. This observation further emphasizes the fact that using a larger number of individual oral medications for PEP is potentially likely to be responsible for poor drug compliance.

In the present study, the completion rate of all subjects for preventive oral drugs was 64.0%, and drug adherence was observed to be 75.7%, indicating that a large proportion of subjects were unable to consume oral drugs on a regular basis, or discontinued the medication. ABT is a long-acting injectable drug approved for antiretroviral use in China [25]. In our study, ABT was administered on the 1st and 15th days. The low-frequency administration, and compulsory hospital infusion resulted in a 28-day drug completion rate (88.9%) and the adherence rate (94.4%) of ABT was significantly more favorable than that of oral drugs. The combination of ABT with DTG showed the highest completion and adherence rates. This signifies that a simplified two-drug regimen which includes a long-acting injectable drug has the potential to improve drug adherence in participants requiring post-exposure prevention. As ABT requires one biweekly administration due to its extended half-life, poor adherence associated with a three-drug regimen may thus be avoided [26].

It is important to note that, in our study, 55.2% (164/297) participants completed the 12-week follow-up visits. Hence, only 73.1% of participants were subjected to HIV antibody testing between Day 15 and Week 12 after the administration of the first prophylactic drug. This emphasizes the importance of patient education and the effective involvement of the attending doctor in HIV PEP treatment. None of the participants were subsequently found to be infected with HIV.

No serious ADR or injection site reactions that could lead to withdrawal from the study were observed in subjects in our study. The most common ADRs were dizziness, diarrhea, and asthenia of severity grade 1–2. The study drugs were well tolerated. Our results showed that subjects had good overall safety and tolerance to the three regimens.

In the present study, the 28-day completion rate of oral drugs was 64.0% and the HIV antibody detection rate was 60–70%, suggesting that organizing HIV post-exposure prevention

education and awareness programs, drug adherence supervision, and high-risk drug monitoring may effectively improve compliance and ensure better prevention and management of HIV.

The efficacy and safety of an ABT-containing 2-drug combination (ABT + LPV/r) have been demonstrated in randomized clinical trials and post marketing studies [20–23]. With the advantages of long-acting, minimal drug–drug interactions, a high barrier to resistance and early blockade of cell fusion mechanism, ABT-containing 2-drug combinations are being considered as a promising HIV PEP option, especially in regions where STRs are not widely available.

The current study had some limitations. Firstly, there were no objective measurements of plasma drug concentration, which would have been able to determine drug compliance more accurately. Secondly, our cohort had a high proportion of participants not presenting for follow-up visits and the high lost-to-follow-up rate observed in our study may have negatively impacted on the regimen completion rate and the individual medication compliance rates seen in our study. The reasons for this are complex, and may be related to preservation and maintenance of privacy and confidentiality, and may contribute to the unfortunately low PEP follow-up rate in China. And, thirdly, our study design was not randomized controlled, and selection bias cannot be avoided. Regimen selection was based on participants preference, which introduces bias, and the results may be skewed, especially with regards to patient-reported tolerability.

CONCLUSIONS

ABT-containing regimens (ABT + DTG or ABT + TDF + 3TC) offered a good option for HIV PEP due to higher completion rates and adherence than the DTG + TDF + 3TC regimen. The overall safety was comparable and acceptable among the three groups.

ACKNOWLEDGEMENTS

participants provided written informed consent.

Data Availability. The datasets generated during and/or analyzed during the current study are not publicly available due to the proprietary nature of the database, but are available from the corresponding author on reasonable request.

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