Preoperative rapid suppression of viral load by elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide regimen in human immunodeficiency virus-positive fracture patients significantly reduces postoperative complications

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To the Editor: There are 1.25 million people living with human immunodeficiency virus (HIV) (PLWH) in China, with more than 135,000 newly diagnosed cases in 2018.[1] HIV-positive patients who suffer a fracture have extremely high complication rates following operations, and medical staff frequently experience occupational exposure during the perioperative period. Therefore, surgeons are often worried about operating on HIV-positive patients. To ensure the safety of surgeons and reduce patients' postoperative complications, we attempted to maximally suppress the viral load (VL) prior to operation. Previous studies have shown that PLWH demonstrated high uptake of highly active antiretroviral therapy (HAART) and rapid VL suppression.[2] In recent years, more rapid VL suppression has been observed with newly introduced antiretroviral drugs, for example, a combination of the integrase strand transfer inhibitor (INSTI), in a single-tablet regimen (STR) containing elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide (E/C/F/TAF) (150/150/200/10 mg).[3] Studies have shown that STRs have more reliable virus suppression success rates than multiple-tablet regimens (MTRs).[4] Generally, patients prefer freely available HAART drugs that are available nationally, containing tenofovir disoproxil fumarate, lamivudine, and efavirenz (TDF/3TC/EFV) (400/300/600 mg). In this study, we compared the preoperative effect of E/C/F/TAF and TDF/3TC/EFV regimens in the treatment for HIV-positive patients to reduce VL and improve the immune function in 7 and 10 days.

From January 2011 to August 2019, 120 HIV-positive patients with closed fracture were admitted to the Beijing Ditan Hospital, Capital Medical University. Our cohort was divided into three groups according to the treatment method used: E/C/F/TAF regimen group ($n = 40$), TDF/3TC/EFV regimen group ($n = 40$), and untreated (before 2015) as a control group ($n = 40$). The median age of the patients was 35 years (range: 20–53 years). All patients underwent an operation for fracture by open reduction and internal fixation.[5] This study was approved by the Ethics Committee of Beijing Ditan Hospital, and all patients signed informed consent forms before participating in this study. The VL and $CD4^+$ T-cell counts of patients in the three groups were detected and compared at diagnosis and after 7 and 10 days. The statistical analyses were performed with SPSS version 24.0 (IBM Inc., Chicago, IL, USA). All continuous variables with non-normal distribution were shown as median (Q_1, Q_3) and analyzed using Kruskal-Wallis H test followed by Nemenyi test. Categorical variables were presented as numbers (%) and compared using the Fisher exact test or Chi-squared test as appropriate. The statistical analyses were performed with SPSS version 24.0 (IBM Inc., Chicago, IL, USA). All tests were two-sided, and $P < 0.05$ was considered to be statistically significant.

The patients were followed-up for 12 months. The follow-up results showed that there was no significant difference in age ($H = 0.411$, $P = 0.714$) and gender ($P = 0.697$) among the three groups. More rapid viral suppression (after 7 days of treatment: 4.86 [4.48, 5.01] $\log_{10}$ copies/ml *vs.* 5.31 [5.03, 5.61] $\log_{10}$ copies/ml, $P = 0.017$; after 10 days of treatment: 3.58 [3.16, 3.79] $\log_{10}$ copies/ml *vs.* 4.05 [3.55, 4.37] $\log_{10}$ copies/ml, $P = 0.038$) and a more rapid increase in $CD4^+$ T-cell count (after 7 days of treatment: 505.6 [385.3, 698.0] cells/mm^3 *vs.* 453.2 [319.2, 700.3] cells/mm^3, $P = 0.021$; after 10 days of treatment: 551.2 [374.2, 710.6] cells/mm^3 *vs.* 483.3

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.1097/CM9.0000000000001185

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Chinese Medical Journal 2020;133(23)

Received: 20-06-2020 **Edited by:** Pei-Fang Wei

Table 1: Characteristics and postoperative complications of HIV-positive fracture patients treated with different regimens.

Characteristics	Total ($n = 120$)	E/C/F/TAF ($n = 40$)	TDF/3TC/EFV ($n = 40$)	Untreated ($n = 40$)	*H* values	*P* values
Age (years)	35 (28–48)	33 (28–43)	32 (27–45)	33 (25–41)	0.411	0.714
Gender					–	0.697
Male	111 (92.5)	37 (92.5)	38 (95.0)	36 (90.0)		
Female	9 (7.5)	3 (7.5)	2 (5.0)	4 (10.0)		
$CD4^+$ T-cell count at diagnosis (cells/mm^3)	407.5 (284.2–674.6)	421.2 (305.5–680.2)	403.4 (299.3–670.5)	417.4 (294.3–690.1)	0.377	0.821
$CD4^+$ T-cell count after 7 days (cells/mm^3)	482.7 (335.2–701.5)	505.6 (385.3–698.0)	453.2 (319.2–700.3)	415.4 (288.7–694.5)	1.493	0.044
$CD4^+$ T-cell count after 10 days (cells/mm^3)	511.6 (355.3–707.3)	551.2 (374.2–710.6)	483.3 (337.6–698.2)	410.4 (300.9–700.2)	1.635	0.032
HIV-1 RNA level at diagnosis (log_{10} copies/ml)	6.63 (5.85–6.38)	6.61 (5.74–6.40)	6.59 (5.74–6.39)	6.72 (5.66–7.34)	0.628	0.725
HIV-1 RNA level after 7 days (log_{10} copies/ml)	5.11 (4.55–5.64)	4.86 (4.48–5.01)	5.31 (5.03–5.61)	6.75 (5.54–7.41)	2.304	0.015
HIV-1 RNA level after 10 days (log_{10} copies/ml)	3.89 (3.47–4.30)	3.58 (3.16–3.79)	4.05 (3.55–4.37)	6.76 (5.41–7.53)	1.756	0.029
Postoperative complications	19 (15.8)	3 (7.5)	7 (17.5)	9 (22.5)	–	0.165

Data are expressed as median (interquatile range) or n (%). E/C/F/TAF: Elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide; HIV: Human immunodeficiency virus; IQR: Interquartile range; TDF/3TC/EFV: Tenofovir disoproxil fumarate, lamivudine, and efavirenz.

[337.6, 698.2] cells/mm^3, $P = 0.046$) were observed in the E/C/F/TAF regimen group than in the TDF/3TC/EFV regimen group. Common postoperative complications included surgical site infection, delayed union and nonunion of fractures, thrombosis, pulmonary infection, and renal failure. Twelve months after operation, there were significantly fewer postoperative complications in the E/C/F/TAF regimen group (3/40) compared with those in the TDF/3TC/EFV regimen group (7/40) (7.5% *vs*. 17.5%, $P = 0.031$) [Table 1].

Our studies have shown that treatment with an E/C/F/TAF regimen can suppress the VL to 4.86 (4.48–5.01) and 3.58 (3.16–3.79) log_{10} copies/ml in 7 and 10 days; at the same time, this regimen increased the $CD4^+$ T-cell count, promoted the reconstruction of immune function, and significantly reduced postoperative complications. We found that the E/C/F/TAF regimen was superior to the TDF/3TC/EFV regimen, producing more rapid viral suppression.[6] However, the TDF/3TC/EFV regimen group also suppressed the VL, reaching to 5.31 (5.03–5.61) and 4.05 (3.55–4.37) log_{10} copies/ml within 7 and 10 days. In summary, the therapeutic effect of the TDF/3TC/EFV regimen is inferior to that of E/C/F/TAF regimen for rapidly suppressing VL in a short time.

Funding

This work was supported by the grants from the Capital's Funds for Health Improvement and Research (No. 2018–2-2174), Scientific Research Common Program of the Beijing Municipal Commission of Education (No. KM201810025029) and the Beijing Municipal Science & Technology Commission (No. Z191100006619060).

Conflicts of interest

None.

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How to cite this article: Ma R, Zhang Q, Zhang YS, Xu B, Tong ZW, Zhao CS, Zhao RG. Preoperative rapid suppression of viral load by elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide regimen in human immunodeficiency virus-positive fracture patients significantly reduces postoperative complications. Chin Med J 2020;133:2892–2893. doi: 10.1097/CM9.0000000000001185