The application of HIV-1 proviral DNA in patients with low-level viraemia under antiretroviral therapy

Lv, Shiyun[1]; Bai, Ruojing[1]; Dai, Man[2]; Hua, Wei[1]; Xin, Ruolei[2]; Dai, Lili [1]

1Beijing You'an Hospital Affiliated to Capital Medical University, No. 8, West Toutiao, outside You'anmen, Fengtai District, Beijing, China ; 2Nstitute for STD/AIDS Prevention and Treatment, Beijing Center for Disease Prevention and Control, No. 16, Hepingli Middle Street, Dongcheng District, Beijing, China

Background

One possible approach to characterize drug resistance of low-level viremia (LLV) patients is to sequence HIV proviral DNA. This study analyzed the drug resistance characteristics in DNA of HIV/AIDS patients who developed LLV after antiretroviral therapy (ART) in a hospital in Beijing and evaluated its reliability compared to RNA genotypic resistance test (GRT).

Materials and methods

Peripheral venous blood was collected from HIV-1 infected patients who had been routinely receiving ART for ≥6 months at the STD/AIDS clinic of Beijing Youan Hospital between January 2020 to September 2021 and who developed LLV. HIV-1 DNA and RNA were extracted from concentrated white blood cells and plasma respectively, and the pol gene region of HIV-1 virus was amplified. Combined with past RNA genotype, DNA and RNA genotypes were categorized into three groups: DNA genotypes compared with past RNA genotypes (group 1); comparing with RNA genotypes on the same day (group 2); comparing with past RNA genotypes and RNA genotypes on the same day (group 3).

Results

A total of 154 plasma samples with a viral load of 50-999 copies/mL were collected from 150 patients (Table 1), and 120 sequences were successfully amplified from 108 patients(77.9% amplification success rate). The resistance mutations were identified in 32 patients, with an overall resistance mutation rate of 29.6% (32/108) among which non-nucleoside reverse transcriptase inhibitors (NNRTIs)-associated resistance mutations predominated, accounting for 24.1% (26/108), followed by nucleoside reverse transcriptase inhibitors (NRTIs)-associated mutations and protease inhibitors (PIs)-associated mutations, accounting for 10.2% (11/108) and 5.6% (6/108) respectively. Of the 56, 89 and 47 patients included in groups 1, 2 and 3, the concordance rate of DNA drug resistance mutations were 73.0% (65/89), 75.0% (42/56) and 66.0% (31/47) respectively. Compared with past RNA genotypes, the loss of drug resistance mutations information in DNA genotypes can be obviously examined within all classes of ARVs (Figure 1).

characteristics	Total (n=150)
Sex	
female	8 (5.3)
male	142 (94.7)
Age	
year, median	37(32-46)
HIV transmission route	
MSM	116 (77.3)
heterosexual	15 (10.0)
IVDU	4 (2.7)
NA	15 (10.0)
HIV-RNA at baseline (copies/mL)	
50-200	118 (78.7)
201-400	16 (10.7)
400-999	16 (10.7)
Virological failure has occurred	
Yes	22 (14.7)
No	128 (85.3)
CD4+T cell count at baseline (cells/μL)	488.19 (289.76-699.86)
Time since ART initiation (years)	3.12 (1.10-5.23)
Number of ARVs since ART initiation	4 (3-5)
A total known number of RNA genotypes	1 (1-2)
Duration of follow-up (months)	5.13 (2.97-8.12)

Table 1. Patient characteristics and clinical features

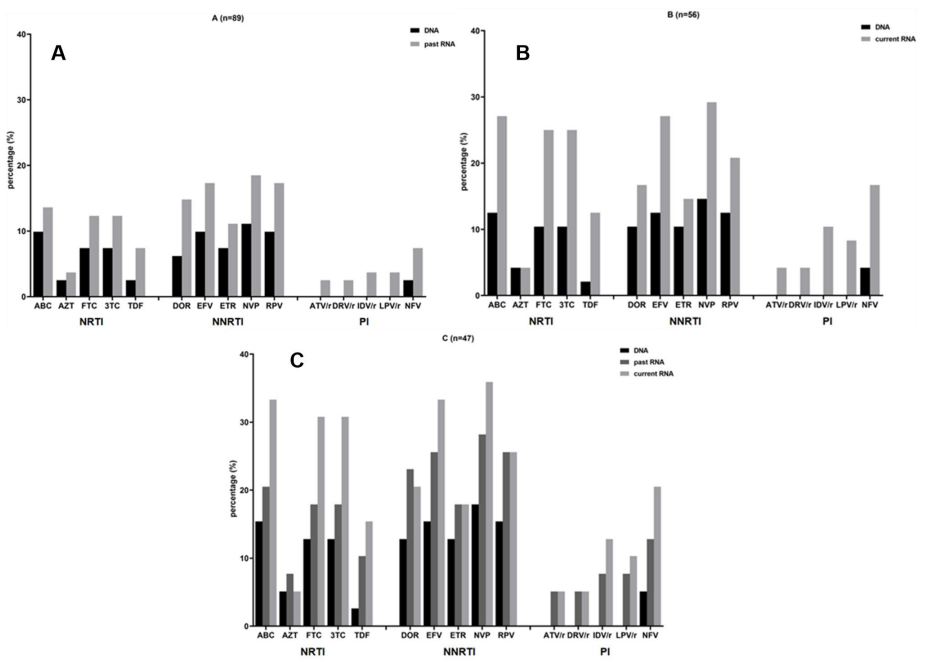

Figure 1. The percentage of proviral HIV-1 DNA genotyping that are resistant to individual ARVs is compared with past RNA genotyping or current RNA genotyping, or past RNA and current RNA genotyping. (A) Group 1, (B) Group 2, and (C) Group 3.

Conclusions

Among LLV patients in Beijing, the drug resistance mutation rate is relatively more common with NNRTIs-related resistance predominating. In the case of LLV, DNA GRT can provide certain resistance information, but the results of RNA GRT is still the gold standard to guide the adjustment of treatment regimens.