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ZDV/3TC to ABC/3TC switch and bone marrow toxicity in the post-HAART era

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ABSTRACT:

The efficacy and safety of HAART regimens based on fixed-dose combination zidovudine/lamivudine (ZDV/3TC) or abacavir/lamivudine (ABC/3TC) have been well studied over the years. Although ZDV is not recommended as first-choice regimen in current guidelines, several patients are still on a ZDV-based regimen. The aim of this retrospective observational study was to evaluate the presence of significant improvements and/or possible side effects after switching from ZDV to ABC in 19 patients with HIV infection on HAART, who switched from a ZDV based regimen to ABC/3TC, at the Outpatient Clinic of Infectious Diseases of the Garibaldi Nesima Hospital, Catania. 13 patients (68%) switched for simplification, 6 (32%) for toxicity. We found no statistically significant changes in HIV viral load, CD4+ count, CD8+ count and CD4/CD8 ratio, hemoglobin levels, creatinine, glucose, GPT, total cholesterol and triglycerides. We found a significant increase in red (p=0.0001) and white (p=0.002) blood cell count and a significant decrease in MCV (p=0.003) and platelet count (p=0.012). This study shows that switching from ZDV to ABC is safe and results in an improvement of MCV, red and white blood cell count. The decrease in platelet count should be confirmed and further analyzed.

Key words: Abacavir, HAART, HIV, Zidovudine.

BACKGROUNDS

The efficacy and safety of the ART regimens based on fixed dose combination zidovudine/lamivudine (ZDV/3TC) or abacavir/lamivudine (ABC/3TC) have been reported over the years. Although ZDV is not recommended as first-choice regimen in current guidelines, several patients are still on a ZDV-based regimen. In fact, patients who are HLA-B5701 negative usually switch from ZDV/3TC to ABC/3TC either for simplification, thus moving from a twice-daily to a once-daily administration, or to avoid drugs toxicity (pre-emptive switch) such as bone marrow impairment.

The aim of this retrospective observational study was to evaluate the clinical and biochemical changes occurring after switch from a ZDV- to an ABC-based regimen.

PATIENTS AND METHODS

All patients switching from a ZDV/3TC to an ABC/3TC-based onewere enrolled in this study at the Outpatient Clinic of Infectious Diseases of the Garibaldi Nesima Hospital, Catania.

The following variables were recorded: gender, age, duration of therapy with ZDV or ABC, reasons for switch and antiretroviral drugs used in association with ZDV or ABC. We also evaluated the following parameters before (T0), 6 and 12 months after switching (T6, T12): HIV RNA viral load (VL), CD4+ and CD8+T-cell count, CD4/CD8 ratio, red blood cell count (RBC), hemoglobin (Hb), MCV, platelet (PLT) count, white blood cell (WBC) count, percentages of neutrophils (N%) and lymphocytes (L%), blood levels of GPT, creatinine, triglycerides, total cholesterol and glucose.

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STATISTICAL ANALYSIS

Non-parametric Wilcoxon testwas used to compare quantitative data. Variables were expressed as number (percentage, %) or median (interquartile range, IQR).

RESULTS

19 patients were enrolled: 8 (42%) were female. Median age was 47 years (IQR 44-58). Median length of therapy with ZDV and ABC was 65 (IQR 55-104.5) and 21 (IQR 14-44.5) months, respectively. 13 patients (68%) switched for simplification (proactive switch), 6 (32%) for toxicity, mainly due to the onset of macrocytic anemia.

Table 1 shows the characteristics of the study population. At T12 no statistically significant changes were observed in HIV viral load, CD4+ count, CD8+ count and CD4/CD8 ratio, hemoglobin levels, creatinine, glucose, GPT, total cholesterol and triglycerides.

On the other hand, we found a significant increase in RBC from 3.6x10^6/µl (IQR 3.5-3.8 x10^6) to 4.2 x10^6/µl (IQR 4.1-4.5 x10^6) (p=0.0001) and WBC from 6000/µl (IQR 4650-7200) to 6800/µl (IQR 6000-9800) (p=0.002), and a significant decrease in MCV, from 112 fl (104-118) to 98 fl (95-99) (p=0.003), and PLT count, from 226000/µl (IQR 198500-255000) to 199000/µl (IQR 180000-216000) (p=0.012).

Table 1. Demographic, viro-immunological and therapeutic parameters of the study population

Parameters	
Age (years), median (IQR)	47 (44-59)
Males/females, n (%)	8 (42)/11 (58)
Lenght of therapy with ZDV/3TC (months), median (IQR)	65 (54-107)
Lenght of therapy with ABC/3TC (months), median (IQR)	21 (12-51)
Switch reason to ABCProactive/ toxicity, n (%)	13 (68)/6 (32)
Number of patients with HIV RNA <20 copies/ml (%)	19 (100%)
CD4 (cells/µl), median (IQR)	615 (368-1104)
CD8 (cells/µl), median (IQR)	777 (529-972)
CD4/CD8, median (IQR)	0,95 (0,56-1,43)

CONCLUSIONS

This study shows that switching from ZDV to ABC is safe and associated with an improvement of the hematological profile of RBC, MCV and WBC values. The decrease in platelet count should be confirmed and further analyzed. Although the small number of patients and the length of the study were not adequate to find other virological or immunological differences, bone marrow toxicity associated with ZDV use should be adequately evaluated and a proactive switch suggested in patients who are still on a ZDV-based regimen.

CONFLICT OF INTEREST:
The authors declare no conflict of interest.

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