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ASSOCIATION BETWEEN NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS RESISTANCE MUTATIONS AND LEVEL OF RESIDUAL HIV-1 VIRAEMIA UNDER ANTIRETROVIRAL TREATMENT IN PATIENTS EXPERIENCING VIROLOGICAL FAILURE

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BACKGROUND: Several studies indicate that viruses carrying nucleoside reverse transcriptase inhibitors (NRTI) mutations show diminished replicative capacity. The aim of this study was to evaluate *in vivo* the virological impact of NRTI resistance mutations on the level of HIV viraemia in patients experiencing virological failure under antiretroviral treatment.

METHODS: A retrospective analysis of 593 treated patients followed in one single institution between 2002 and 2004 was performed. Genotypic resistance testing was performed for all patients in the context of virological failure. According to the French ANRS resistance testing algorithm, the Genotypic Sensitivity Score (GSS) was defined as the number of drugs presumed still effective. The impact of NRTI resistance mutations (thymidine analogue mutations (TAMs), K65R, L74V, Q151M and M184V/I) on the HIV RNA level was studied in univariate analysis. Associate factors with the HIV viraemia were determined using a linear regression model. Factors with a P-value <0.10 in univariate analysis were entered in the multiple linear regression model.

RESULTS: Overall, the main characteristics were: median HIV RNA=4.18 log copies/mL (IQR: 3.72;4.74) and median CD4 cell count=278/mm³ (IR:148;412). According to the IAS-USA list, the median number of NRTI, NNRTI and PI resistance mutations were 4, 0 and 5, respectively. In univariate analysis, the level of HIV RNA was significantly associated with the number of NNRTI and PI mutations, the GSS and the presence of the Q151M or M184I mutations. Inversely, the level of HIV RNA was negatively associated with the CD4 cell count and the presence of the M184V mutation.

The total number of NRTI resistance mutations, the number of TAMs, the K65R and the L74V mutations were not associated with the HIV viraemia level. In multivariate analysis, four factors remained independently associated with the level of HIV RNA: CD4 cell count, GSS and M184V mutation with a lower HIV viraemia and the M184I mutation with a higher HIV viraemia.

CONCLUSION: Among the main NRTI resistance mutations, only the 184 mutation was associated with the level of viraemia: the M184V mutation with reduced viraemia and the M184I mutation with elevated viraemia.

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