

Poster presentation

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Mitochondrial effects of 3 years of CD4-guided HIV treatment interruption

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Purpose of the study

Mitochondrial toxicity of antiretroviral treatment (ARVT), especially nucleoside-analogues' capacity to inhibit DNA-polymerase gamma, has been proposed as the ethio-pathological mechanism which underlies many of the secondary effects of HIV therapy. The aim of the present study was to evaluate whether a prolonged CD4 cell-guided ARVT interruption could reverse mitochondrial toxicity.

Methods

We included 38 patients from the TIBET study whose peripheral blood mononuclear cells (PBMCs) had been collected at baseline, at 96 and at 144 weeks throughout the study period; 18 of them discontinued ARVT along this time and 20 maintained therapy. Mitochondrial DNA (mtDNA) content was measured by real-time PCR and mitochondrial function through the spectrophotometric measurement of cytochrome C oxidase (COX) enzymatic activity normalised by mitochondrial content using citrate synthase (CS) activity (COX/CS ratio).

Summary of results

Whereas mtDNA content showed a similar progressive decrease throughout the study period in both study arms,

only for the control group was this significant either at week 96 (15% decrease, $p = 0.03$) or at week 144 (34% decrease, $p = 0.01$). The COX/CS ratio significantly improved in patients who interrupted antiretroviral therapy in comparison with those who did not, especially at week 96 (130% increase, $p = 0.06$). The univariate and multivariate analysis performed showed that only CD4+ T-cell value at the time of ARVT initiation and time with viral suppression before the study were associated with changes in the COX/CS ratio.

Conclusion

PBMCs' mitochondrial function improved during a prolonged ARVT interruption in spite of mtDNA content decrease. The absence of correlation between mitochondrial parameters suggests the existence of a mitochondrial transcriptional or translational upregulation mechanism which could be increasing mitochondrial protein expression in the absence of mtDNA content improvement, or also could be the reversion of an ARV-mediated mitochondrial toxicity mechanism that was previously disturbing mitochondrial function through a DNA polymerase gamma-independent way.

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