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MITOCHONDRIAL IMPAIRMENT IN MONONUCLEAR CELLS OF HYPERLACTATEMIC PATIENTS ON HAART

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OBJECTIVES: Hyperlactataemia is one of the most serious secondary effects developed by HIV patients on HAART. Mitochondrial toxicity of antiretroviral drugs, especially nucleoside analogues, has been suggested to underlay HAART-related hyperlactataemia. Hyperlactatemic mitochondrial impairment has been demonstrated on liver and muscle invasive studies. However, few approaches have been performed on peripheral blood mononuclear cells (PBMC), all containing reduced numbers of patients and exclusively based on mitochondrial DNA (mtDNA) quantification. We herein show mitochondrial genetic and biochemical analysis in PBMCs of HIV patients on HAART during an acute hyperlactatemic episode and after recovery.

METHODS: We studied PBMCs of 20 HIV patients on HAART undergoing an hyperlactatemic crisis and after clinical recovery with respect to asymptomatic HIV subjects on HAART, naïve individuals and non-infected controls. All subjects were matched by age, gender and those on treatment had similar HAART backgrounds. We measured mtDNA and mtRNA content by quantitative real- time PCR, enzymatic activities of mitochondrial respiratory chain (MRC) complexes II, III, IV and mitochondrial content by spectrophotometry and mitochondrial protein synthesis by western blot.

RESULTS: MtDNA content and mitochondrially encoded enzymatic activities (III and IV) were decreased during the hyperlactatemic phase (1.49 ± 0.22 versus 1.65 ± 0.21 , $P=ns$; 143.72 ± 22.82 versus 214.12 ± 27.63 , $P=0.002$; 49.18 ± 6.83 versus 84.44 ± 9.84 , $P=0.001$, respectively), as well as mitochondrial amount (72.82 ± 7.97 versus 106.35 ± 14.48 , $P=0.009$) and mitochondrial protein

expression (0.9 ± 0.06 versus 1.03 ± 0.05 , $P=0.039$), all with respect to clinical recovery. Conversely, mtRNA content was increased (32.5 ± 14.86 versus 20.61 ± 3.67 , $P=ns$) and the nuclear-encoded MRC complex II was conserved and similar to controls. After clinical recovery, studied parameters tend to achieve values found on asymptomatic individuals, which were lower than ranges of naïve or non-infected controls.

CONCLUSIONS: HAART-related hyperlactataemia is associated with decreases in mtDNA content (although non-significant), mtDNA-encoded MRC enzymatic activities III and IV, mitochondrial amount and mitochondrial protein synthesis, despite the increase in mtRNA content (although non-significant). After the crisis all these parameters tend to normality.

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