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Neurotoxic effect of antiretroviral agents on CNS

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Background

Toxic effects of highly active antiretroviral therapy (HAART) emerge in all organs and are well known in the peripheral nerve system. The neurotoxic impact of the antiretroviral agents ddI, ddC, and d4T as part of HAART on neurocognitive function during HIV-infection was studied.

Methods

In a retrospective cross-sectional study, parameters of event-related potentials (ERPs) were analysed from patients receiving HAART with ddI, ddC, d4T for at least 3 month (n = 60) with a mean intake of 24 ± 6 months (mv ± 1 SD). Results were compared to a control group receiving HAART without these substances. The latency of P2, N2, P3 and the amplitude of P3 of ERPs and the mean reaction time were analysed. Cognitive impairment (CI) and distal-symmetric polyneuropathy (DSP) were investigated using routine clinical and neurophysiological methods.

Summary of results

Statistical analysis revealed no significant difference for age, sex, CDC-stages, CD4+-cell count and plasma viral load between both groups. Patients treated with ddI, ddC and d4T showed a significant latency prolongation of the P3 component of ERP of 448 ± 45 vs. 431 ± 33 msec (mv ± 1 SD) ($p < 0.02$). Routine clinical and neurophysiological methods revealed significant higher prevalence of CI and DSP in the group receiving HAART with ddI, ddC or d4T ($p < 0.009$).

Conclusion

In concordance with earlier publications, these results show using clinical and neurophysiological methods that ddI, ddC and d4T cause additionally, besides HIV infection itself, cognitive impairment in HIV-infected patients. It is assumed that these alterations are induced by the toxic impact of ddI, ddC, and d4T on β-polymerase in mitochondriae of the CNS. As shown in newborns, this effect may last up to 2 years after finishing HAART. Neurotoxic effects of ddI, ddC, and d4T represent an additional factor in the development of newer forms of HIV-associated neurocognitive disorders.