IS HIV-NEUROPATHY THE SAME IN PATIENTS TREATED WITHOUT STAVUDINE?

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Background: HIV patients can experience a debilitating neuropathy (HIV-SN) that reflects both their HIV status and neurotoxic NRTI (usually stavudine). However in the era of ART without stavudine, there are reports of patients with numbness and burning sensations in their legs consistent with HIV-SN. We are addressing the prevalence of HIV-SN and the underlying mechanisms in patients on ART without neurotoxic NRTIs.

Methods: We present data from Cipto Mangunkusumo Hospital, Jakarta. HIV patients (n=197) who had received ART without stavudine for >12 months, and who submitted to neurological examinations. The Brief Peripheral Neuropathy Screening Tool was used to assess HIV-SN. A sub-group of patients provided distal leg skin biopsies to examine peripheral nerves. These were stained to visualise CCR2, CCR5, CXCR3, CXCR4 or CX3CR1, and CD3 or CD14 using 4-colour confocal microscopy.

Results: The prevalence of HIV-SN was 14%, - below half that seen in the same clinic when patients received stavudine (34% in 2006). A HIV burden >500 copies/ml and nadir CD4 count <200 cells/ul were significant risk factors for HIV-SN ($p<0.05$), which is in – in contrast with 2006 when age and height were the clearest determinants. CCR2, CCR5, CXCR3 and CXCR4 were upregulated in HIV+ patients' skin. Some positive cells associated with damaged nerves suggesting a role in the pathogenesis of HIV-SN. Others were distributed along small blood vessels in a pattern consistent with extravasation. CX3CR1 was minimally upregulated but was also seen in HIV-SN skin sections. CX3CR1 was more evident on CD14+ cells, whilst other receptors were expressed on CD3+ cells.

Conclusion: HIV-SN affects a reduced number of HIV patients treated without stavudine but remains a significant debilitating condition. Chemokines may contribute to the underlying pathology as receptors were visualized on inflammatory cells adjacent to damaged nerves. The relative roles of HIV itself and non-stavudine ART are now being explored in longitudinal cohorts of patients treated in South Africa. As in Indonesian, HIV-SN prevalence is halved in Africans on ART without stavudine. However there remains a two-fold greater prevalence of the neuropathy in patients of African ancestry relative to Indonesians. Ongoing studies of the genetic factors affecting neuropathy in South African and Indonesian patents treated with and without stavudine may reveal common or distinct pathogenic mechanisms. Early data will be presented and the many people who have contributed to these programmes will be acknowledged

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