SENSORY NEUROPATHY AFFECTS 40% OF HIV+ SOUTH AFRICANS DESPITE SAFER TREATMENTS AND 46% OF RISK IN THIS GROUP CAN BE PREDICTED BY ONE GENOTYPE PLUS DEMOGRAPHIC FACTORS!

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Background: HIV-associated sensory neuropathy (HIV-SN) is a small fibre neuropathy seen in 60% of South African HIV+ patients treated with stavudine. We established age, height and polymorphisms in adjacent genes - P2X7R, P2X4R and CAMKK2 - as markers of susceptibility of HIV-SN in South African HIV+ patients receiving stavudine (model p<0.0001, n=143, Pseudo R²=0.19).

Stavudine has now been phased out worldwide. The incidence of HIV-SN decreased from 34 to 14% in Jakarta, Indonesia. Susceptibility was then most clearly linked to lower CD4 T-cell counts, persistent HIV replication and three SNP in CAMKK2. Here we address whether the incidence of HIV-SN and its risk factors remain the same in South African patients treated without stavudine.

Methods: 75 HIV+ patients with African ancestry were recruited at clinics in Johannesburg as they commenced HIV treatment. Patients were assessed for neuropathy and thorough clinical details recorded at an initial visit and at follow-up appointments at 2, 4 and 6 months. Patients were genotyped for polymorphisms in the genes P2X7R, P2X4R, CAMKK2 and ANAPC5.

Results: 29 of the 75 patients (38.7%) developed HIV-SN with 9/29 (12%) diagnosed prior to commencing HIV treatment. Two P2X7R, one P2X4R, four CAMKK2 and one ANAPC5 SNP associated with HIV-SN in bivariate analyses. The optimal logistic regression model predicting HIV-SN included one P2X7R and three CAMKK2 SNP independently associated with HIV-SN after correcting for greater weight, lower CD4 T-cell count and a history of tuberculosis (model p<0.0001, n=69, pseudo R²=0.457). This model explains a staggering 45.7% of the risk of HIV-SN in this group.

Conclusion: Our findings confirm a role for CAMKK2 in HIV-SN independent of stavudine and ethnicity. We are now evaluating whether the effects of CAMKK2 extend to the brain by assessing neurocognitive loss in Indonesian HIV+ patients treated without stavudine.

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