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BETTER ANTIRETROVIRAL PENETRATION INTO THE CENTRAL NERVOUS SYSTEM IS ASSOCIATED WITH LOWER CSF VIRAL LOAD

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BACKGROUND: The importance of ART penetration into the central nervous system (CNS) for HIV suppression in cerebrospinal fluid (CSF) and neurological improvement is controversial. The objective of this study was to evaluate whether CNS ART penetration, as measured by an overall index, the total penetration score, is associated with lower CSF viral load.

METHODS: We enrolled 374 HIV⁺ persons in the CHARTER study, a North American observational cohort where taking at least 1 ART and having CSF and plasma viral loads measured. Their ART were assigned a penetration score of 0 (low), 0.5 (intermediate), or 1 (high), based on published data on CSF concentrations and/or chemical properties (see Table). Summing the individual penetration scores for each ART in a regimen yielded a total penetration score.

Increasing CNS Penetration			
→			
	0	0.5	1
NRTIs:	TFV	d4T	ZDV
	ddl	3TC	
	ddC	FTC	ABV
NNRTIs:		EFV	DLV
			NVP
PIs:	NFV	APV	APV-r
	SQV	f-APV	f-APV-r
	SQV-r	ATV	ATV-r
	RTV	IDV	IDV-r
	TPV-r		LPV-r
Fusion Inhibitors:	T-20		

RESULTS: The median penetration score was 1.5 (IQR 1 to 2). Higher penetration scores correlated with lower CSF viral load ($p = 0.006$). In contrast, penetration scores did not correlate with plasma viral load ($p = 0.26$). Since higher penetration scores also correlated with larger numbers of ART, a multivariate regression was performed to determine if this accounted for the observed effect. Higher penetration scores (parameter $p = 0.001$) were still associated with lower CSF viral load even after adjusting for total number of ART and plasma viral load (model $r^2 = 0.34$, $p < 0.0001$).

CONCLUSIONS: These findings support that better penetration of ART across the blood-CSF barrier leads to better control of HIV replication in CSF. Since inhibition of HIV replication in the CNS is important in treating patients who have HIV-associated neurocognitive disorders, they may benefit from CNS-targeted ART therapy.

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