Implications of Cognitive Impairment on Antihypertensive Medication Use in HIV

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BACKGROUND

- Age-related comorbidities, such as cardiovascular disease and neurocognitive impairment, are more common among people with HIV (PWH). [1]
- Hypertension (HTN) has been implicated in cognitive decline.
- Hypertension is a risk factor for cognitive decline, and certain antihypertensives with anticholinergic properties may exacerbate this risk, particularly in PWH who are already vulnerable to neurocognitive impairment.[2]
- We hypothesized that worsening neurocognitive performance would be associated with increasing numbers of antihypertensives prescribed to hypertensive PWH and compared this in PWH and PWoH.

METHODS

- This longitudinal analysis encompassed seven visits over five years, enrolled between 1999 and 2022.
- Participants were included if they reported HTN or used antihypertensives. All participants underwent comprehensive cognitive assessments, and their global cognitive performance was evaluated using demographically corrected T-scores.
- The association between the global T-score and the number of antihypertensives was evaluated using generalized linear mixed-effects models. Summary regression-based change score (sRCS) was analyzed as an indicator of global performance over time.

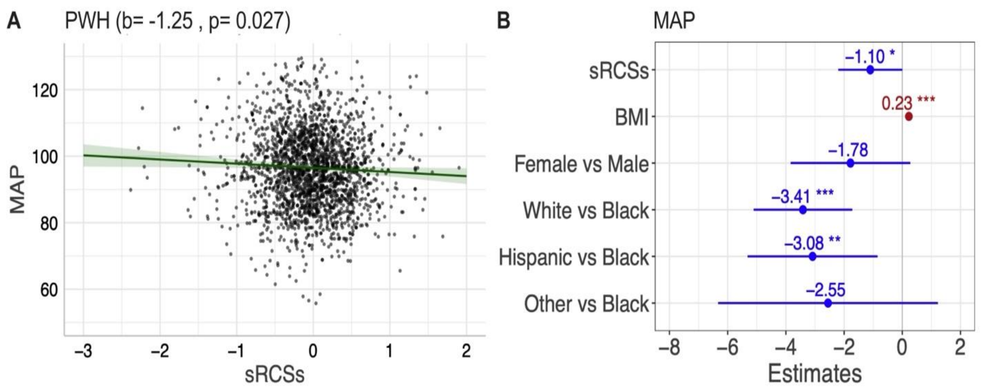
Table 1. Baseline demographics and clinical characteristics by HIV serostatus

Variables	All (n=1457)	PWH (n=1158)	PWoH (n=272)	P-value*
Demographic Characteristics				
Age (years), M (SD)	50.7 (10.8)	49.67 (10.4)	55.15 (12.3)	**<0.0001**
Education (years), M (SD)	13.3 (2.84)	13.21 (2.79)	13.58 (3.01)	0.052
Male, N (%)	1171(79.88%)	987 (83.29%)	178 (65.44%)	**<0.0001**
Ethnicity, N (%)	-	-	-	**<0.0001**
- White, non-Hispanic	745 (50.85%)	581 (49.07%)	160 (58.82%)	
- Black	432 (29.42%)	383 (32.35%)	48 (17.65%)	
- Hispanic	242 (16.52%)	179 (15.12%)	(21.69%)	
- Other	46 (3.14%)	41 (3.46%)	5 (1.84%)	
On antihypertensive medication	711 (59.15%)	548 (59.51%)	156 (57.35%)	
-Beta blockers	234 (19.46%)	191 (20.73%)	42 (15.44%)	
-CCB	137 (11.34%)	95 (10.31%)	41 (15.07%)	0.055
-ARB	57 (4.75%)	38 (4.12%)	19 (7.00%)	
-ACE inhibitor	247 (20.47%)	183 (19.87%)	61 (22.42)	
-Alpha blockers	47 (3.68%)	41 (4.01%)	6 (2.00%)	
-Alpha agonist	32 (2.88%)	28 (3.27%)	4 (1.27%)	
-Diuretics	90 (7.48%)	74 (8.00%)	15 (5.55%)	
-Potassium sparing	30 (2.12%)	25 (2.11%)	5 (2.23%)	
-Combination therapy	204 (17.00%)	149 (16.17%)	53 (19.50%)	-
On anticholinergic meds	1114 (76.00%)	930 (78.51%)	177 (65.04%)	**<0.0001**
Neurocognitive impairment	612 (41.67%)	542 (44.21%)	84 (30.88%)	**<0.0001**
Global T-scores	46 (7.46)	45.7(7.61)	47.8 (6.53)	**0.004**
HIV Characteristics				
Duration of HIV (years), M (SD)	-	14.4 (8.44)	-	
AIDS diagnosis, N (%)	-	828 (70.17%)	-	
Current CD4, median (IQR)	500 (276, 752)	462 (256, 699)	-	
Nadir CD4, median (IQR)	169 (36, 350)	127 (28, 270)	-	
ART ON, n (%)	-	938 (79.9%)	-	
Plasma HIV RNA ≤ 200 copies/mL, n (%)	-	738 (67.3%)	-	

*The chi-square and independent samples t-test were used to compare categorical variables and group means, respectively. CCB: calcium channel blockers; ARB: Angiotensin II receptor blockers; ACE: angiotensin-converting enzyme

PWH with declining neurocognitive function were prescribed increasing numbers of antihypertensives over time. Regular monitoring of neurocognitive function in PWH on antihypertensive therapy could help reduce polypharmacy, minimize side effects, and avoid drug-drug interactions.

Figure 1. Association between MAP and sRCS in univariable (A) and multivariable analyses in PWH (B) sRCS: summary regression change score; MAP: mean arterial pressure.



RESULTS

- Among 1158 hypertensive PWH (79.9% were on ART), every 10-unit increase in global T-score was associated with a decrease of 8.4% in antihypertensive count; that is, a higher global T-score was associated with lower antihypertensive medication count in PWH (p=0.027). The significant association remained after adjusting for covariates in multivariable analysis (p=0.014). Global T-score was not associated with the antihypertensive count in PWoH (p=0.50).
- PWH had lower mean arterial pressure (MAP) than PWoH after adjusting for demographics (β=-5.05, p=2.3e-11). In PWH, an association between MAP and sRCS suggested that those with cognitive improvement had lower MAP (p=0.027). PWH taking more anticholinergics were more likely to have worse cognitive performance over time (p<0.001). This relationship was not seen in PWoH (p=0.68).

Table 2. Associations between antihypertensive medication count and global T-score and demographic and clinical variables using Poisson GLMM, stratified by HIV status.

	Univariable analysis		Multivariable analysis	
Predictor	**RR (95% CI)**	**p-value**	**RR (95% CI)**	**p-value**
PWH				
Global T-score[a]	0.916 (0.848,0.990)	**0.027**	0.907 (0.840,0.981)	**0.014**
Age (decades)[a]	1.14 (1.07,1.21)	**<0.001**	1.13 (1.07,1.21)	**<0.001**
BMI	1.004 (0.994,1.015)	0.41	1.008 (0.997,1.018)	0.15
Sex	0.93 (0.77,1.123)	0.45	-	-
Ethnicity		**0.003**		**0.005**
Hispanic (vs. Black)	0.734 (0.592,0.91)	**0.005**	0.722 (0.582,0.896)	**0.003**
White (vs. Black)	1.04 (0.888,1.219)	0.62	0.988 (0.843,1.159)	0.89
Other (vs. Black)	1.187 (0.836,1.687)	0.34	1.174 (0.829,1.663)	0.37
Nadir CD4[b]	1.004 (0.994,1.013)	0.45	-	-
plasma HIV RNA[c]	0.989 (0.946,1.035)	0.65	-	-
PWoH				
Global T-score[a]	0.994 (0.977,1.012)	0.50	0.995 (0.978,1.013)	0.58
Age (decades)[a]	1.26 (1.13,1.39)	**<0.001**	1.305 (1.16,1.438)	**<0.001**
BMI	1.01 (0.994,1.026)	0.24	1.019 (1.003,1.036)	**0.02**
Sex	1.022 (0.79,1.324)	0.87	-	-
Ethnicity		0.52	-	-
Hispanic (vs. Black)	0.923 (0.629,1.354)	0.68	-	-
White (vs. Black)	0.813 (0.588,1.126)	0.21	-	-
Other (vs. Black)	0.68 (0.297,1.56)	0.36	-	-
Nadir CD4[b]	1.006 (0.978,1.035)	0.66	-	-

[a] The unit is 10; square root and log10 transformation; BMI = body mass index; RR = rate ratio

Table 3. Association between global T- score and anticholinergic medications in a stratified analysis by HIV status using mixed-effects models, adjusting for covariates.

		PWH		PWoH	
Outcome	**Predictor**	**ES (95% CI)**	**p-value**	**ES (95% CI)**	**p-value**
Global T-score	anticholinergic count	-0.27 (-0.38, -0.15)	**<0.001**	0.07 (-0.26,0.40)	0.68
	Ethnicity	-	**<0.001**	-	**<0.001**
	Hispanic (vs. Black)	-1.52 (-2.03, -1.00)	**<0.001**	-2.37 (-3.50, -1.25)	**<0.001**
	White (vs. Black)	-1.15 (-1.54, -0.76)	**<0.001**	-1.77 (-2.73, -0.82)	**<0.001**
	Other (vs. Black)	-0.88 (-1.62, -0.14)	**0.02**	-2.75 (-4.16, -1.33)	**<0.001**
	Nadir CD4[a]	0.03 (0.01, 0.05)	**0.005**	-	-
	Plasma HIV RNA[b]	-0.04 (-0.10, 0.01)	0.14	-	-
	BMI	-	-	0.04 (0.01,0.07)	**0.004**
	Time		0.087	-	-

CONCLUSIONS

PWH with declining neurocognitive performance over time were prescribed increasing numbers of antihypertensives, suggesting that their providers were increasing the number because of either treatment refractory HTN or poor adherence. Providers should monitor neurocognitive performance in PWH on antihypertensives to optimize treatment regimens, reduce polypharmacy, and avoid anticholinergic burden.

References

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