Anticholinergic Drug Use in Patients ≥65 Years Old of the Swiss HIV Cohort Study

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Introduction

- Exposure to medications with anticholinergic (ACH) activity has been associated with neurocognitive impairment (NCI) and dementia.[1-4]
- Concomitant use of ACH medications may result in increased ACH burden, but there is lack of consensus regarding the most appropriate method for identifying ACH drugs and calculating ACH burden.[5-12]
- Elderly patients are at increased risk for ACH medication side effects due to reduced cholinergic function and reduced number of cholinergic receptors.[13]
- People living with HIV (PLWH) are also more likely to have NCI as they age.[14] Additional risk factors for NCI in PLWH include duration of HIV infection, CD4 cell count, chronic inflammation, antiretroviral therapy (ART) toxicity, higher rates of depression, cardiovascular events, previous central nervous (CNS) infections and education level, making this population especially vulnerable to ACH effects.[15-19]
- Study aims:
  1. Identify medications with ACH activity.
  2. Determine the prevalence of prescribed ACH drugs for patients ≥65 years of age within the Swiss HIV Cohort Study (SHCS).
  3. Ascertain if there is an association between ACH medication use and self-reported neurocognitive impairment using the European AIDS Clinical Society (EACS) cognitive screening questions.

Methods

Identification of Anticholinergic Medications

- A review of the literature and commonly used ACH drug lists/scales was performed by two investigators with expertise in pharmacology to identify potential medications with ACH activity.
- Further review of the literature was conducted to confirm documented ACH activity and supporting ACH side effect profile; CNS penetration was also evaluated. Medications without documented evidence were excluded.
- ACH medications were given a score of 1 to 3 based on evidence of ACH activity and potential cognitive side effects; 1 indicating low activity; 3 indicating high activity.

Assessment of Anticholinergic Medication Use in SHCS

- This was a cross-sectional medication review performed in July 2019.
- Patients were included if they were ≥65 years of age and were actively followed in the SHCS (≥2 visits within 12 months).
- Anticholinergic medication use was collected and scored.
- Additional data collected included: demographics, non-ACH medications, and responses to the EACS cognitive screening questions.
- Association between ACH burden and neurocognitive complaints was evaluated using the self-reported NCI questions addressing memory loss, attention difficulties, and slowing of reasoning ability.

Results

Table 1. Patient Characteristics

	All Patients (N=1019)	Patients with ACH Drug (N=200)	Patients with no ACH Drug (N=819)	p-value*
Median age (IQR)	70 (67-74)	70 (67-75)	70 (68-74)	0.58
Male sex, %	82.0	78.5	82.9	0.15
CD4 cell count <200 cells/mm^3, %	3.3	5.5	2.8	0.06
Nadir CD4 <200 cells/mm^3, %	60.0	59.5	60.1	0.88
HIV viral load <50 copies/mL, %	95.5	96.0	95.4	0.69
Depression symptoms**, %	10.6	33.0	5.1	<0.001
ART Type, %				0.47
NNRTI-based	22.2	18.5	23.1	
PI-based	4.7	3.5	5.0	
INSTI-based	50.2	50.2	49.8	
Other	21.7	24.5	21.0	
No ART	1.2	1.5	1.1	
Mean # co-medications	5.13 ± 3.6	7.96 ± 4.1	4.44 ± 3.0	<0.001
Polypharmacy, %	50.2	81.0	42.7	<0.001

*Determined using independent-samples median test to compare medians, chi-square for categorical variables, and student t-test for continuous variables
**Self-reported symptoms within preceding 6 months
IQR = interquartile range; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; INSTI = integrase strand transfer inhibitor; polypharmacy = ≥5 non-HIV medications

- 200 (19.6%) patients in SHCS were receiving ≥1 medication with ACH activity (average ACH score of 1.7).
- Antidepressants were the most commonly prescribed class of medications with ACH activity (see Table 2).
- Gender and age were not associated with ACH drug use.
- Polypharmacy was associated with ACH drug use (OR 5.71; 95% CI 3.91-8.35).

Table 2. Most Commonly Prescribed Medications with Anticholinergic Activity (N=256)

ACH Score 1	%	ACH Score 2	%
Mirtazepine	9.8	Quetiapine	2.7
Citalopram	8.6	**ACH Score 3**	**%**
Escitalopram	7.5	Trimipramine	3.9
Duloxetine	6.6	Paroxetine	3.1
Sertraline	5.5		
Glycopyrronium	3.5		
Ranitidine	2.7		
Fluoxetine	2.7		

ACH Score 1 = low ACH activity; ACH Score 2 = moderate ACH activity; ACH Score 3 = high ACH activity

Results

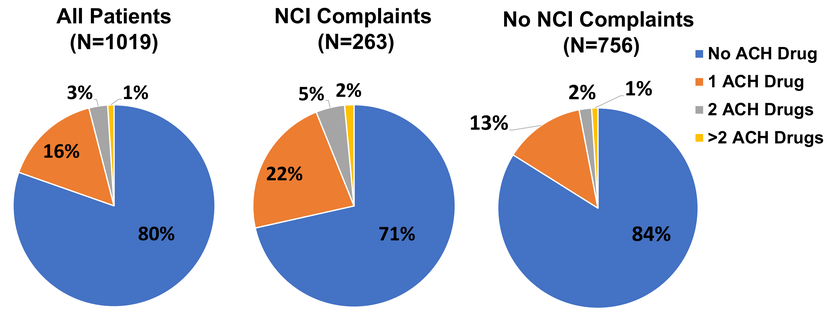

Figure 1. Total Number of Anticholinergic Drugs

In the multivariate analysis patients were more likely to have self-reported NCI if they were ≥70 years of age and had self-reported symptoms of depression within the preceding 6 months. The use of an ACH drugs had an adjusted OR of 1.42 (95% CI 0.97-2.09; p=0.06).

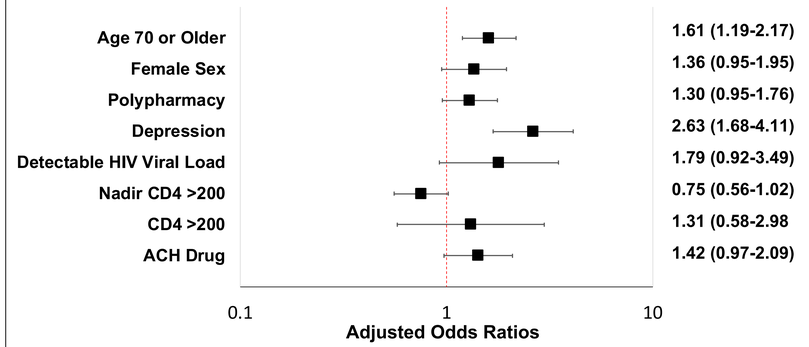

Figure 2. Predictors of NCI in All Patients

In a subgroup analysis of participants without depression (N=911), adjusted for age, gender, CD4, nadir CD4, viral load, and polypharmacy, self-reported NCI was associated with the use of an ACH drug (OR = 1.64; 95% CI 1.08-2.51; p=0.02)

Conclusion

- **ACH drug use is common in elderly PLWH and may contribute to self-reported NCI.**
- **The effect of ACH drugs on NCI warrants further evaluation using more comprehensive neurocognitive tests.**

References

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