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Polypharmacy, anticholinergic burden, and drug-drug interaction assessment in people living with HIV harboring a 4-class resistance: data from the PRESTIGIO Registry

M. Mazzitelli[1], D. Pontillo[2], T. Clemente[2], A. Di Biagio[3], G. Cenderello[4], S. Rusconi[5], B. Menzaghi[6], C. Fornabaio[7], E. Garlassi[8], M. Zazzi[9], A. Castagna[2], A. Cattelan[1] on behalf of the PRESTIGIO Study Group

1.Padua University Hospital, Padua 2. San Raffaele Scientific Institute, Milan, 3. San Martino Hospital, Genova, 4. Sanremo Hospital, Sanremo, 5. ASST Ovest Milanese, Legnano, 6. ASST della Valle Olona, Busto Arsizio, 7. ASST Cremona, Cremona, 8. Acrispedale S. Maria Nuova, Reggio Emilia, 9. University of Siena, Italy

Purpose

Over the last years, assessment of drug-drug interactions (DDIs) and anticholinergic burden (ACB) has emerged as a clinical problem, especially in people living with HIV (PLWH) on polypharmacy. PLWH and a resistant virus to all 4 classes of antiretrovirals (4DR-PLWH) often require complex treatment regimens[1], potentially causing DDIs.

Methods

This is a cross-sectional study, including 4DR-PLWH of the PRESTIGIO Registry (multicenter Italian cohort) taking at least one non-antiretroviral drug. Polypharmacy was defined as taking ≥ 5 non-antiretroviral drugs/person. The cumulative ACB of one or more drugs with anticholinergic activity, was calculated using the ACB scale: 0= no AC effect, 1-2= low/moderate risk, ≥3= high anticholinergic risk. DDIs evaluated from the Liverpool database. Characteristics of people classified according to ACB score were compared using the Kruskal-Wallis test; Spearman's correlation coefficient calculated to assess linear relationship.

Results (I)

Overall, 172 4DR-PLWH were evaluated: 62 (27.1%) on polypharmacy, 109 (63.4%) treated with an INSTI-based regimen, 124 (72.1%) using a boosting agent, and 72 (41.8%) with 4 or more antiretrovirals. Other characteristics in Table 1. Based on ACB scale, 33/172 (19.2%) and 11/172 (6.4%) had a low/moderate and high AC risk, respectively. The most common drugs for ACB are reported in Table. 2.

Results (I)

The high ACB was significantly related to the number of drugs/person (r =0.327, p=<.0001) and the number of previous clinical event (r =0.222, p=0.004). Overall, we found 258 DDIs between ARVs and comedications in 115 (66.8%) PWH, and 14 (8.1%) PLWH received contraindicated drug combinations (Table 3).

Table 1. Demographic, immunologic, virologic characteristics according to ACB score.

Variable	Overall (N=172)	Score ACB ≥3 (n=11)	Score ACB=1-2 (n=33)	Score ACB=0 (n=128)	P-value
Age (years), median (IQR)	49.95 (45.6 – 56)	51.25 (45.34 – 55.2)	49.87 (46.3–56)	49.82 (45.5–54)	0.726
Male Gender, n (%)	130 (75.6)	10 (90.9)	26 (78.8)	94 (73.4)	0.386
ART duration (years), median (IQR)	25.76 (22.3–28.7)	26.16 (19.4–29)	26.25 (22.3–29)	25.72 (22.3–28.4)	0.744
CD4+ cell count (cells/µL), median (IQR)	537 (331.5–818)	574 (372 - 628)	414 (326-740)	537 (338.5–843)	0.657
HIV-RNA <50 (copies/mL), median (IQR)	121 (70.3)	9 (81.8)	25 (75.8)	87 (68)	0.187
History of MACEs, n (%)	22 (12.9)	1 (9.1)	10 (30.2)	11 (8.7)	0.114
History of Malignancies, n (%)	25 (14.5)	3 (27.3)	5 (15.2)	17 (13.3)	0.126
History of Hypertension, n (%)	35 (20.3)	2 (18.2)	7 (21.2)	26 (20.3)	0.977
History of Neuropsychiatric diseases, n (%)	39 (22.7)	9 (81.8)	7 (21.2)	23 (18)	0.0008

Table 3. Summary of DDIs in the PRESTIGIO Registry

	Overall n=258		Potential weak		Potential		Do not coadminister	
Antiretroviral causing DDIs	n	%	n	%	n	%	n	%
Ritonavir	115	44,6	42	16,5	65	25,2	8	3,1
Cobicistat	79	30,6	28	11,0	47	18,2	4	1,6
Etravirine	27	10,5	14	5,5	13	5,0	0	0,0
TAF/FTC or TDF/FTC	7	2,7	6	2,4	1	0,4	0	0,0
Dolutegravir	8	3,1	2	0,8	6	2,3	0	0,0
Bictegravir	3	1,2	0	0,0	3	1,2	0	0,0
Fostemsavir	7	2,7	2	0,8	5	1,9	0	0,0
Doravirine	1	0,4	1	0,4	0	0,0	0	0,0
Rilpivirine	4	1,6	2	0,8	2	0,8	0	0,0
Lamivudine	2	0,8	2	0,8	0	0,0	0	0,0
Atazanavir	3	1,2	0	0,0	1	0,4	2	0,8
Maraviroc	1	0,4	0	0,0	1	0,4	0	0,0
Zidovudine	1	0,4	0	0,0	1	0,4	0	0,0

Conclusion

In 4DR-PLWH, polypharmacy, and proportion of people with moderate/high AC burden were high, as well as the number of DDIs detected. As the use of boosted agents is often not avoidable in PLWH with multidrug resistance, a multidisciplinary approach among specialists of different fields is strongly encouraged.

Table 2. Description of polypharmacy/comedication according to ACB score.

Variable	Overall (N=172)	Score ACB ≥3 (n=11)	Score ACB=1-2 (n=33)	Score ACB=0 (n=128)	P-value
Antidepressants	26 (15.1%)	10 (90.9%)	5 (15.1%)	11 (8.6%)	<0.0001
Dyslipidaemia drugs	68 (39.5%)	6 (54.5%)	12 (36.4%)	50 (39.1%)	0.552
Beta-blockers	51 (29.7%)	4 (36.4%)	17 (51.5%)	30 (23.4%)	0.006
Diuretics	23 (13.3%)	1 (9.1%)	14 (42.4%)	8 (6.3%)	<.0001
Other Hypolipidemic Drugs	26 (15.1%)	2 (18.2%)	6 (18.2%)	18 (14%)	0.924
Antiplatelets	40 (23.4%)	3 (27.3%)	11 (33.3%)	26 (20.3)	0.053
Ace-inhibitors	42 (24.4%)	2 (18.2%)	6 (18.2%)	34 (26.6%)	0.536
Sartans	17 (9.9%)	1 (9.1%)	4 (12.1%)	12 (9.4%)	0.891
Calcium channel blockers	20 (11.6%)	0 (0%)	7 (21.2%)	13 (10.2%)	0.097

References

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Corresponding author: m.mazzitelli88@gmail.com