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Editorial

Mind the polypharmacy in people living with HIV. A new challenge for the fourth 90



Atención a la polifarmacia en las personas que viven con VIH. Un nuevo reto para el cuarto 90

The efficacy of antiretroviral therapy (ART) has improved the life expectancy of people living with HIV (PLWH) ¹. However, they experience premature aging compared to those of the same biological age who are not infected ². This leads to a higher prevalence of comorbidities, multiple physician involved in patient care and usually increasing polypharmacy ³ with high level of medication regimen complexity. All of them are risk factors for adverse events and drug-drug interactions. ATHENA observational cohort ⁴ estimates that by 2030, 84% of PLWH will have at least one non-communicable disease (NCD) and 28% three or more NCD. Related to medication, 54% will be receiving a non-HIV medication and 20% three or more non-HIV medications.

In this regard, Morillo et al. ⁵ analyzed not only the prevalence of polypharmacy but also the complexity of treatment in outpatient PLWH who were attended in the pharmacy services of different hospitals in Spain. The authors analyzed more than 1200 PLWH, 79% male, 47% 50 years or older, and most of them with undetectable viral load. Comorbidities were present in 67% and more than half of them had two or more comorbidities; 32.4% showed polypharmacy (defined as using 6 or more different drugs) and 5.5% major polypharmacy (11 or more different drugs).

The data reported by Morillo et al. ⁵ also reflect the growing concern in the average of drugs and complexity of overall pharmacotherapy in PLWH and the need to optimize it. We are used to think about polypharmacy in a quantitative way, based on the number of drugs prescribed. However, a much more qualitative analysis is important, since other conditioning factors such as administration patterns, pharmaceutical forms, etc. contribute to difficult adherence. To address this problem, the Medication Regimen Complexity Index (MRCI) ⁶ was developed. In recent years, multiple articles focus on HIV infection has been published ^{7–9} noting, among others, that total non-adherence to treatment was an independent factor associated with a higher MRCI. This situation is further complicated, as Manzano-García et al. pointed out ⁸, by incorporating a new concept such as pharmacotherapeutic complexity that would include not only the MRCI score but also the score perceived by the own patients (i.e. through the visual analog scales). Given the

importance of pharmacotherapeutic optimization, and in order to transfer it to daily clinical practice, it would be necessary to establish new lines of research based on multidisciplinary coordination and the use of new technologies for patient follow-up.

Polypharmacy does not always imply inappropriate treatment, but sometimes it brings several challenges, as dealing with significant negative effects for the patient and the health-care system (loss of adherence to ART, cognitive impairment, hospitalization and mortality. . .) ^{10–12}, or increasing the risk of prescribing drugs to treat adverse effects of established treatments (prescribing cascade) ¹³. Many of these adverse events could be potentially preventable. For this reason, reconciliation, prioritization and ensuring the correct use of the pharmacotherapy should be a priority and part of routine clinical practice focused on preventing unnecessary polypharmacy. In this context, specific guidelines ¹⁴ and tools have been developed to identify potentially inappropriate prescriptions (Beers Criteria, STOPP / START tool, anticholinergic load scale. . .) ^{15–17} to prioritize the most dangerous ones. Therefore, efforts will focus on those in which they are specifically contraindicated ³. Special mention should be made of anticholinergics ¹⁸ and opioids for the treatment of chronic pain ¹⁹. The EACS guideline has included a “Selected Top 10 Drug Classes to Avoid in Older PLWH” because of the problems they can cause in this population. The list included first-generation antihistamines, tricyclic antidepressants, benzodiazepines, atypical antipsychotics, urological spasmolytic agents, laxatives, stimulant laxatives, non-steroidal anti-inflammatory drugs, digoxin (dosage >0.125 mg/day), long-acting sulfonyleureas and cold medicines ²⁰. However, in a small study carried out by Contreras-Macías et al. ⁹ in PLWH aged 65 years or older, and having into account the previous list, a potential inappropriate prescription was identified in 47.4%.

In Spain, specialized clinical pharmacists and primary care services should be provided with the tools necessary for deprescribing and eliminate potential barriers to their application (time constraints, complexity of the approach that affects different specialties, communicational barriers. . .). Overcoming these barriers and being proactive on deprescription could help on many levels providing clear health benefit to these people. In fact, comorbidity and polypharmacy are included yet in the stratification scores of PLWH ^{21,22}.

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As a take-home message, no more “missed opportunities”, so the suitability of drug therapy should be periodically evaluated to assess the adequacy of pharmacotherapy. This is not only a drug burden problem, but also an overall health improvement issue.

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