Challenges of medication-related harm in older adults: not always in plain sight

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The report by Barbara Bień¹ in this issue of Polish Archives of Internal Medicine (Pol Arch Intern Med) successfully highlights the complexity of the growing challenge of medication-related harm (MRH) affecting older adults. It adds to the growing literature drawing attention to the key “third player,” patient susceptibility to MRH, besides medications and prescribers.

Bień used observational data from 301 consecutively admitted older hospital patients (mean age of 82.4 years, 2/3 women, highly multimorbid) to investigate the prevalence and types of MRH and the contributory role of non–medication-related factors. In 106 patients (35%), 153 MRH cases of different types were identified after a comprehensive geriatric assessment. Similar rates in such patients are not uncommon.²

Using the categorization adopted by the World Health Organization,³ most cases would be regarded as type A adverse drug reactions (ADRs)—adverse effects at either normal or excessive dosage. Most cases were recognizable medication–syndrome dyads such as antidiabetics–hypoglycemia.

Polypharmacy dropped out from the logistic model, tranquilizers, patient-related factors, and specific condition–medication combinations are of greater importance. Many medications associated with each of the individual MRH types were not the usual culprits, and the causal relationship is unclear from the traditional approach. Overall, patients with MRH, regardless of its type, more frequently reported dizziness, syncope, fainting/falls before admission, orthostatic hypotension, multimorbidity, and polypharmacy, which suggests that these features represent the underlying vulnerabilities.

Patients with frailty, susceptibility to adverse health outcomes, and with or without multimorbidity are subject to multiple physiological mechanisms impacting the loss of physiological reserve, increasing the risk of MRH, with additional, even small medication-induced changes. Cullinan et al⁴ found that the increasing level of frailty⁵ among 711 hospitalized older patients was associated with a higher likelihood of polypharmacy, potentially inappropriate prescriptions (PIPs), and ADRs, but polypharmacy was not linked to ADR likelihood, which suggested that physiological vulnerability was the major determinant of the variable ADR risk. A recent study using a stringent approach to identifying MRHs in the period after hospital discharge demonstrated that frailty predicts MRH requiring healthcare support.⁶

The logic of the Beers⁷ and STOPP / START criteria⁸ is that the reduction of PIPs is crucial to avoid MRHs, but evidence to support this is poor. Neither a recent meta-analysis⁹ nor the 2018 Cochrane Review¹⁰ of community-based interventions following those principles found a consistent benefit regarding hospitalization, mental or physical function, quality of life, or mortality.

Why might these approaches not work? Larroche et al¹¹ identified PIPs in 1331 of 2018 patients aged 70+ who were admitted to a French hospital geriatric unit. Adverse drug reactions occurred more frequently (20.4% versus 16.4%) in those with PIPs, but PIPs were not associated with the risk of ADRs after taking multimorbidity and renal function into account.

Psychosocial factors also contribute to MRHs through their impact on medication adherence¹² or loss of psychosocial reserves or support. The patient’s ability to respond may be low, leading to deterioration and hospital presentation. Multifaceted, individually targeted interventions adjusted to the changing needs of the patient, such as that delivered in the Pharm2Pharm study,¹³ may help. The authors of that study monitored medicines management issues in the context of health literacy, cultural practices, and social support with regard to the patient’s changing vulnerability. The number of admissions due...
to MRH was reduced by over 1/3. Again, a minority of admissions were associated with PIPs.

So, while PIPs and ADRs are of importance, the spectrum of MRH goes beyond this. Medication-related harm should be considered a factor in the clinical presentation of all frail older patients, not only in those with easily recognizable patterns, and should always be part of a comprehensive geriatric assessment. Medications that are apparently appropriate will constitute a factor in many older patients. A key insight is that, like common geriatric syndromes, MRHs are usually multifactorial in origin, with the balance of contributory factors being uncertain and variable between individuals and over time. The response in clinical practice is to ameliorate any potential contributing factors, be flexible, and live with the uncertainty.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

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