Farmacia HOSPITALARIA
Órgano oficial de expresión científica de la Sociedad Española de Farmacia Hospitalaria

EDITORIAL
Bilingual edition English/Spanish

Bolstering the safety profile of patients with multiple morbidities receiving polypharmacy: explicit tools to address drug-drug interactions

Avanzando en la seguridad del paciente con multimorbilidad y polimedicación: herramientas explícitas para las interacciones fármaco-fármaco

Daniel Sevilla-Sánchez

Specialist hospital pharmacist. PhD in Health Sciences. Department of Pharmacy, Parc Sanitari Pere Virgili, Barcelona. Spain.

Author of correspondence
Daniel Sevilla-Sánchez
Servicio de Farmacia
Parc Sanitari Pere Virgili
c/ Esteve Terrades, 30
08023 Barcelona. Spain.

Email:
danielsevillasanchez@gmail.com

Received 1 June 2021;
Accepted 10 June 2021.
DOI: 10.7399/fh.11738

How to cite this paper
Sevilla-Sánchez D. Bolstering the safety profile of patients with multiple morbidities receiving polypharmacy: explicit tools to address drug-drug interactions. Farm Hosp. 2021;45(4):161-2.

Ageing is often associated with multiple morbidities, which often require multiple medications. Instances of polypharmacy or polymedication must be managed effectively, `particularly in the more advanced stages of life, characterized by increasing frailty, as in such patients drugs are often subjected to pharmacokinetic and pharmacodynamic modifications[1]. Effective management of polymedicated patients requires an effective tool to address the so-called potentially inappropriate prescribing practices, typically associated with negative health outcomes[2]. From 1991, when Beers developed her criteria for the systematic and uniform detection of inappropriate medication in nursing home residents[3], to the present, where we can avail ourselves of a wide range of tools to improve prescribing practices in elderly patients[4], systematic efforts have been made to define situations that could result in an unfavorable risk/benefit balance for these patients.

However, until now no explicit tool[5] was able to specifically detect clinically significant drug-drug interactions (DDIs), one of the most potentially harmful problems of our patients[6]. Although it is true that some of Beers' explicit criteria did contemplate these situations, they were not specifically designed for that purpose. Moreover, it should not be forgotten that it is not only explicit tools that have been used in an attempt to address DDIs. Implicit tools, i.e., those formulated on the basis on the physician's clinical judgement using "open questions" (avoiding the closed-item checklists typical of explicit criteria), have also frequently focused their attention on DDIs[7].

It was only recently that Anrys *et al.*[5] published an international consensus based on a series of explicit criteria that for the first time included 66 particularly significant DDIs, many of them potentially avoidable. This tool makes specific reference to the most widely used drugs among the geriatric population such as those used for problems with the cardiovascular system or the central nervous system, antithrombotics, and drugs with a narrow therapeutic margin, selecting those situations where DDIs may cause potentially life-threatening events. From a methodological point of view, Anrys *et al.* developed these new criteria following an approach similar to the one used for the already published explicit criteria, i.e., a systematic review of the available evidence and a subsequent consensus by an expert panel (Delphi methodology). The tool is the result of contributions from experts from different European countries, including Spain, with pharmacists outnumbering all the other healthcare providers on the expert panel, which indicates the urgent need for increased specialization in this area of pharmacotherapy.

It is important to underscore the huge benefits that may be derived from a tool that has been designed specifically to prevent DDIs in geriatric patients. On the one hand, from the point of view of patient safety the tool should be conceived as a starting point for detecting, resolving and preventing potentially dangerous situations as it makes it possible to anticipate adverse drug reactions which, in the most serious cases, could lead to hospital admissions[8]. On the other hand, this tool could assist in pharmacoepidemiologic research[9] as it could allow the standardization of the different studies and reviews on DDIs and be used as an outcome variable related with medication reviews in patients with multiple morbidities and polypharmacy[10], constituting a quality indicator in these processes.

From the point of view of implementation, application of the tool in the healthcare system should be led by a pharmacist[11] working as part of a multidisciplinary team at the various levels of care: hospital care, intermediate care and primary care, and the different transitional stages patients may find themselves in. The tool is accompanied by information on the recommendations that must be made when a DDI is detected, which may consist in modifying the prescribed treatment or implementing strict monitoring. The tool could also be introduced into the existing computerized support systems for drug monitoring and administration so that pharmacists may be warned about potential DDIs.

Nevertheless, the tool is not without limitations. Firstly, although the methodology used to develop it (Delphi methodology) is standard for tools of its characteristics and contributes a high degree of robustness, it is not devoid of biases and possesses some intrinsic limitations in terms of form, content and evidence[12]. In addition, given that an explicit tool must be agile and easy to implement, it cannot be excessively lengthy (in this case 66 DDIs are included) and must do without some potentially relevant interactions. This means that, although the tool is capable of a rapid screening of the most concerning interactions, a more in-depth analysis will require recourse to other sources of information. Furthermore, it must be said that the tool only includes DDIs, excluding drug-disease interactions, of great importance given the profile of these criteria, and therapeutic cascades[13].

In short, the new tool contains a series of consensual criteria that may potentially contribute to optimizing drug therapy in elderly patients who are frail, have multiple morbidities and receive polypharmacy. Implementation of these criteria should result in an improvement of health outcomes and a decrease in the negative clinical outcomes associated with inappropriate use of medication, with the pharmacist playing the leading role in detecting, preventing, and resolving DDIs, at all levels of healthcare.

Bibliography

1. Mangoni AA, Jarmuzewska EA. Incorporating pharmacokinetic data into personalised prescribing for older people: challenges and opportunities. Eur Geriatr Med. 2021;12:435-42. DOI: 10.1007/s41999-020-00437-5
2. Xing XX, Zhu C, Liang HY, Wang K, Chu YQ, Zhao LB, *et al.* Associations Between Potentially Inappropriate Medications and Adverse Health Outcomes in the Elderly: A Systematic Review and Meta-analysis. Ann Pharmacother. 2019;53:1005-19. DOI: 10.1177/1060028019853069
3. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. Arch Intern Med. 1991;151:1825-32. DOI: 10.1001/archinte.1991.00400090107019
4. Motter FR, Fritzen JS, Hilmer SN, Paniz ÉV, Paniz VMV. Potentially inappropriate medication in the elderly: a systematic review of validated explicit criteria. Eur J Clin Pharmacol. 2018;74:679-700. DOI: 10.1007/s00228-018-2446-0
5. Anrys P, Petit AE, Thevelin S, Sallevelt B, Drenth C, Soiza RL, *et al.* An International Consensus List of Potentially Clinically Significant Drug-Drug Interactions in Older People. J Am Med Dir Assoc. 2021:S1525-8610(21)00315-7. DOI: 10.1016/j.jamda.2021.03.019
6. De Oliveira LM, Diel JDAC, Nunes A, da Silva Dal Pizzol T. Prevalence of drug interactions in hospitalised elderly patients: a systematic review. Eur J Hosp Pharm. 2021;28:4-9. DOI: 10.1136/ejhpharm-2019-002111
7. Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, *et al.* A method for assessing drug therapy appropriateness☆. J Clin Epidemiol. 1992;45:1045-51. DOI: 10.1016/0895-4356(92)90144-C
8. Dechanont S, Maphanta S, Butthum B, Kongkaew C. Hospital admissions/visits associated with drug-drug interactions: a systematic review and meta-analysis. Pharmacoepidemiol Drug Saf. 2014;23:489-97. DOI: 10.1002/pds.3592
9. Liau SJ, Lalic S, Sluggett JK, Cesari M, Onder G, Vetrano DL, *et al.* Medication Management in Frail Older People: Consensus Principles for Clinical Practice, Research, and Education. J Am Med Dir Assoc. 2021;22:43-9. DOI: 10.1016/j.jamda.2020.05.004
10. Beuscart JB, Knol W, Cullinan S, Schneider C, Dalleur O, Boland B, *et al.* International core outcome set for clinical trials of medication review in multi-morbid older patients with polypharmacy. BMC Med. 2018;16:21. DOI: 10.1186/s12916-018-1007-9
11. De Oliveira Santos Silva R, Macêdo LA, Dos Santos GA, Aguiar PM, De Lyra DP. Pharmacist-participated medication review in different practice settings: Service or intervention? An overview of systematic reviews. PLoS One. 2019;14:e0210312. DOI: 10.1371/journal.pone.0210312
12. Sinha IP, Smyth RL, Williamson PR. Using the Delphi Technique to Determine Which Outcomes to Measure in Clinical Trials: Recommendations for the Future Based on a Systematic Review of Existing Studies. PLoS Med. 2011;8:e1000393. DOI: 10.1371/journal.pmed.1000393
13. McCarthy LM, Visentin JD, Rochon PA. Assessing the Scope and Appropriateness of Prescribing Cascades. J Am Geriatr Soc. 2019;67:1023-6. DOI: 10.1111/jgs.15800