

Pharmacotherapy Pearls in Rheumatology for the Care of Older Adult Patients

Focus on Oral Disease-Modifying Antirheumatic Drugs and the Newest Small Molecule Inhibitors

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KEYWORDS

- Geriatrics • DMARDs • Rheumatology • Rheumatoid arthritis • Tofacitinib
- Apremilast

KEY POINTS

- Older patients with rheumatic disorders are at increased risk for therapeutic misadventure because of age-related pharmacokinetic and pharmacodynamic changes, polypharmacy, comorbidities, impaired health literacy secondary to decreased cognition, and provider age bias.
- Rheumatologists along with other members of the allied health care team can most effectively minimize the risk for medication-related adverse reactions in older patients.
- Familiarity with dosing, monitoring, adverse reactions, medication interactions, and amelioration strategies can improve the safety of disease-modifying antirheumatic drugs in the older rheumatology patient.

INTRODUCTION

Providing safe and effective pharmacotherapy to the geriatric patient population is an ongoing struggle for health care providers. The incidence of rheumatologic disorders increases with advancing age. Recent National Health Interview Survey data

Disclosure Statement: This work was supported by the Intramural Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health. The authors do not have any conflicts of interest related to this work. This article reflects the views of the authors and should not be construed to represent FDA's views or policies.

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Rheum Dis Clin N Am ■ (2018) ■-■
<https://doi.org/10.1016/j.rdc.2018.03.010>
0889-857X/18/Published by Elsevier Inc.

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(2013–2015) observed a prevalence of physician-diagnosed arthritis among adults aged 65 years and older approaches 50% with 44% of these patients having related activity limitation.¹ It is estimated that rheumatoid arthritis (RA) affects 0.5% to 1% of the adult population in developed countries. This translates to approximately 1.3 million Americans, with an increasing prevalence with advancing age.²

Oral disease-modifying antirheumatic drugs (DMARDs) are not only effective in reducing morbidity and improving quality of life but can also have a positive impact on mortality.³ However, DMARDs alter the host immune system and could create a risk of significant adverse events including infection and malignancy. A rheumatologist involved in the care of the elderly should be aware of specific adverse reactions and drug interactions associated with the use of oral DMARDs.

Older patients are at increased risk for adverse drug reactions. Budnitz and colleagues⁴ found individuals older than the age of 65 were more likely than younger persons to have adverse drug reactions requiring emergency room visits and hospitalization. Such therapeutic misadventures in geriatric patients are caused by age-related changes in pharmacokinetics and pharmacodynamics, polypharmacy contributing to increased risk of clinically significant drug-drug interactions, and alterations in cognitive faculties that impair health literacy and therapeutic adherence.^{5–11} These problems are likely compounded by age bias, manifesting as a reluctance to aggressively treat older patients, and economic barriers.^{12,13} Management of rheumatologic conditions also carries special risk because of rapidly evolving use of novel therapeutic agents with limited data guiding their use in geriatric patients.

This article provides an update regarding commonly used oral DMARDs for the treatment of inflammatory arthritis, including methotrexate (MTX), hydroxychloroquine (HCQ), sulfasalazine (SSZ), and leflunomide, and the newer oral antirheumatic agents tofacitinib and apremilast. Although nonsteroidal anti-inflammatory drugs, prednisone, and injectable biologic agents are commonly used in the management of inflammatory arthritis, these are outside the scope of this article.

AGE-RELATED CHANGES IN PHARMACOKINETICS AND PHARMACODYNAMICS

Pharmacokinetics is the study of drug absorption, distribution, metabolism, and excretion in the body. Geriatric patients experience physiologic changes at every step of the pharmacokinetic process.^{7,9} However, understanding of the age-related changes on pharmacokinetic properties of particular medications has been hampered by the general lack of inclusion of older adults in clinical trials and drug-specific pharmacokinetic studies. The most clinically significant pharmacokinetic alteration in the geriatric population is a decline in renal function that decreases metabolite excretion. Several commonly used antirheumatic medications, such as MTX, require monitoring of renal function.

Pharmacodynamics is the study of the biochemical and physiologic effects of drugs in the body. The pharmacodynamic changes with aging are more difficult to study and less characterized than pharmacokinetic alterations. In general, the response in elderly is less predictable and subject to more interindividual variability.¹¹ Aging patients experience changes at multiple levels including receptor, signal transduction, or homeostatic mechanisms. This not only affects the effectiveness but also the risk of adverse reactions. For example, a decrease in cell density and cell proliferation in the bone marrow in elderly individuals⁷ makes these patients especially sensitive to the hematologic side effects of MTX.

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