Pharmacotherapy Pearls for the Geriatrician

Focus on Oral Disease-Modifying Antirheumatic Drugs Including Newer Agents

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KEYWORDS

• Geriatrics • DMARDs • Rheumatology • Tofacitinib

KEY POINTS

- Older rheumatology patients are at increased risk for therapeutic misadventure due to age-related pharmacokinetic and pharmacodynamic changes, polypharmacy, impaired health literacy secondary to decreased cognition, and provider age bias.
- Geriatricians, working in partnership with rheumatologists and other members of the allied health care team, can most effectively minimize the risk for medication-related adverse events in older patients.
- Familiarity with dosing, monitoring, medication interactions, potential for commonly encountered adverse effects and amelioration strategies can improve the safety of disease-modifying antirheumatic drugs and tofacitinib 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 chronic health conditions such as rheumatological disorders increases with advancing age.[1] Data from the annual 2014 National Health Interview Survey indicate that 47.4% of adults ages 65 to 74 carry a diagnosis of arthritis. This estimate rises to 50.9% in adults ages 75 years and greater.[1] It is estimated that rheumatoid arthritis affects 0.5% to 1% of the adult population in developed countries. In the United States, this translates to approximately 1.3 million adults, with an increasing prevalence with older age.[2]

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Oral disease-modifying antirheumatic drugs (DMARDs) can ameliorate some autoimmune diseases and improve morbidity and mortality. The geriatrician should be aware of specific issues associated with the use of oral DMARDs in aging patients. For example, newer agents such as Janus kinase (JAK) inhibitors for treatment of rheumatoid arthritis and urate transporter inhibitors for treatment of gout require special consideration before their use in the elderly patient.

Older patients are at increased risk for adverse drug reactions. Despite that people older than the age of 65 years make up 14% of the US population, Budnitz and colleagues[3] found that patients older than 65 years of age accounted for 25% of emergency room visits for adverse drug reactions. Such therapeutic misadventures in geriatric patients can be due to 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.[4–9] These problems are likely compounded by age bias, manifesting as a reluctance to aggressively treat older patients, as well as economic barriers.[10,11] In addition to the physiologic and social factors contributing to the risk of adverse drug events in the elderly, management of rheumatologic conditions carries special risk due to rapidly evolving use of novel therapeutic agents and limited data supporting their use in geriatric patients.

This review article provides an update regarding commonly used oral DMARDs for the treatment of inflammatory arthritis, including methotrexate, hydroxychloroquine (HCQ), sulfasalazine (SSZ), and leflunomide, as well as serves to review pertinent information regarding the newest oral anti rheumatic agent, tofacitinib. Special considerations regarding the role of the developing field of pharmacogenetics, immunization practices for the older rheumatology patient and areas of future research are also discussed. Although nonsteroidal anti-inflammatories, 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 DRUG METABOLISM

Geriatric patients experience physiologic changes at every step of the pharmacokinetic process. However, the general lack of inclusion of older adults in clinical trials and drug-specific pharmacokinetic studies has been a great obstacle in the understanding of the age-related changes on pharmacokinetic properties of particular medications. Physiologic pharmacokinetic changes in elderly patients have been outlined extensively in prior review articles.[6,8] The most clinically significant pharmacokinetic alteration in this population is a decline in renal function that inhibits excretion of metabolites. Many commonly used antirheumatic medications require monitoring of renal function, including methotrexate.

Aging patients also experience changes in pharmacodynamic processes or in the magnitude of end organ effects. Mechanistically, these changes can occur at a receptor level or secondary to the age-related blunting of other compensatory systems.[6] Older patients are more sensitive to the effects of a multitude of medications, including antihypertensives such as beta-blockers, diuretics, anticoagulants, antihyperglycemics, and NSAIDs. For example, due to a decrease of cell density of bone marrow, elderly patients may be more sensitive to the development of anemia during methotrexate therapy. Therefore, selecting more conservative initial doses and more gradual increases in dose titration is a common clinical strategy for managing antirheumatic therapy in older individuals.[6]