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Discontinuing Medications Late in Life

Kevin T. Bain, PharmD, MPH, BCPS, CGP, FASCP

There is extensive use of medications in patients late in life. It is estimated that polypharmacy, defined as taking five or more different medications, is present in 20-40% of older adults.[1-3] While the potential benefits of polypharmacy are understood, the risks associated with it are also recognized. Polypharmacy is often considered the most important risk factor for adverse drug reactions.[4-7] Adverse drug reactions account for a substantial proportion of injuries and deaths in the United States,[8] as well as substantially increase the healthcare costs of older adults.[9] Intuitively, one might think it best to reduce polypharmacy in patients late in life to prevent adverse drug reactions. However, there is little information to guide discontinuing medications that patients are taking. The purpose of this article is to discuss the steps, risks, benefits, and challenges associated with discontinuing medications late in life.

What are the steps associated with discontinuing medications?

There are four distinct steps associated with discontinuing medications:

(1) recognizing an indication that may warrant discontinuing a medication,

(2) prioritizing the medication to discontinue,

(3) discontinuing the medication, and

(4) monitoring the patient for beneficial or harmful effects.[10]

Late in life, especially for patients with a limited remaining life expectancy and whose goals of care are mainly palliative and treatment targets are focused primarily on symptom management, medications should have the shortest time until benefit.[11] Medications used for symptom management, such as analgesics, generally have a short time until benefit – hours to days – and would continue to benefit all patients, particularly those close to death. On the other hand, medications used for primary or secondary prevention usually have a longer time until benefit – months to years – and therefore these medications may be indicated for discontinuation in patients with a limited remaining life expectancy.[11] Other medications that may be indicated for discontinuation include those causing adverse drug reactions, those being used for conditions that have resolved, and those that are not being used for palliation or to improve quality of life.[10] Although it may be indicated to discontinue several medications concurrently, it is recommended that medications be prioritized and that discontinuation be performed sequentially. Higher priority should be given to discontinuing medications that are causing adverse drug reactions.[10] Once the decision is made to discontinue a medication, the clinician should develop a discontinuation plan, which includes monitoring. This plan should be guided by the consideration of the patient (e.g., comorbid conditions) and medication (e.g., pharmacokinetics) characteristics. Failure to account for these characteristics can result in adverse drug withdrawal events.[12]

What are the risks associated with discontinuing medications?

Adverse drug withdrawal events are defined as a clinically significant set of symptoms or signs caused by the removal of a medication.[13] These events may manifest as a physiological withdrawal reaction, an exacerbation of the underlying condition for which the medication was prescribed, or a new set of symptoms. In some cases, adverse drug withdrawal events can result in major morbidity and even mortality. The manifestations, frequency, timing, severity, and factors associated with adverse drug withdrawal events after discontinuing medications have been described in more detail elsewhere.[13-15] In summary, medications most commonly associated with adverse drug withdrawal events are those from the cardiovascular (e.g., beta-blockers) and central nervous system (e.g., benzodiazepines) drug classes. Although not all medications need to be tapered prior to discontinuation, tapering medications over the course of days to weeks is a logical approach to reduce the likelihood of an adverse drug withdrawal event, especially for medications from the cardiovascular and central nervous system drug classes. To further reduce the likelihood of an adverse drug withdrawal event discontinuing medications should be undertaken as a team approach, involving prescribers, pharmacists and, where appropriate, nurses, as well as the patient.[10]

What are the benefits associated with discontinuing medications?

Several studies indicate that most medications can be discontinued in a substantial proportion of patients late in life without generating any harm.[13, 15, 16] Even when adverse drug withdrawal events occurred in some studies, these events were easily mitigated by recommencing the medication.[15] Furthermore, there is some clinical trial evidence indicating that discontinuing certain medications has benefits, such as reducing the risk of falling[17, 18] and improving cognitive function.[19-21]

Despite the relative lack of literature regarding the clinical benefits of discontinuing medications, it is reassuring that in one study of medication discontinuation among a managed care cohort of patients, polypharmacy was reduced resulting in a lowered risk for adverse drug reactions and substantial cost savings.[22] Investigators found that pharmacists-driven interventions reduced the rate of polypharmacy events by 67.5% after the first intervention and 39.0% after the second intervention. After the first intervention, overall medication costs were reduced by $4.8 million, and six months after the second intervention, the corresponding medication cost reduction was $1.3 million.

What are the challenges associated with discontinuing medications?

Discontinuing medications can be challenging. Factors that discourage discontinuing medications ("barriers") are numerous, complex, and often overlapping. Some barriers relate to patients and prescribers and others are the result of aspects of the healthcare system. While a detailed discussion of each of these is beyond the scope of this article, the major themes will be discussed here.

Patients may become physically dependent on a medication, especially when used on a chronic basis. Oftentimes, patients can be weaned off a chronically-used medication; however, physical dependency may preclude the complete discontinuation of the medication. In addition to physical dependency, patients often become psychologically attached to a medication they have been taking for years to manage a chronic condition. Convincing patients (and their families) that a medication they have been taking for years is no longer beneficial and, in fact, could be harmful is challenging.[12] Increased communication with their prescriber could address the patient's concerns about discontinuing a medication. Ideally, this communication should occur when the medication is first prescribed and periodically thereafter.

Prescribers have clinical inertia with regard to medications.[11] Once a medication is prescribed, it may be difficult to discontinue, even if the medication is no longer clinically beneficial. This is due, in part, because the act of prescribing a medication is a socially understood expression of the prescriber-patient relationship. A prescriber may be reluctant to discontinue a patient's medication out of concern that doing so would damage this relationship. [12] Prescribers care profoundly about providing good patient care, yet they have been hampered in providing this care because they often lack the time and patient-specific information that they need to make complex medical decisions.[23] Successfully discontinuing medications is a time-consuming process. Integrating the processes of discontinuing and prescribing medications throughout the patient's lifespan is likely to reduce the time prescribers spend on discontinuing medications late in life.

In terms of the healthcare system, there is little incentive for patients and prescribers to discontinue medications. This is evidenced by the astronomical number of medications purchased and annual rate of growth in medication spending in the United States. In 2005, approximately 3.6 billion prescription medications were purchased,[24] and in 2006, prescription medication spending increased 8.5% from the prior year to reach $216.7 billion.[25] Most medications are prescribed and dispensed in 30- or 90-day supplies, in part due to insurance requirements. Attacking the issue from the supply end would require a major change in attitude and behavior among prescribers, payers, pharmacies, and patients, which is likely to be met with tremendous opposition. Furthermore, there is a paucity of data available from a relatively limited number of high-quality studies to assess the benefits and risks of discontinuing medications, and most studies undertaken have only included medications from the cardiovascular and central nervous system drug classes.[15] Without compelling evidence to support discontinuing many medications, such a change is unlikely to occur. One potential means to build the evidence base is to incorporate a double-blind, randomized discontinuation phase into early efficacy studies of medications.[12]

What is the take-away message?

Every medication that is prescribed involves a trade-off between the intended benefits and the inherent risks, both of which come at a price. Discontinuing medications also involves a trade-off between benefits and risks, the main risk being adverse drug withdrawal events. Following the steps described in this article, the overwhelming majority of medications can be discontinued safely and effectively without causing an adverse drug withdrawal event. Still, there are many barriers that must be overcome to optimally discontinue medications late in life. Some of these barriers occur early on in the medication-development

and medication-use process. Given that patients late in life are at substantial risk for adverse drug reactions, there is an increasing need to devote and invest more resources that will guide medication discontinuation in the future.

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