Evolving Pharmacological Management of Persistent Pain in Older Persons

Pain medicine is among the youngest subspecialties of medicine and is still in the midst of defining itself. In this process, it is very important to address the needs of the most vulnerable patient populations who have increased burden of illness and pharmacological intake with many potential adverse consequences; one such population is the older patient with persistent pain. The updated guidelines for the pharmacological management of persistent pain in older persons is an important step in keeping the developments in pain management in the older person known to those health care providers who are responsible for their care. Especially useful for the practicing clinicians is the very insightful overview about the general context of pain management, including the crucial role of an adequate pain assessment as the starting point.

One of the challenges in publishing guidelines is the goal to be comprehensive and practical while following information from rigorous clinical trials as the gold standard. This guideline, similar to a previous guideline on this topic, is based on clinical standards in the field and on existing data that is often limited in scope and quality. The end product is necessarily a synthesis of the best available evidence [1].

Because the science of pain medicine has evolved slowly, pain guidelines in general and this one in particular are fraught with limitations. In the introductory section, it is stated that the focus is on those age 75 years and older, yet the quality of evidence in this subset of older adults is perhaps more limited than any other. It becomes difficult for the practitioner caring for these individuals who often have multiple and varied coexisting pain conditions and attendant comorbidities to turn to the guidelines for help. While the purpose of the guidelines is to present recommendations on the use of pharmacological agents for frail older adults, it is precisely these individuals for whom pharmacotherapy should be used only when absolutely necessary and virtually always prescribed along with evidence-based nonsystemic medication treatment options. The guidelines state, “Although some nonpharmacological interventions have been shown to reduce pain when used alone, their benefit is usually enhanced when combined with drug strategies”.

One of the most common persistent pain conditions in patients of all ages is myofascial pain syndrome—a condition that may be effectively and appropriately treated with nonpharmacological modalities [2]. These syndromes often complicate other chronic pain conditions and, therefore, their treatment must be prioritized.

Another limitation of the guidelines is that while precise recommendations are offered for the starting dose of analgesics, details are not provided regarding titration. Pain undertreatment in older adults is in part contributed by practitioner’s fear of inducing adverse effects. “Start low and go slow” is a time-honored tradition in the field of geriatric medicine, but too often, this adage is interpreted as “start low and stay low.” If practitioners are expected to roll up their sleeves and use these guidelines to help their patients, more detailed instructions are needed.

Some of the specific pharmacotherapeutic recommendations offered in the guidelines are arguable as summarized in the next section of this editorial:

Table 2 has several misstatements about age-related changes in drug pharmacokinetics [3]. First, to the best of our knowledge, there are no evidence-based data that suggest aging further slows the gastrointestinal absorption of sustained-release drugs (e.g., opioids) nor does change in gastric pH effect analgesic absorption [3,4]. However, there is a decreased first pass effect that results in higher bioavailability of drugs such as morphine, even though the table indicates that first pass effect is usually unchanged. Table 2 also does not mention age-related decrease in liver blood flow [3]. This is extremely important as morphine is a high hepatic extraction ratio drug whose clearance is significantly decreased resulting in prolonged half-life in older adults [5].

Table 3 lists recommended drugs for persistent pain in older adults but does not indicate for which drugs specific aging-associated pharmacokinetic and/or pharmacodynamic data exist. For nabumetone, hydrocodone, oxymorphone, and methadone, there are no pharmacokinetic studies in older adults, thus prescribing these medications for older adults with persistent pain becomes an
individual experiment not guided by data. Table 3 also provides insufficient detail about several issues involving the known pharmacokinetics of various other analgesics. A number of analgesic drugs are hepatically metabolized by CYP2D6 (e.g., codeine, hydrocodone, oxycodone, tricyclic antidepressants, tramadol, venlafaxine) [4]. While age-related changes in CYP2D6 have not been demonstrated, significant interactions with other drugs that are metabolized by this same enzyme can occur. For example, amiodarone, bupropion, fluoxetine, quinidine, and ritonavir can inhibit the metabolism of most of the analgesics mentioned above and, therefore, lead to increased toxicity. For tramadol that must be metabolized to a more active metabolite, reduced analgesic efficacy may result.

Table 3 lists naproxen as a recommend drug. It is important to note that naproxen’s free clearance is reduced by 50% in older adults. Given its long half-life and increased risk of gastrointestinal and renal toxicity, naproxen is generally not recommended for use in older adults [4,6].

While a comment appears in Table 3 about increased potential toxicity with morphine and milnacipran because of accumulation of the parent compound or active metabolites with decreased renal function, no specific details are provided about the need to reduce the dosage of the following primarily renally cleared medications or their active metabolites: duloxetine, gabapentin, oxycodone, pregabalin and tramadol. Readers are referred to the following references for further information about dosing these renally cleared medications [7–9].

Two other points about nonsteroidal anti-inflammatory drugs (NSAIDs) not mentioned in the guidelines are worth highlighting. First, an important relative contraindication to their use is concomitant warfarin that is associated with an increased risk of bleeding [10]. Second, it should be noted that the comment about avoiding ibuprofen in those taking aspirin also applies to naproxen but not to celecoxib [11,12].

With regard to opioids, readers should be aware that long half-life/duration agents (e.g., fentanyl patch, methadone, sustained release oxycodone, and morphine, etc.) should be avoided in opioid naïve patients to reduce the risk of late onset toxicity [13].

While the guidelines provide explicit recommendations regarding appropriate medications for various pain conditions, providers also need explicit recommendations regarding which medications should be avoided. For example, specific NSAIDs such as indomethacin, ketorolac, naproxen, oxaprozin, piroxicam, specific opioids such as pentazocine, propoxyphene, or meperidine, and specific skeletal muscle relaxants such as methocarbamol, cyclobenzaprine, carisoprodol, chlorzoxazone, methocarbamol should not be prescribed for older adults as it is generally accepted that the risks of prescribing these medications outweigh their potential benefits [6].

The guidelines nicely highlight the evolving nature of pain medicine. Until a decade ago, nonsteroidal anti-inflammatory agents were a staple of pain management. Rapidly evolving recognition that adverse effects of medications in general, including those that are considered safe enough to be available as over-the-counter drugs, such as certain NSAIDs and acetaminophen, has increased recently and brought in focus the large health care burden and costs of these adverse effects. As a consequence, the landscape of rules and regulations related to pain pharmacotherapy has been rapidly changing. Growing information has lead to the recognition that opioids might be a relatively safer choice, although studies that directly compare these management approaches are not available.

As traditionally prescribed analgesics have come under increased scrutiny and face potential limitations in the way they will be prescribed, there will be an increasing need for medications that have specific mechanisms of action different from traditional analgesics, as well as evidence-based guidance regarding how to best use multimodal therapeutic approaches. As noted in a recent review, little evidence is available regarding the use of multimodal treatment, although this is commonly utilized by prescribers [14]. Without an evidence base, the AGS guidelines are unable to address this common approach to treatment even while progress has been made, much more is needed. Studies that focus exclusively on older adults, especially the frail older adults on which these guidelines focus, are sorely lacking. Such studies are needed to create future guidelines that are based upon solid evidence that can give practitioners the confidence they need to provide high-quality care to this understudied and vulnerable population.

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References


