Potentially inappropriate medications in geriatric population: a clinical update for oral medicine and orofacial pain practitioners

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The American Geriatric Society has periodically published guidelines, known as the *Beers Criteria*, for identifying potentially inappropriate medications (PIMs) for the geriatric population. In addition, the Screening Tool of Older Person's Potentially Inappropriate Medications is another list that was developed on the basis of hospital admissions resulting from adverse drug events in geriatric adults. This review paper provides a summary of these PIMs that are commonly prescribed to the geriatric population by dental practitioners, with a focus on medications prescribed by oral medicine and orofacial pain specialists. Five classes of medications have been identified and discussed in this review, namely, tricyclic antidepressants, benzodiazepines, muscle relaxants, anticonvulsants, and nonsteroidal anti-inflammatory drugs. Alternative medications in lieu of PIMs for geriatric adults have also been provided, along with the required dosage modifications. (Oral Surg Oral Med Oral Pathol Oral Radiol 2017;124:600–608)

Advances in biomedical technology and health care delivery have significantly raised life expectancy in the population. It is projected that geriatric adults aged 65 years and above will constitute approximately 21% of the total US population by the year 2040.[1] In 2009, the Task Force in Aging Research demonstrated that although geriatric adults represent 13% of the current US population, they consume 40% and 35% of prescription and over-the-counter medications, respectively.[2] In addition, data also showed that individuals aged 65 years and above obtain, on average, 14 to 18 prescriptions per year.[2,3]

Decline in physiologic functioning is a phenomenon of the natural aging process. Pharmacokinetic activities, including gastrointestinal (GI) absorption, drug distribution, hepatic metabolism, and renal clearance, diminish with age.[4] Pharmacodynamic functions, such as drug–receptor interaction, signal transduction, protein transcription, and cellular response, can also be compromised with advancing age.[4] Moreover, the coexistence of several health problems and polypharmacy increases the risk for adverse drug events (ADEs) and drug interactions.[5]

Dental practitioners should be cautious when prescribing pharmacologic agents and must be aware of any potential hazards or side effects of medications. Guidelines, known as the *Beers Criteria*, for identifying potentially inappropriate medications (PIMs) for geriatric patients have been periodically published. The American Geriatric Society has assumed sponsorship of the Beers Criteria since 2012.[6] The most recently updated Beers Criteria for PIMs were released in November 2015.[7] These criteria are utilized by the National Committee for Quality Assurance and the Pharmacy Quality Alliance that the Centers for Medicare/Medicaid Services uses to identify drugs likely to cause harmful effects in older adults. Furthermore, the American Geriatric Society, in consultation with the National Committee for Quality Assurance and Pharmacy Quality Alliance, has published alternative medications and regimens for the recently published PIMs list.[5,6]

The Screening Tool for Older Person's Potentially Inappropriate Medications (STOPP) is another list that was developed to assess hospital admissions resulting from ADEs in geriatric adults.[8-10] It was developed independently of the Beers Criteria and is based on clinical data, rather than study-reported outcomes. The tool also addresses some of the shortcomings of the Beers Criteria by including medications not commonly prescribed in the United States.[8-10]

The aim of this review paper was to provide a summary of PIMs for the geriatric population that are commonly prescribed by dental practitioners, with a focus on medications prescribed by oral medicine and orofacial pain specialists. Five classes of medications have been identified on reviewing the Beers Criteria and the STOPP list, namely, tricyclic antidepressants, benzodiazepines, muscle relaxants, anticonvulsants, and nonsteroidal anti-inflammatory drugs (NSAIDs). Alternative medications in lieu of PIMs for geriatric adults have also been summarized.

Statement of Clinical Relevance

Some of the medications commonly used in the practice of oral medicine and orofacial pain are potentially inappropriate for the geriatric population. Caution should be taken when prescribing these medications, and alternative pharmacologic and nonpharmacologic therapeutic modalities should be considered.

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TRICYCLIC ANTIDEPRESSANTS

Indication

Tricyclic antidepressants (TCAs) have wide therapeutic indications, including anxiety disorders, post-traumatic stress disorders, and panic attacks.[11] Currently, they are commonly used for the management of chronic neuropathic pain in the head and neck region, postherpetic neuralgia (PHN), persistent dentoalveolar pain (PDAP) (formerly referred to as *atypical odontalgia* and *persistent idiopathic facial pain*) and burning mouth syndrome (BMS) respond to these agents.[12-14] Amitriptyline and nortriptyline are the first and the most commonly used medications of this class in the practice of oral medicine and orofacial pain. Doxepin and imipramine are relatively newer agents with very similar chemical structure and pharmacodynamic effects.

Mechanism of action

TCAs are tertiary amines with broad pharmacologic actions. They exert their effect by inhibiting presynaptic reuptake of serotonin and noradrenaline from the synaptic cleft in addition to antagonizing sodium channels and voltage-dependent calcium channels.[15-19]

Level of evidence against use in the geriatric population

According to the Beers Criteria and the STOPP list, it is highly recommended that prescribing amitriptyline, nortriptyline, and imipramine be avoided because of their potent anticholinergic, hypotensive, and sedating effects.[7,20] CYP450 interactions and cardiotoxicity are also among the major concerns with the use of TCAs.[21] Oral medicine and orofacial pain clinicians should be vigilant when prescribing these agents, especially when there is coexistence of cardiovascular disease. The evidence for this recommendation is relatively strong and is based on consistent findings from high-quality randomized controlled trials (RCTs) and consistent observational studies.[22-24]

Side effects and interaction

The commonly reported side effects of TCAs are related to their antagonist effects on the H1 histamine receptors, α_1-adrenergic receptors, and muscarinic receptors. Xerostomia, constipation, and urine retention are the most common side effects and, for most, the first to appear. Weight gain, blurred vision, erectile dysfunction, muscle weakness, and cognitive impairment are also common and, in many instances, can persist after drug discontinuation.[21] Larger doses of TCAs are associated with cardiotoxicity manifesting as ventricular conduction abnormalities and arrhythmias.[25]

Alternatives

Gabapentin and pregabalin. Both agents are blockers of the voltage-gated Ca^{++} channel α_2-δ ligands that reduce the release neurotransmitters.[26] Their high safety profile comes from the sparing effect of plasma protein binding and hepatic metabolism (excretion is exclusively renal) that make their use favorable in patients with polypharmacy.[27]

Both agents have proven effectiveness in treating diabetic peripheral neuropathy and PHN, as well as neuropathic pain associated with spinal cord injury and some fibromyalgia cases.[28-30] In orofacial pain, they have shown efficacy in treating cases of trigeminal neuralgia, PDAP, and BMS.[13,31-36] They are also used as one of the therapeutic agents to treat short-lasting unilateral neuralgiform headache with conjunctival injection and tearing.[37,38]

Gabapentin initiation dose is 300 mg, 3 times per day, and can be gradually titrated up to 3600 mg daily. Pregabalin is started at 150 mg in divided daily doses and can be increased up to 300 mg/day.[39] In the geriatric population, dose adjustment, based on estimated glomerular filtration rate values, maybe necessary in cases of compromised renal function. Details regarding definition of renal impairment and medication dose adjust are provided in Table I.[40,41]

The side effects of gabapentin and pregabalin include sedation, dizziness, confusion, peripheral edema, and possible sexual dysfunction.[39]

Duloxetine and milnacipran. Duloxetine and milnacipran are contemporary antidepressants of the serotonin-noradrenaline reuptake inhibitors class.[26] On clinical trials, serotonin-noradrenaline reuptake inhibitors demonstrated significant efficacy in alleviating painful diabetic neuropathy, mixed painful polyneuropathy, and fibromyalgia.[42-46] In the head and neck region, some open label noncomparative studies showed significant efficacy of milnacipran at 15 to 100 mg/day in alleviating symptom of BMS.[47,48] Moreover, a trial of duloxetine at 2 to 40 mg/day and up to 40 mg/day also showed significant pain reduction in both BMS and PDAP cases.[49]

Milnacipran and duloxetine appear to be safe for patients with cardiovascular conditions. Milnacipran, specifically, appears to be more favorable for those with polypharmacy because of its lack of interaction with hepatic CYP450 enzymes.[50-54] Milnacipran is started at 12.5 mg once daily and gradually increased up to 50 mg twice a day (even in patients with moderate renal impairment). It can be prescribed to those with severe renal impairment but should not exceed a dose of 25 mg, twice a day.[55]

Duloxetine initiation dose is 30 mg/day. Although it can be increased up to 60 mg twice a day, it is preferable to keep the dose at 60 mg once a day for geriatric adults, especially those with comorbid moderate renal impairment. It should be completely avoided in cases of severe renal impairment.

Common side effects of both duloxetine and milnacipran include nausea, vomiting, constipation, dry