Review

Prescribing opioids in older people

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Abstract

People are living to older age. Demographic pressures are driving change. Opiate analgesics are the most powerful known pain relievers. Persistent pain, both cancer and non-cancer types, is frequent in older adults. The use of opioid analgesics is appropriate in the treatment of moderate to severe persistent pain. The challenge of prescribing opioids in older adults is to understand the factors involved in making appropriate choices and monitoring the beneficial effects of pain relief while managing the side-effects. This article will review the current concepts, evidence and controversies surrounding opiate use in the elderly. An approach is outlined which involves: pain assessment, screening for substance abuse potential, deciding whether you are able to treat your patient without help, starting treatment, monitoring effectiveness of pain control and managing opioid-associated side-effects. The goal of pain management using opioids is the attainment of improved function and quality of life.

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1. Introduction

This article is a focused review of the topic of prescribing opioids in older adults. We will highlight the current concepts, evidence and areas of uncertainty. This article is targeted to clinicians who are navigating therapeutic options for older adults, a significant number of whom are becoming vulnerable and frail. The objectives are to provide the reader with information about the effectiveness, side-effects and appropriateness of prescribing opioid analgesics for their older adults with the goal of improving the function and quality of life of those individuals.

2. The challenges of prescribing in older adults

People are living to older age. In late 2011, the world population reached 7 billion. As estimated by the World Health Organization in 2009, based on the reports of its 193 member states, this population had a median age of 29 years, with 11% of people currently older than 60 years. Older adults are also the fastest growing segment of the global population. This demographic pressure is driving different health care needs and exposing new issues.

There are several challenges when prescribing in older adults. The first challenge is the presence of physiologic changes related to normal aging that mimic or amplify medication side effects. Dizziness symptoms and constipation is common. Bowel and bladder function is compromised by pelvic floor muscle laxity. Renal and hepatic function declines. However decline in cognitive functioning is not a universal phenomenon. The second challenge is older patients frequently have multiple co-morbidities such as heart disease, hypertension, diabetes, arthritis, stroke, hypothyroidism, prostatic hypertrophy, and dementia [1,2]. This burden of co-morbidities may also impact on an older patient’s response to medications. Patients studied in a variety of settings (hospitalized, emergency department, nursing homes, community-dwelling) may represent heterogeneous cohorts because of different burdens of co-morbidities and limits the findings to those groups. Past clinical trials have routinely excluded older adults, especially those 80 years and older with multiple co-morbidities. The lack of rigorous studies into the effects of therapeutics in this important segment of the population has led to the emergence of organizations such as PREDICT (http://www.predict.eu.org) and the drafting of the European Charter for Older People in Clinical Trials [3,4]. The third challenge is represented by polypharmacy. Older adults use more medications because of the co-existence of multiple diseases [5]. Polypharmacy as defined by the use of four or more medications, is highly prevalent in this population [6]. Even though the multiple medications a patient is taking may be deemed appropriate this polypharmacy is often the cause of iatrogenic complications if not managed properly. Elderly patients who visit multiple prescribing physicians and fill their prescriptions at multiple pharmacies also increase their risk of polypharmacy and of inappropriate and undesirable prescribing [7].

3. Methods

This review is based on high quality articles chosen from the results of targeted searches using the OvidSP search engine (Wolters Kluwer, P.O. Box 1030, 2400 BA, Alphen aan den Rijn, the Netherlands) for literature published between 2000 and 2012 accessing the MEDLINE and EMBASE bibliographic databases, the Cochrane Library (http://www.thecochranelibrary.com) and citations from key articles.

3.1. Opioid analgesics

Opioids are the most powerful known pain relievers. Evidence of their use and abuse date back to antiquity and history is filled with conflict and crime related to the narcotics industry. Opioid analgesics are among one of the most frequently prescribed drugs. In the United States, the combination medication hydrocodone/acetaminophen is the number one individual dispensed prescription medication during 2007–2011 while the class of narcotic analgesics is overall ranked third [8,9]. Global sales in 2011 of prescribed opioid analgesics was 12.3 billion US dollars, ranked fifteenth [10]. The rise in opioid prescribing is a concern in many countries, with reports coming from Australia [11] the United States [12] and Norway [13] as examples. However the “prescription opioid crisis” [14] should be considered an appropriate reality once it is understood that opioid prescribing must increase to respond to the clinical needs of more older patients who require effective relief from their moderate to severe persistent pain. The following sections present factors that should be considered when prescribing opioids in older adults so evidence-informed decisions can be made to provide the best care.

3.2. Pharmacology of opioids in older adults

The effect of normal aging on the pharmacokinetic and pharmacodynamic properties of drugs is well described [15–19]. Changes in body composition, such as a reduction in total body water, a decrease in total body mass and an increase in body fat results in an increase in the volume of distribution for liposoluble medications (e.g. antipsychotics and antidepressants) and a lower volume of distribution for water soluble drugs such as morphine. Malnutrition and sarcopenia are states that can lower serum albumin concentration which can increase the free fraction of drugs which are highly protein-bound (e.g. phenytoin, valproic acid) which then leads to potentially increased side effects.

Reduced hepatic function due to a reduced hepatic mass and blood flow can increase the bioavailability of drugs such as morphine which undergo a high first-pass extraction. Reduced levels of hepatic monoxygenases and cytochromes can result in a 30–40% reduction of hepatic drug clearance.

A reduction in renal function due to the decline in kidney mass, renal blood flow, glomerular filtration rate and tubular secretion rate is universal. However an accompanying decrease in creatinine production due to a reduction in muscle mass may offset these changes and lead to an apparent preservation in plasma creatinine measurement. An estimation of the creatinine clearance or actual measurement by inulin clearance analysis is needed to guide clinicians in dosage adjustments for drugs that are cleared by the kidneys.

Individual variability due to genetics, lifelong living habits and the environment can result in significant heterogeneity in the response to drugs in elderly patients.

3.3. Pharmacokinetics of opioids

Table 1 lists the comparative duration of action of opioid drugs and their different formulations. Table 2 lists the comparative
metabolism of opioid drugs. We are unable to present a table listing the equivalent potencies of the opioid drugs because of the absence of rigorous studies in older adults in this area.

3.3.1. Morphine

The oral bioavailability of morphine in older patients is increased because of a decrease in first-pass metabolism [20]. Only 10% of the dose of morphine is eliminated unchanged in the urine. Glucuronidation is the major pathway for morphine biotransformation with the production of two metabolites morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G). M6G has a high affinity for the μ-opioid receptor (whose activation is mainly responsible for the analgesic effects of opioids) and is six times more potent than morphine. The M3G metabolite is inactive but is responsible for the neurotoxic effects. Both metabolites are completely excreted by the kidneys and may accumulate in the presence of renal impairment [21]. The observation of increased sensitivity of older adults to the effects of morphine is not fully explained by the pharmacokinetic changes. Continued research for other factors, including the role of genetic variation in the human μ-opioid receptor gene is needed [22].

3.3.2. Codeine

Codeine is a weak opioid analgesic structurally related to morphine. It is metabolized primarily by the liver to codeine-6-glucuronide and norcodeine, and approximately 10% is O-demethylated to morphine. Codeine itself has a very weak affinity for μ-opioid receptors. Its analgesic activity relies on the conversion of codeine to morphine, via cytochrome P450 (CYP) 2D6. Individuals with decreased CYP2D6 activity (6–10% in white population) are expected to have an impaired conversion and therefore a decrease in the analgesic effect [20].

Table 1
Comparison of various formulations of opioid drugs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route of administration</th>
<th>Onset of action</th>
<th>Peak</th>
<th>Duration of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>Transdermal patch</td>
<td>24–36 h</td>
<td>3 days</td>
<td>7 days</td>
</tr>
<tr>
<td>Codeine</td>
<td>Oral: short acting preparation</td>
<td>30–60 min</td>
<td>1–1.5 h</td>
<td>4–6 h</td>
</tr>
<tr>
<td></td>
<td>Oral: long acting preparation</td>
<td>30–60 min</td>
<td>3–4 h</td>
<td>12 h</td>
</tr>
<tr>
<td></td>
<td>Subcutaneous (SC)</td>
<td>15–30 min</td>
<td>30–60 min</td>
<td>4–6 h</td>
</tr>
<tr>
<td></td>
<td>Intramuscular (IM)</td>
<td>10–30 min</td>
<td>30–60 min</td>
<td>4–6 h</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Transdermal patch</td>
<td>6–8 h</td>
<td>24 h</td>
<td>72 h</td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>7–15 min</td>
<td>–</td>
<td>1–2 h</td>
</tr>
<tr>
<td></td>
<td>Intravenous (IV)</td>
<td>Immediately</td>
<td>–</td>
<td>30–60 min</td>
</tr>
<tr>
<td></td>
<td>Sublingual tablet (SL)</td>
<td>5–15 min</td>
<td>15–30 min</td>
<td>2 h</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Oral: short acting preparation</td>
<td>15–30 min</td>
<td>30–60 min</td>
<td>4–5 h</td>
</tr>
<tr>
<td></td>
<td>Oral: long acting preparation (12 h)</td>
<td>15–30 min</td>
<td>4–5 h</td>
<td>12 h</td>
</tr>
<tr>
<td></td>
<td>Oral: long acting preparation (24 h)</td>
<td>15–30 min</td>
<td>8 h</td>
<td>24 h</td>
</tr>
<tr>
<td></td>
<td>SC and IM</td>
<td>15 min</td>
<td>30–60 min</td>
<td>&gt;5 h</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>5–10 min</td>
<td>15 min</td>
<td>4–5 h</td>
</tr>
<tr>
<td>Methadone</td>
<td>Oral: short acting preparation</td>
<td>30–60 min</td>
<td>1.5–2 h</td>
<td>24–36 h</td>
</tr>
<tr>
<td></td>
<td>Oral: short acting preparation</td>
<td>30 min</td>
<td>60 min</td>
<td>4–5 h</td>
</tr>
<tr>
<td></td>
<td>Oral: short acting preparation liquid</td>
<td>20 min</td>
<td>60 min</td>
<td>4–5 h</td>
</tr>
<tr>
<td></td>
<td>Oral: long acting preparation (12 h)</td>
<td>60 min</td>
<td>4–5 h</td>
<td>12 h</td>
</tr>
<tr>
<td></td>
<td>Oral: long acting preparation (24 h)</td>
<td>60 min</td>
<td>10 h</td>
<td>24 h</td>
</tr>
<tr>
<td></td>
<td>SC</td>
<td>50–90 min</td>
<td>1–1.5 h</td>
<td>4–5 h</td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>30–60 min</td>
<td>0.5–1 h</td>
<td>4–5 h</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>5–10 min</td>
<td>15 min</td>
<td>4–5 h</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>Long acting preparation</td>
<td>–</td>
<td>–</td>
<td>12 h</td>
</tr>
<tr>
<td></td>
<td>Oral: short acting preparation</td>
<td>60 min</td>
<td>2–4 h</td>
<td>3–6 h</td>
</tr>
<tr>
<td></td>
<td>Oral: short acting preparation with acetaminophen</td>
<td>&lt;60 min</td>
<td>2–3 h</td>
<td>Up to 9 h</td>
</tr>
<tr>
<td></td>
<td>Oral: long acting preparation (24 h)</td>
<td>7</td>
<td>4–8 h (Zytram, Tridural) 12–15 h (Ralivia)</td>
<td>24 h</td>
</tr>
</tbody>
</table>

Table 2
Comparison of metabolism of opioid drugs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Metabolic pathway</th>
<th>Active metabolite</th>
<th>Metabolite with toxic effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine</td>
<td>CYP3A4</td>
<td>Yes</td>
<td>–</td>
<td>Potential drug–drug interactions via CYP3A4</td>
</tr>
<tr>
<td></td>
<td>CYP2D6</td>
<td>Yes</td>
<td>–</td>
<td>Metabolism to morphine required for analgesic effect. Individuals with impaired CYP2D6 activity will have less or no analgesic effect</td>
</tr>
<tr>
<td>Codeine</td>
<td>CYP3A4</td>
<td>No</td>
<td>–</td>
<td>Hydromorphone-3-glucuronide (H3G)</td>
</tr>
<tr>
<td></td>
<td>Glucuroconjugation</td>
<td>No</td>
<td>–</td>
<td>Potential neuroexcitatory effects of H3G metabolite</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>CYP3A4</td>
<td>Limited</td>
<td>Morphine-6-glucuronide (M6G)</td>
<td>Numerous drug–drug interactions via CYP3A4</td>
</tr>
<tr>
<td></td>
<td>Glucuronidation</td>
<td>Active metabolites</td>
<td>Morphine-3-glucuronide (M3G)</td>
<td>Potential neuroexcitatory effects of M3G metabolite</td>
</tr>
<tr>
<td>Methadone</td>
<td>CYP3A4</td>
<td>Limited</td>
<td>Morphine-6-glucuronide (M6G)</td>
<td>Analgesic effects are maintained despite genetic polymorphism or inhibition of CYP2D6 because both oxycodone and its metabolites are active</td>
</tr>
<tr>
<td></td>
<td>Glucuronidation (70%) oxidation (15%) via CYP2D6, CYP2C9 and CYP2C19</td>
<td>Limited</td>
<td>Morphine-3-glucuronide (M3G)</td>
<td>More studies are needed to evaluate safety in geriatric patients</td>
</tr>
</tbody>
</table>
| Oxycodone | CYP2D6 | Yes | – | Active metabolite has greater affinity for μ-opioid receptors than parent drug. Potential drug–drug interactions via CYP2D6.
| Tapentadol | Glucuronidation (70%) oxidation (15%) via CYP2D6, CYP2C9 and CYP2C19 | No | – | |
| Tramadol | CYP2D6 and CYP3A4 | Yes | – | |
3.3.3. Oxycodone

Oxycodone is a semi-synthetic μ-opioid agonist. There is limited information on the pharmacokinetics in the oldest old and frail elderly patients. It is metabolized via the oxidative enzymes, CYP3A4 and CYP2D6, which transform oxycodone to noroxycodone and to oxymorphone, respectively. Both metabolites are active and accumulate in renal impairment. A reduction in the formation of the active metabolite oxymorphone is found in individuals with decreased CYP2D6 activity. Further studies are needed to evaluate the effect of age, genotype and drug interactions on the variability in oxycodone pharmacokinetics [20,21].

3.3.4. Hydromorphone

Hydromorphone is a semi-synthetic opioid that undergoes significant first-pass metabolism. Since this pathway decreases in aging an increase in the plasma concentration of hydromorphone is common. Hydromorphone is primarily metabolized by glucuronidation to hydromorphone-3-glucuronide (H3G) which is neuroexcitatory and can accumulate in renal impairment [20].

3.3.5. Fentanyl

Fentanyl is a highly lipophilic semi-synthetic opioid which rapidly penetrates the blood–brain barrier. It has a high first pass metabolism making it unsuitable for oral administration. Fentanyl undergoes extensive metabolism by CYP3A4 to an inactive metabolite norfentanyl which is renally excreted. Fentanyl is most commonly administered via the transdermal route using a patch. After application of the patch a depot of fentanyl accumulates in the subcutaneous layers of the skin with subsequent absorption into the general circulation. Factors such as the site of patch application, skin temperature, sweat gland distribution and function and skin integrity may influence drug absorption. The effects of normal aging, sarcopenia and malnutrition on the pharmacokinetic parameters of fentanyl is unknown or conflicting [21]. One study with a small sample size reported a longer plasma fentanyl concentration doubling time (11.1-h in the elderly compared to 4.2-h in younger subjects) and a longer elimination half-life after removal of the patch (30.5-h in the elderly compared to 21.2-h in younger subjects) [23].

3.3.6. Tramadol

Tramadol is metabolized extensively by the liver. More than 80% of tramadol is transformed by CYP2D6 to a main metabolite, O-demethyl tramadol. The mechanism of action of tramadol is bimodal: modulation of the central monoaminergic pathways and activation of μ-opioid receptors. Tramadol has higher monoaminergic activity, whereas its metabolite O-demethyl tramadol has higher affinity and activates μ-opioid receptors [20].

3.3.7. Methadone

Methadone is extensively metabolized by hepatic N-demethylation to an active metabolite, 2-ethylidene-1,5-dimethyl-3,4-diphenylpyrrolidine (EDDP). Involvement of CYP3A4 and to a lesser extent CYP2D6 are responsible for the conversion of methadone to EDDP and other inactive metabolites. The elimination of methadone and its metabolites are mainly in the urine [17].

3.3.8. Buprenorphine

Buprenorphine undergoes significant first-pass metabolism and is only available in the sublingual, parenteral or transdermal formulations. One third of the drug is metabolized by the liver to norbuprenorphine, norbuprenorphine-glucuronide and buprenorphine-3-glucuronide by CYP3A4. The elimination is mainly through the feces (80–90%). Two-thirds of buprenorphine is eliminated via the enterohepatic circulation and one-third via renal excretion. In patients with renal impairment, buprenorphine appears to be safe since the kidney elimination of the metabolites of buprenorphine is very limited. In patients with hepatic impairment, careful monitoring is recommended [17].

3.3.9. Tapentadol

Tapentadol is a centrally acting μ-opioid receptor agonist and inhibits norepinephrine reuptake. It undergoes important first-pass metabolism and it is extensively metabolized in the liver by conjugation to tapentadol-O-glucuronide and tapentadol sulphate. Fifteen percent of the metabolism of tapentadol is via CYP2C9, CYP2C19 and CYP2D6. The use of this drug is contraindicated in severe renal insufficiency [20]. Opioids metabolized by the CYP system (e.g. codeine, oxycodone, hydrocodone, fentanyl, tramadol, and methadone) are associated with numerous drug interactions that can result in either a reduction or enhancement in opioid effects. Conversely, opioids that are not metabolized by that system (morphine, oxymorphone, hydromorphone) tend to be involved in fewer CYP-associated drug interactions [24].

3.4. Appropriate use of opioids in older adults

Persistent pain in older adults is common. A survey conducted in the United States found 18% of older Americans were taking analgesic medications and 63% of those had been taking for six months or more [25]. Similar proportions of one in five people reporting persistent pain has come from Europe and Israel [26], Canada [27], and Singapore [28]. The use of opioid analgesics in the treatment of moderate to severe cancer pain including in older adults is an integral component of the World Health Organization three-step ladder strategy [29–32]. High quality information is also available about the use of opioids in older adults [33,34]. Both a consensus statement by Pergolizzi et al. [17] and the American Geriatrics Society 2009 guidelines [35] promotes the use of opioids for persistent severe pain in older adults. Documentation of pain assessment is essential for regulatory and health care quality oversight associated with prescribing opioids as well as for monitoring their effectiveness. Assessment tools are available, including those that are useful in assessing pain in patients with cognitive impairment [25,36,37].

3.5. Risks of opioids in older adults

The inclusion of opioids on lists of potentially inappropriate medications (PIMs) is changing. The 2012 updated Beers criteria from the American Geriatrics Society [38] identifies only meperidine as inappropriate. The STOPP/START criteria recommends only caution when using high-potency opioids for extended use [39]. The association between opioid use and post-operative delirium is unclear. The use of opioids can increase the risk of falls [40]. The use of codeine combinations was shown to have the highest risk of injury, a 127% greater risk, [HR=2.27(2.21–2.34)] per one adult dose equivalent increase [41]. The addition of opioid analgesics, especially those metabolized by the CYP system may increase the potential for drug–drug interactions and adverse events [42].

3.6. Management of opioid-related side-effects

Opioid overdose management relies on using general supportive measures and treatment with naloxone [43]. The most common side-effects of opioid administration are nausea and constipation. Other side-effects can include sedation, dizziness and respiratory depression. Less common side effects may include physical dependence, delayed gastric emptying, hyperalgesia, immunologic and hormonal dysfunction, muscle rigidity, and myoclonus [44]. An association has been made between chronic opioid use and cognitive decline [45] but these findings need to be further validated.
Advanced age, immobility, dehydration and the use of other medications which slow bowel motility can magnify opioid-induced constipation. Prophylactic treatment with an osmotic agent or a stimulant cathartic is appropriate, and can then be titrated to an individual patient’s response. The use of the combination of oxycodone + naloxone (fixed ratio 2:1) may be considered [46]. Newer agents such as methylnaltrexone (peripheral opioid antagonist) [47–50] and prucalopride (5-HT4 receptor agonist with enterokinetic properties) [51,52] are available and may be considered in difficult cases. However data are lacking for use in frail elderly patients [53].

Respiratory depression is rare if low drug doses and slow titration are used during treatment initiation. Pre-existing pulmonary conditions, drug–drug interactions and cumulative effects from other drugs can increase this risk. Morphine, oxycodone, hydro- morphine, fentanyl, and methadone produce a dose-dependent respiratory depression with apnea at high doses, while buprenorphine has a ceiling effect [17].

Large doses of opioids can increase histamine release which can cause flushing, sweating or itching around the head, neck, or the chest [53]. Other bothersome side effects include nausea, dry mouth and urinary retention [17,35].

Opioid-induced hyperalgesia is observed as increasing pain symptoms in the absence of worsening pathology during opioid treatment. This phenomenon is not well studied and its clinical relevance is uncertain [54,55].

Opioid-induced immunosuppression is a curious phenomenon, mediated by the presence of μ-opioid receptors in the central nervous system and on immune cells. Morphine and fentanyl appear to have the most immunosuppressive effects [17,56,57]. Selection of an opioid drug for long-term treatment may need to consider this effect.

The use of the combination of buprenorphine + naloxone (fixed ratio 4:1) has mainly been targeted for use in managing opioid abuse conditions [58].

When side-effects of a drug outweigh the beneficial effects, regulatory agencies can proceed to withdraw marketing approval for a particular drug or formulation. For example the oxycodone sustained release formulation OxyContin (Purdue Pharma) was replaced by OxyNEO (Purdue Pharma) after a redesign of the formulation to make the tablet more tamper-proof. Propoxyphene or dextropropoxyphene (Darvon, US; Doloxene, Australia; Paradox, Capadex, New Zealand, others) was originally approved for use worldwide in 1957. This drug was withdrawn from the global markets between 2004 and 2010 because of having an extremely narrow therapeutic index, a high abuse, addiction and overdose potential, potential for triggering cardiac arrhythmias and the presence of safer and effective alternate drugs [59,60].

3.7. Approach to using opioids in older adults

The following steps can help guide the clinician who is considering prescribing opioid analgesics in older adults:

1. Pain assessment
   (a) Tools for general patients [25]
   (b) Tools for patients with cognitive impairment [37]

2. Screen for current aberrant drug-behavior problems or potential future substance abuse
   (a) Opioid Risk Tool (ORT) [61], revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R) [62]

3. Decide whether you are able to treat the patient without help
   (a) Presence of complex medical co-morbidities, complex behavioral or social circumstances would support referrals
   (b) Availability of appropriate specialists in pain management, geriatric medicine to help co-manage

4. Start treatment
   (a) Acetaminophen regular dosing, maximum daily dose 2400–3000 mg
   (b) Short-acting opioids titration. Select drug based on availability of dose range, formulation, and favorable metabolism. Avoid the use of meperidine
   (c) Switch to long-acting preparations if possible to minimize pill counts and to improve medication adherence and adjust for breakthrough pains
   (d) Monitor for safety and efficacy
      (i) Adjust dose to manage side-effects or toxicity
      (ii) Dose changes need to consider drug and formulation duration of action (Table 1)
      (iii) Consideration of opioid rotation strategy [63,64] if loss of effectiveness or hyperalgesia occurs

5. Constipation management
   (a) Stepped approach starting with osmotic cathartics
   (b) Combination of oxycodone/naloxone may be considered
   (c) In difficult cases consider adding methylnaltrexone, or prucalopride

4. Summary and conclusions

Opioids should be considered in older adults who have moderate to severe persistent pain, regardless of etiology. Therapeutic nihilism should be avoided, since advanced age, the presence of multiple co-morbidities and cognitive impairment does not diminish suffering and distress. Careful assessment of pain, monitoring of effectiveness and management of side-effects is essential. Buprenorphine is recommended because of its favorable pharmacokinetic properties. Opioid overdose is managed by supportive measures and naloxone treatment. Monitoring and aggressive management of constipation is important, because this condition can increase a patient’s discomfort and distress and lead to various cascades. Administration of prucalopride and methylnaltrexone may be considered in difficult cases. In patients with multiple co-morbidities and complex behavioral or social situations referral to specialized pain management services should be considered. If the clinician is successful in using opioids to manage pain, anxiety and distress, patients can live more comfortably, be more functional and reap the benefits of a better quality of life for the remainder of their individual lifespan. More research is needed to validate the safety, efficacy and targeted appropriate use of opioid analgesics in older people, especially those 80-years and older.

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Contributors

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Competing interests

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