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Opioids and the management of chronic severe pain in the elderly: consensus statement of an International Expert Panel with focus on the six clinically most often used World Health Organization Step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone).

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Abstract

SUMMARY OF CONSENSUS: 1. The use of opioids in cancer pain: The criteria for selecting analgesics for pain treatment in the elderly include, but are not limited to, overall efficacy, overall side-effect profile, onset of action, drug interactions, abuse potential, and practical issues, such as cost and availability of the drug, as well as the severity and type of pain (nociceptive, acute/chronic, etc.). At any given time, the order of choice in the decision-making process can change. This consensus is based on evidence-based literature (extended data are not included and chronic, extended-release opioids are not covered). There are various driving factors relating to prescribing medication, including availability of the compound and cost, which may, at times, be the main driving factor. The transdermal formulation of buprenorphine is available in most European countries, particularly those with high opioid usage, with the exception of France; however, the availability of the sublingual formulation of buprenorphine in Europe is limited, as it is marketed in only a few countries, including Germany and Belgium. The opioid patch is experimental at present in U.S.A. and the sublingual formulation has dispensing restrictions, therefore, its use is limited. It is evident that the population pyramid is upturned. Globally, there is going to be an older population that needs to be cared for in the future. This older population has expectations in life, in that a retiree is no longer an individual who decreases their lifestyle activities. The "baby-boomers" in their 60s and 70s are "baby zoomers"; they want to have a functional active lifestyle. They are willing to make trade-offs regarding treatment choices and understand that they may experience pain, providing that can have increased quality of life and functionality. Therefore, comorbidities—including cancer and noncancer pain, osteoarthritis, rheumatoid arthritis, and postherpetic neuralgia—and patient functional status need to be taken carefully into account when addressing pain in the elderly. World Health Organization step III opioids are the mainstay of pain treatment for cancer patients and morphine has been the most commonly used for decades. In general, high level evidence data (Ib or IIb) exist, although many studies have included only few patients. Based on these studies, all opioids are considered effective in cancer pain management (although parts of cancer pain are not or only partially opioid sensitive), but no well-designed specific studies in the elderly cancer patient are available. Of the 2 opioids that are available in transdermal formulation—fentanyl and buprenorphine—fentanyl is the most investigated, but based on the published data both seem to be effective, with low toxicity and good tolerability profiles, especially at low doses. 2. The use of opioids in noncancer-related pain: Evidence is growing that opioids are efficacious in noncancer pain (treatment data mostly level Ib or IIb), but need individual dose titration and consideration of the respective tolerability profiles. Again no specific studies in the elderly have been performed, but it can be concluded that opioids have shown efficacy in noncancer pain, which is often due to diseases typical for an elderly population. When it is not clear which drugs and which regimes are superior in terms of maintaining analgesic efficacy, the appropriate drug should be chosen based on safety and tolerability considerations. Evidence-based medicine, which has been incorporated into best clinical practice guidelines, should serve as a foundation for the decision-making processes in patient care; however, in practice, the art of medicine is realized when we individualize care to the patient. This strikes a balance between the evidence-based medicine and anecdotal experience. Factual recommendations and expert opinion both have a value when applying guidelines in clinical practice. 3. The use of opioids in neuropathic pain: The role of opioids in neuropathic pain has been under debate in the past but is nowadays more and more accepted; however, higher opioid doses are often needed for neuropathic pain than for nociceptive pain. Most of the treatment data are level II or III,

and suggest that incorporation of opioids earlier on might be beneficial. Buprenorphine shows a distinct benefit in improving neuropathic pain symptoms, which is considered a result of its specific pharmacological profile. 4. The use of opioids in elderly patients with impaired hepatic and renal function: Functional impairment of excretory organs is common in the elderly, especially with respect to renal function. For all opioids except buprenorphine, half-life of the active drug and metabolites is increased in the elderly and in patients with renal dysfunction. It is, therefore, recommended that--except for buprenorphine--doses be reduced, a longer time interval be used between doses, and creatinine clearance be monitored. Thus, buprenorphine appears to be the top-line choice for opioid treatment in the elderly. 5. Opioids and respiratory depression: Respiratory depression is a significant threat for opioid-treated patients with underlying pulmonary condition or receiving concomitant central nervous system (CNS) drugs associated with hypoventilation. Not all opioids show equal effects on respiratory depression: buprenorphine is the only opioid demonstrating a ceiling for respiratory depression when used without other CNS depressants. The different features of opioids regarding respiratory effects should be considered when treating patients at risk for respiratory problems, therefore careful dosing must be maintained. 6. Opioids and immunosuppression: Age is related to a gradual decline in the immune system: immunosenescence, which is associated with increased morbidity and mortality from infectious diseases, autoimmune diseases, and cancer, and decreased efficacy of immunotherapy, such as vaccination. The clinical relevance of the immunosuppressant effects of opioids in the elderly is not fully understood, and pain itself may also cause immunosuppression. Providing adequate analgesia can be achieved without significant adverse events, opioids with minimal immunosuppressive characteristics should be used in the elderly. The immunosuppressive effects of most opioids are poorly described and this is one of the problems in assessing true effect of the opioid spectrum, but there is some indication that higher doses of opioids correlate with increased immunosuppressant effects. Taking into consideration all the very limited available evidence from preclinical and clinical work, buprenorphine can be recommended, while morphine and fentanyl cannot. 7. Safety and tolerability profile of opioids: The adverse event profile varies greatly between opioids. As the consequences of adverse events in the elderly can be serious, agents should be used that have a good tolerability profile (especially regarding CNS and gastrointestinal effects) and that are as safe as possible in overdose especially regarding effects on respiration. Slow dose titration helps to reduce the incidence of typical initial adverse events such as nausea and vomiting. Sustained release preparations, including transdermal formulations, increase patient compliance.

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