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Benefitted Reduction of Neuropathic and Non-Neuropathic Pain

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Abstract

Muscle relaxant drugs include cyclobenzaprine, carisoprodol, chlorzoxazone, methocarbamol, and others. Cyclobenzaprine is essentially identical to amitriptyline, with potential adverse effects similar to those of amitriptyline. In addition, carisoprodol has been removed from the European market because of concerns about drug abuse. Although these drugs may relieve skeletal muscle pain, their effects are nonspecific and not related to muscle relaxation. Therefore, they should not be prescribed in the mistaken belief that they relieve muscle spasm.

Introduction

Muscle relaxants may inhibit polysynaptic myogenic reflexes in animal models, but whether this is related to pain relief remains unknown. If muscle spasm is suspected to be at the root of the patient's pain, it is probably justified to consider another drug with known effects on muscle spasm [1]. Clinicians should be aware that many of these drugs may be associated with greater risk for falls in older persons. Addiction is a chronic, neurobiological disease characterized by one or more of the following behaviours, impaired control over drug use, compulsive use, continued use despite harm, and craving. The likelihood that a patient will abuse opioid medications correlates with a number of genetic and environmental factors, and for those who are genetically pre-disposed, certain factors will precipitate the addiction [2].

Methodology

Although the risks are exceedingly low in older patients with no current or past history of substance abuse, it is impossible to identify every patient who will abuse or divert prescribed opioids. Therefore, many clinicians have adopted a Universal Precautions approach to pain management. This paradigm stresses that every patient should be assessed for risk factors related to the potentially problematic use of pain medication [3]. Such an approach seeks to protect patients from the harm of substance abuse and helps primary care providers meet their legal and regulatory responsibilities. Various sources, including published guidelines and statements from state medical boards, are available to help clinicians assess and monitor patients with persistent pain for responsible opioid use as shown in (Figure 1). Scores on the ORT and the SOAPP-R are used to stratify patients as low, medium, or high risk, which in turn informs their treatment plan [4]. Patients who have already been prescribed opioid medications can be assessed using the Current Opioid Misuse Measure, a 17-question self-assessment designed to identify on-going patient misuse of opioid medication. These tools should be used to supplement a physical examination, patient interviews, the healthcare provider's clinical experience, and diligent monitoring as a component of a comprehensive initial and on-going risk assessment. The patient interview may help to validate claims of pain, explore drug and alcohol use, and determine the safety of opioids within the patient's home while also helping to identify potential risk factors in treatment [5]. Stratification of patients is not meant to deny treatment to those classified as being at high risk for abuse. Rather, it allows the clinician to consider who can be treated without consultation, who should be co-managed with the assistance of a specialist, and who should be referred to medical providers with extensive experience in pain medicine or addiction medicine. Although clinicians should remain vigilant about the possibility of misuse or abuse of opioid agents in all patients irrespective of age, older age is significantly associated with lower risk for opioid misuse and abuse. Some authors suggest that underuse of opioids in older populations constitutes a greater problem [6].

Figure 1: Clinicians assess and monitor patients for responsible opioid use.

Discussion

Given that older patients may not fill prescriptions or may take opioid medications sparingly because of multiple concerns, clinicians are encouraged to query patients about their beliefs and prior experiences with this class of medications before beginning an opioid medication as shown in (Figure 2). A number of drugs from various classes that were developed for purposes other than pain relief have been found in traditional experimental pain models to alter or attenuate pain perception in many pain-producing conditions without raising the pain threshold [7]. These agents, now conventionally termed adjuvant drugs, originally appeared in the cancer pain

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Figure 2: Encouraged clinicians to query patients before beginning opioid medication.

literature, although the term is now used regardless of pain etiology. Drug classes include antidepressants, anti-convulsants, and other agents that alter neural membrane potentials, ion channels, cell surface receptor sites, synaptic neurotransmitter levels, and other neuronal processes involved in pain signal processing [8]. Adjuvant drugs may be used alone or co-administered with non-opioid or opioid analgesics and are used in a variety of persistent pain conditions, especially neuropathic pain. Tricyclic antidepressants were the first drugs found to reduce pain associated with post therapeutic neuralgia and painful peripheral diabetic neuropathy, but the adverse-effect profile of this class of drugs often contraindicates their use in older patients. More recent pharmacological advances in the treatment of depression have included selective serotonin-reuptake inhibitors and mixed serotonin- and norepinephrine-uptake inhibitors [9]. The SNRIs are particularly effective in the treatment of various neuropathic pain conditions and fibromyalgia, with a better side-effect profile than the tricyclic antidepressants. In contrast, SSRI drugs have not proved to be effective against pain. Gabapentin, pregabalin, and other anticonvulsant agents with similar mechanisms of action at voltage-gated calcium ion channels have been found to have beneficial effects in various neuropathic pain conditions more-benign side-effect profiles than older anticonvulsant and antidepressant tricyclic drugs. To minimize adverse effects, all pain-modulating drugs must be carefully titrated and monitored frequently. Regular phone contact and follow-up visits should be scheduled to assess therapeutic effects and monitor for adverse reactions. Anecdotal evidence and a limited number of studies have indicated that other drugs, as a group, are less reliable than opioids and traditional analgesics in the treatment of persistent pain [10]. These observations are often based on small patient populations in which subjects may be less responsive to other drugs or have a higher likelihood for side effects or a slower onset of action. In the absence of data from well-controlled clinical trials that are easily applicable to a given clinical situation, the use of these non-opioid, non-traditional drugs is largely a matter of clinical judgment. Analgesic effects have been described for a variety of systemically administered corticosteroids in a broad range of dosages for a variety of conditions [11]. Clinical observations and the evidence provided by numerous published clinical trials have led to the development of clinical guidelines regarding the use of opioids in patients with persistent non-cancer pain by the American Pain Society, American Academy of Pain Medicine, AGS, and others. Furthermore, the evidence that use of NSAIDs and COX-2 inhibitors may result in serious and life-threatening gastrointestinal and cardiovascular adverse events or gastrointestinal bleeding has shifted attention to opioids, especially for older patients who may be at particular risk for NSAID-related adverse effects. Controlled trials have established the efficacy of various opioids in the treatment of persistent pain associated with musculoskeletal conditions, including osteoarthritis and low back pain, and in the management of several neuropathic pain conditions, such as diabetic peripheral neuropathy and post therapeutic neuralgia [12]. Nonetheless, evidence of long-term effectiveness for persistent non-cancer pain conditions in all age groups is lacking. Two recent meta-analyses and a number of systematic reviews highlight the difficulties of assessing clinical trial data in support of opioid therapy for long-term management of persistent pain. The proper positioning of opioid therapy for older patients with persistent non-cancer pain is based on comparing the potential efficacy and risks with those of other modalities and balancing them against the harms of unrelieved pain and potential adverse effects of opioid therapy. All practitioners who care for older patient's geriatricians, pain specialists, and primary care providers must consider their own clinical experience along with published evidence when deciding whether and how they will prescribe opioids [13]. Use of opioids in older patients with persistent pain should be prescribed on a trial basis with clearly defined therapeutic goals. The trial may involve serial attempts to titrate the opioid to an efficacious dose without intolerable adverse effects. It should be understood that opioids will be discontinued if the trial is unsuccessful. In most persistent pain conditions that warrant opioid therapy, optimum management requires a comprehensive treatment program that also involves functional restorative and psychosocial modalities. Patients and their caregivers must understand that opioids are not a panacea or substitute for non-pharmacological therapies [14]. The potential adverse effects associated with opioids can present a barrier to long-term treatment. Although most of the adverse effects decrease with long-term use, adverse events can be sufficiently debilitating to cause patients to discontinue therapy. With long-term opioid therapy, respiratory depression usually results from excessively rapid dosing increases, drug–drug interactions with other central nervous system depressants, and drug accumulation or accidental overdose from opioids with variable pharmacokinetic profiles, such as methadone. Recent evidence has also shown that long-term opioid therapy may suppress the production of several hypothalamic, pituitary, gonadal, and adrenal hormones, manifesting most commonly as testosterone deficiency in men, with associated fatigue, depression, and decreased libido. When used over a protracted period of time, prescription opioid abuse may become a concern, especially in patients with a prior history of a substance use disorder [15].

Conclusion

Prescription opioid diversion and use of these agents outside specified medical indications and directions has placed an increasingly significant burden on the healthcare system and on society as a whole. Associated financial costs, including medical costs, lost productivity, and the additional burden on the criminal justice system, reached an estimated $9 billion in the United States in 2005.

Acknowledgement

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Conflict of Interest

None

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