Treatment of Cancer-Related Pain

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There is a wide range of specific and nonspecific treatments for pain related to cancer. These treatment approaches fall into two major categories: tumor specific and pain specific. Tumor-specific treatments include radiotherapy, chemotherapy, and surgery and have as their goal reducing or eliminating the cause of the pain. Pain-specific therapies include analgesic and other pharmacologic therapies, anesthetic and neurosurgical antitumor and ablative procedures, cognitive behavioral approaches, and complimentary and alternative therapies and have as their goal the reduction or elimination of pain independent of the cause.

There is an extensive body of descriptive data demonstrating the effectiveness of specific antitumor therapies to reduce pain. For example, radiotherapy for bone metastases has been demonstrated to provide significant pain relief across various tumor types and sites. In contrast, there is limited data comparing the effectiveness of radiotherapy to surgery or chemotherapy or other analgesic and pharmacologic approaches. Existing guidelines select one approach over the other and are currently based on best practices and documented clinical experience.

There is a lack of use of consistent validated assessment and measurement tools, limiting the evaluation of treatment effectiveness and comparative studies. There are a series of extant methodological approaches to relate pain assessment to treatment outcomes, including, for example, the Pain Management Index, the Edmonton Staging System, and the Memorial Symptom Assessment Scale; but these tools have not been sufficiently integrated into antitumor clinical trials, and relief of symptoms is often not the primary focus of the trial but rather survival.

Pharmacological therapies with analgesic and adjuvant drugs are considered the mainstay of treatment for acute and chronic pain, focused on reducing or eliminating pain symptoms over the continuum of the illness. Drug therapy is the primary treatment approach in patients whose disease is not responsive to antitumor therapies. Current national and international guidelines are based on validated, well-designed analgesic trials in acute, chronic, and breakthrough pain, using pain intensity as the defining pain criteria. Increasing attention has focused on developing clinical trials using mechanism-based entry criteria as a way to address and differentiate somatic, neuropathic, and visceral pain. However, the lack of a clearly defined mechanistically based classification schema has prevented the development of evidence-based protocols for drug selection and sequential trials. Further complicating this methodologic issue is the fact that many cancer patients have mixed pain syndromes, with both neuropathic and somatic components. A major step forward would be to set as a priority the development of large clinical trials for some of the common somatic and neuropathic cancer pain syndromes, using common assessment and treatment outcome methodologies to compare analgesic drug therapy with nonsteroidal anti-inflammatory drugs, opioids, antidepressants, anticonvulsants, and other adjuvant drugs. This approach would serve as a first step to the development of evidence-based sequential drug trial guidelines.

The pervasive lack of comparative trials has led to a series of what have been referred to as the controversies in analgesic drug therapy, specifically with opioid drugs. The controversies range from how to choose an appropriate analgesic and the starting dose, to what is the most appropriate route of administration, to the specific protocols for opioid rotation, and to the better understanding of tolerance development and risk of addiction. To address these controversies, there is a need for both novel and sophisticated methodologies and population-based studies to compare efficacy, side effects, routes of administration, tolerance development, and risk of addiction of the commonly used drugs. A recent multinational study has compared conventional medical management with oral opioid drugs to intrathecal opioid drug therapy and serves to demonstrate the challenges of implementing such comparative studies. Interindividual variation in response to analgesic drugs is significant, and pharmacokinetic and pharmacodynamic factors and genetic correlates have been identified. There is a need to further define the molecular biologic aspects of these differences among patients as we develop rational drug therapy guidelines.

To date, studies of the development of clinical tolerance and assessment of addiction risk are based on either clinical descriptive data without long-term follow-up or retrospective studies. The lack of such studies has the potential to negatively influence the approval of new preparations of opioid analgesics, and a recent U.S. Food and Drug Administration (FDA) Advisory Panel recommended the development of a National Institutes of Health multicenter–FDA partnership to study how to address these issues through novel experimental design and long-term studies in chronic pain patients.

In summary, there is a critical need to define the state of the science in the clinical management of cancer-related pain. A better understanding of the molecular biology of pain and its genetic correlates, coupled with mechanistically based trials using experimental study design methodology, will lead the way. The specific issues of opioid rotation, tolerance, and risk of addiction require a concerted effort of basic and clinical researchers to develop research priorities and cooperative projects that utilize the expertise of the drug researcher and clinician.
BIBLIOGRAPHY


