Gregory B Crawford
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Cancer Pain and Opioids—Past, Present, and Future

Gregory B Crawford, MBBS, MPHC, MD, FRACGP, FAChPM

Senior Consultant in Palliative Medicine, Director of Research & Education, Northern Adelaide Palliative Service, Adelaide, Australia; Associate Professor of Palliative Medicine, Discipline of Medicine, University of Adelaide, Australia

Abstract

The Cancer Council Australia and Cancer Institute New South Wales are two Australian organizations that are providing useful resources to support evidence-based prescribing of opioids in cancer pain. Morphine remains the preeminent medication for nociceptive cancer pain. Our understanding of the action of opioids, and how relatively recently these developments are, assists in putting pain and suffering in the context of "total pain." Increasing understanding of the how pain is understood is leading to new insights with an increasing emphasis on the neuro-immuno-pharmacology of pain.

Keywords

Cancer pain, morphine, opioid conversion, neuro-immuno-pharmacology

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Correspondence: Gregory B Crawford, MBBS, MPHC, MD, FRACGP, FAChPM, Associate Professor of Palliative Medicine, Discipline of Medicine, University of Adelaide, 5005 Australia. E: gregory.crawford@adelaide.edu.au

Recent Australian initiatives have improved the use and safety of opioid prescribing. The Cancer Council Australia has recently produced evidence-based clinical practice guidelines for the management of cancer pain in adults. They are intended to guide community prescribers in the rational management of pain with advice on the assessment and nonpharmacologic management of pain as well as opioid prescribing. This is a resource well worth exploring.[1]

It is well structured and emphasizes the need for a patient-centred approach to care. There are detailed sections on screening, assessment, and history taking. One would be surprised if it did not have a well-structured comprehensive component on the pharmacologic management of cancer pain. The emphasis on nonpharmacology and self-management, as well as practice improvement and quality control and opioid formulations, make this a valuable resource available to anyone with access to the Internet.

The Cancer Institute New South Wales provides another excellent Australian resource. Practicing oncologists will generally be well aware of eviQ,[2] the cancer treatment online resource that provides current evidence-based, peer-reviewed, best practice cancer-treatment protocols and information. The opioid calculator included in this resource is extremely useful, not just for the occasional prescriber of opioids but is a valuable method of confirming difficult or perhaps less commonly made conversions from one opioid to another,[3] not withstanding the continuing debate and uncertainty about opioid conversions.[4]

Morphine, named after Morpheus, the classical God of Dreams,[5] has held a preeminent place in the pharmacologic repertoire for pain management in cancer pain. The understanding of pain has developed within multiple scientific domains. Initially it was centered on the neuroanatomy, physiology, and pharmacology of opioids. In early history the benefit of opium and derivatives of the poppy were well known but the isolation of morphine in 1806[6] and the determination of its chemical structure in 1923 led to an explosion of knowledge.[7] The poppy and its effects were known as far back as 3400 BCE. Hippocrates,[8] in 460 BCE, dismissed the magic attributes of opium but acknowledged its usefulness as a narcotic, styptic, or antihemorrhagic agent in treating internal diseases and its useful for diseases of women and epidemics.

History reveals trade competitions and wars and the medicinal use in more recent times, includes opium tinctures, such as laudanum and then Brompton Cocktail, and cough and teething preparations such as Bonnington's Irish Moss.[9] The opioid ingredient no longer exists in the preparation of the same name now currently available!

We take for granted that opioids have isomers[10] and binding sites.[11] Equally we assume knowledge of stereoselectivity[12] and an ability to measure the strength of binding.[13] And the population in general know about endogenous opioids, despite their discovery as recently as 1974.[14] And only in the 21st century have we understood concepts such as excitation and also inhibition of pain signals. And we are

beginning to grapple with the concepts that opioids might not only provide analgesia, but also cause antalgesia and hyperalgesia, i.e. they stimulate further pain.

Dame Cicely Saunders,[16] with the modern hospice movement, pioneered an understanding of the available pain-relieving medications in terminal illness but also provided an insight into the anticipation and prevention rather than just the alleviation of pain.[17,18] An increasing understanding of mechanisms other than pure nociception only add weight to her concept of the total nature of pain—strengthening the importance of the physical, social, psychologic, and spiritual components of pain and, more widely, of suffering.[19]

Opioids are available in a confusing array of preparations. Naturally cultivated and synthetic opioids exist. We have access to routes of administration that include oral, transdermal, buccal, mucosal, nasal, subcutaneous, intramuscular, intravenous, and inhaled. And preparations may be immediate-, modified-, or even sustained-release. And there are combinations or opioids and preparations combined with other pharmacologic agents to alleviate possible side effects or to prevent diversion.

And increasingly the impact and involvement of the immune system is taking importance, with knowledge of the involvement of microglia, mitochondria, and multiple inflammatory cytokines. A new area of research, the neuro-immuno-pharmacology of opioids, is expanding.[20–22]

But despite these exciting advances, there is, particularly for many clinicians, still a sense of bewilderment. Do we really understand what initiates and maintains pain? In other areas of medical science there are developments that have lead to changing the nature of the condition and even preventing its occurrence. Perhaps one day we will see a super analgesic—the super opioid. A preparation that would relieve all pain, have no side effects, and be able to perhaps even prevent the "disease of pain." With the rapid growth in our understanding of pain and its mechanisms and modifications, we have to look to neuro-immuno-pharmacology. ■

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