



## Life in The Time of Opioids

Steven D Waldman<sup>1-3\*</sup>

<sup>1</sup>Associate Dean of International Medicine, University of Missouri-Kansas City School of Medicine, USA

<sup>2</sup>Chairman and Professor of Medical Humanities and Bioethics, University of Missouri-Kansas City School of Medicine, USA

<sup>3</sup>Clinical Professor of Anesthesiology and Pain Management, University of Missouri-Kansas City School of Medicine, USA

Just as HIV forever changed the way we approached every aspect of patient care, the pervasive use of opioids for chronic non-cancer pain is now altering the way we care for the patient suffering from acute and chronic pain of malignant origin and has made the care of this important patient population much more challenging. It seems that it was but a very few years ago that the alleviation of pain in cancer patients seemed within our reach. As clinicians began to understand the nature of cancer pain and how to treat it, the number of patients with uncontrolled cancer pain began to decrease. This was accomplished in large part by the widespread implementation of the World Health Organization Three Step Therapeutic Ladder. This Ladder provided clinicians with a logical step-wise approach to the pharmacologic management of cancer pain. While the Ladder has been subsequently modified to add a fourth step to include interventional pain management modalities and a fifth step to include reversible neuroaugmentation modalities, the mainstay of the Ladder's efficacy in the management of cancer pain remains the rational use of opioid analgesics.

Unfortunately, the rapidly increasing number of patients taking long-term opioids for a variety of non-cancer pain complaints has led to an entire population of opioid tolerate individuals, some of whom will inevitably develop cancer-related pain. Unlike the opioid naïve patients suffering from cancer pain of yesteryear, the high incidence of opioid tolerance encountered in today's patients has seriously compromised our ability to effectively use opioids when they are needed to treat cancer pain. This fact has serious implications for both the patient and the clinician as the treatment aims for cancer pain management have not changed in tandem with the increasing chronic use of opioids for non-cancer pain. Furthermore, the additional problem of the prevention of drug withdrawal in these opioid dependent patients has now been added to the mix.

While basic scientists unravel the neurobiologic basis of why the chronic administration of opioids for non-cancer pain causes opioid tolerance by looking at receptor regulation, desensitization, internal signaling, pro-inflammation and glial activation, clinicians are still left the task of treating this challenging group of opioid tolerant patients who suffer cancer pain. The starting point for the care of this unique and ever growing patient population is a targeted pain management assessment that must at a minimum include:

- Identification and input from all providers who prescribe the patient opioids and other controlled substances
- An accurate quantification of all legal, over-the-counter, and illicit drugs that the patient is actually taking (this is often different than what may be prescribed) including a careful assessment of the potential for drug diversion
- A history of drug allergies and reported "drug reactions" ... "I'm allergic to everything but Oxycontin"
- An assessment of medical and psychiatric co-morbidities including hepatitis, HIV, psychiatric illness, etc.
- A pain diagnosis that carefully identifies causes of acute, incident related, chronic non-cancer, and cancer pain etiologies

- The patient's prognosis from both a cancer and non-cancer perspective
- A careful search for a history of medication misuse or addiction
- An assessment of the patient's psycho-social and spiritual beliefs regarding cancer, pain control, coping strategies, and end-of-life issues.
- A clear understanding of what the patient's expectations are regarding pain relief

Once the clinician has the information gleaned from this targeted pain management assessment, it is then possible to begin implementation of a cogent treatment plan that provides the patient with effective relief of any acute or incident related pain, assures the continuation of current or equivalent analgesics, includes the prevention of drug withdrawal, and uses the early addition of adjuvant analgesics, interventional pain management, and neuroaugmentive modalities if appropriate. In order to accomplish these goals, it is usually necessary not only to continue the patient's maintenance opioids, benzodiazepines, barbiturates, and other controlled substances, but to titrate additional opioids, often at higher than expected doses to obtain pain relief. During titration, the addition of non-opioids and adjuvant analgesics may be beneficial. Monitoring and quantification of pain levels, functional capacity, and side effects is mandatory. If initial pain control is difficult to achieve, opioid rotation, interventional pain procedures with long acting local anesthetics, spinal opioids, and the use of ketamine and psychostimulants such as amphetamines may be useful strategies to attenuate the effects of opioid tolerance. If the patient is to undergo procedures under anesthesia, the potential for awareness under anesthesia due to drug tolerance remains a real possibility and needs to be considered. Once pain control is achieved and antineoplastic therapies such as chemotherapy and radiation therapy have been implemented, consideration should be given to the implementation of a Reverse Therapeutic Ladder which has as its goal the tapering of added opioids and other modalities used to treat the patient's acute cancer pain to provide future pain treatment options should they be needed. The prescription of immediate release opioids as rescue doses and to treat activity related or incident pain should be considered.

While the treatment of this rapidly growing special population of

**\*Corresponding author:** Steven D. Waldman, M.D., J.D, Associate Dean of International Medicine, University of Missouri-Kansas City School of Medicine, USA, E-mail: [waldmans@umkc.edu](mailto:waldmans@umkc.edu)

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opioid tolerate patients who present with cancer pain is challenging, the above strategies can make the care of these patients more successful and rewarding. As clinicians are in the process of assessing

the appropriateness of the continued use of opioids to treat chronic non-cancer pain, we should remember the collateral damage that this treatment approach causes for patients suffering from cancer pain.

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