



Opioids for CRPS? Think again.

By R. Norman Harden, MD

WHETHER OR NOT TO PRESCRIBE OPIOIDS for chronic and non-malignant pain conditions, such as CRPS, remains controversial¹⁻³. After years of thoughtless and over-aggressive use of these compounds for pain, most practitioners have become cautious, primarily due to the emergence of serious side effects and adverse events associated with chronic opioid therapy³⁻⁶. Although the quality of research addressing this clinical controversy has improved, there still have been no definitive studies performed^{3,7,8}. Nonetheless, this class is sometimes used in complex regional pain syndrome (CRPS) as a “rescue” or an “as needed” medicine.

One has to question when opioids are used in chronic pain maintenance and

prophylaxis in CRPS (around-the-clock therapy)⁹. The standard for scientific evidence of any therapy in medicine is the Randomized Controlled Trial (RCT) and unfortunately, only one has been conducted evaluating the use of any opioid in CRPS. Harke et al studied controlled-release morphine in CRPS and reported no difference in pain reduction when compared to placebo.^{11,12} In other words, morphine did not relieve CRPS pain in this trial. More research is needed to definitively address this question, considering that the Harke trial was complicated and may have been underpowered¹².

There are a few high-quality studies of opioids for neuropathic pain that suggest marginal efficacy¹³. However,

evidence also suggests that neuropathic pain does not respond as well to opioids as nociceptive pain (pain from skin, muscles, joints) and often requires higher doses^{15,16}. Consequently, neuropathic pain states (especially the neuropathic component of CRPS) often require much higher doses of opioids, which in turn greatly increase the risk of side effects and adverse events. Thus, a very careful and thoughtful analysis of the risk (ie, side effects, adverse events, cost) to benefit (efficacy/effectiveness) ratio is critical in the decision to use opioids in CRPS.

Since there is no evidence supporting the use of opioids in CRPS and the literature is not particularly supportive of opioids for CRPS, we must conclude the Efficacy/Effectiveness (benefit) part of this equation does not favor opioids in the CRPS population⁹⁻¹². Opioids are clearly not a panacea, and there are many unresolved concerns about long-term efficacy in any chronic condition, efficacy in neuropathy, tolerance, cognitive impairment (especially with “rescue dosing” or initial titration), long-term toxicity and opioid-induced hyperalgesia^{3,9}.

Good practice and common sense requires that we critically and continuously assess the risks and side effects of opioid therapy in order to maintain that primal tenet of medicine and our Hippocratic Oath: “first do no harm.” Furthermore, our patients must be fully informed of the risks considering that there is no compelling research supporting the use of these compounds for CRPS.

Side Effects of Opioid Therapy

The many risks of opioid therapy are well known, from the very common occurrence of constipation and itchiness to the more recently-identified hypogonadism (shrunken testicles)^{3,17}.

Long-term cognitive impairment, personality changes, tolerance, and long-term toxicity are unresolved issues at the moment. Any general pharmacological reference, such as a recent edition of the Physicians' Desk Reference, will have a good list of the problems associated with opioids. One particular side effect of opioid use in CRPS is opioid-

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induced hyperalgesia (increased pain perception)^{18,19}. Since hyperalgesia is an important diagnostic and clinical feature of CRPS, it makes little sense to use a class of drugs that cause this symptom for treatment of CRPS. Thus, a CRPS patient on high-dose opioids may have a worsening of signs and symptoms due to opioid therapy. Simply said, high-dose chronic opioid therapy may make CRPS pain worse.

Optimal CRPS care preferably entails the use of non-drug therapies, non-opioid medications for maintenance, and occasional opioids for crisis management, specifically when overwhelming pain prevents progress in functional restoration and if injection therapy has been considered and/or fails^{20, 21}. Opioids should never be used in isolation, and must always be used only with a comprehensive functional restoration program^{20, 21}. Thus, clinicians should not become over-enthusiastic or overzealous about opioids and should keep them in perspective within therapeutic techniques. A critical assessment of the literature and the risk to benefit ratio suggest that opioid therapy in CRPS is extremely questionable.

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