Opioid Induced Hyperalgesia

Introduction
Pain is one of the main reasons that people seek medical attention, and it is estimated to affect tens of millions of Americans. Chronic pain management commonly includes the use of opioid type medications. This is in spite of the fact that this class of drugs has well known adverse effects including the development of dependence, tolerance, and addiction. Recently, however, a troubling clinical phenomenon known as opioid-induced hyperalgesia (OIH) is gaining more and more attention with medical providers. As a consequence, there has been a noted increase in the number of clinical studies exploring the mechanisms of action and clinical significance of OIH, although prevalence has yet to be determined. For example, one small prospective study of six opioid-naïve chronic pain patients developed hyperalgesia to cold pressor pain within 4 weeks of starting moderate doses of morphine. In another study, OIH was described in multiple patients following acute opioid exposure in a peri-operative setting. Despite the debates on clinical relevance, it is clear that OIH presents a clinical challenge in acute, chronic, and cancer pain treatment settings.

Diagnosis and Presentation
OIH is characterized by a significant intolerance to pain, often among patients that are receiving repeated doses of opioids. It can present as allodynia or hyperesthesia, and is often times mistaken for opioid tolerance. It differs from opioid tolerance in that the pain intensity is stronger than initially reported, occurs relatively quicker, and worsens with an increased opioid dose. Common characteristics of OIH include nociceptive sensitization, the area of pain is more diffuse, has lesser quality, and is harder to pinpoint. It has been reported that pain can manifest beyond the original region of injury. A major concern with this condition is that a prescriber may often times continue to increase the dosages of opioids in an effort to control the patient’s pain symptoms. However, this can be extremely dangerous as it can result in drug overdose or death.

Etiology
Although the exact mechanism is unknown, several mechanisms have been proposed and are currently being studied. OIH can occur under a number of varying treatment situations involving opioid medications (e.g. cancer patients, and with both acute and chronic exposure). It has been reported with different types of opioids and with all different routes of administration such as oral, intravenous, intrathecal, and epidural. Therefore, it is likely that there are multiple mechanisms involved. One of the most commonly proposed mechanisms is the activation of the NMDA receptor. This causes an influx of calcium and increases excitability of the neuron, therefore causing the neurons to be more active and to readily transmit painful impulses. Another proposed mechanism is the increased production of the endogenous opioid peptide, dynorphin, which activates the kappa and NMDA receptors and has been shown to be increased with prolonged opioid use.

Treatment Options: The following are examples of some suggested treatment strategies
- Referral of the patient to a pain management specialist.
- Discontinuation of the offending opioid using a gradual tapering method. This strategy is usually complicated by the fact that underlying pain issues persist and still require an effective treatment plan. To complicate matters further, opioid withdrawal can sometimes paradoxically produce hyperalgesia.
- Reducing the current opioid dose has been shown to reduce hyperalgesia while also improving the analgesic effects in some patients.
- Switching from one structural class of opioids to another has also been an effective strategy in some studies. Switching to methadone has been one of the most popular treatment alternatives thus far. (Phenanthrene opioids have shown a higher association with OIH, so try non-phenanthrene opioid such as buprenorphine, fentanyl, tramadol, or methadone)
- Supplementing opioid therapy with a non-opioid pain reliever such as acetaminophen or a COX-2 inhibitor/NSAID is another tactic that has gained some support.
Conclusion: Future Directions
In order to better understand the clinical relevance of OIH, a number of important questions remain to be answered. For example; what patient population is at highest risk to develop OIH? Which opioids are or are not associated with the development of OIH? What is the typical duration of OIH? What is the prevalence of OIH? What is the root cause of OIH? Further research is clearly needed to determine the answers to these questions. Until that time, timely and accurate diagnosis of this condition and development of an effective treatment cannot be fully established.

References:


