LASIE COLUMN

The long-term negative effects of opioid utilization

Prior to the 1990s most physicians rarely prescribed narcotics or opioids beyond a short window unless the individual had cancer. Since then there has been a growth explosion in the pain industry. The premise of long-term utilization of opioids is that there is a source of ongoing pain that never ceases in an individual and that requires constant mu receptor treatment with narcotics.

Over time, this concept has become accepted and spawned the industry of 'pain management'. Prior to the 1980s and 1990s most physicians treated pain without narcotics. If narcotics were utilized, they were usually for patients with active and growing tumors. Cancer tumors do produce ongoing and active pain that does need control.

Recently, non-cancer chronic pain has become prevalent as a diagnosis and consequently opioids too have become prevalent. Obviously there is a problem with the use of these synthetic narcotics in this country. We usually look at death statistics to understand the negative implications of long-term use of opioids. For instance, for the first time ever, male life-expectancy has dropped in this country; this is due primarily to early death via overdose.

Beyond death there is a host of problems associated with the long-term application of opioid and narcotic medication to the human body. We will discuss some of these in this article.

Long-term use of opioids may be considered to be more than 7 days at this point. However, historically, we think of this as lifetime use or the use of narcotics for years. Narcotics attach to mu receptors to achieve the effect of pain relief. These receptors are not just located in the pleasure center of the brain, but also in the spinal cord and throughout the body. The medications prescribed do not preferentially attach to receptors associated only with the pain being treated; rather, they attach to any and all receptors encountered. One of the primary effects of narcotics and opioids is euphoria.

Even considering DSM IV or V criteria, the lifetime prevalence of opioid abuse among chronic pain patients is about 35% (*Boscarino 2011)* The seminal article by Portenoy that ushered in the era of 'pain as the 5th vital sign' had warning signs within it regarding this potential. In the article, 2 of 38 patients with prior known substance abuse became addicted. None of the 38 patients treated for non-cancer pain with opioids gained employment or social function. Only 24 described partial relief of pain and 14 had no relief (*Portenoy 1986*). Despite this study, because there was no toxicity reported, it was determined that opioids were to be considered safe.

Unfortunately, the current model of pain management is to escalate dosage. That is, if some individual presents to a physician and states that they are having more pain, the typical response of a provider is to

increase (escalate) the dose or frequency of utilization of narcotics. It has become clear that this is how pain is 'managed' today in our country. There is no good evidence to support this practice. There is evidence that demonstrates no improvement in actual pain scores with escalation. There is also evidence that shows no improvement in function or ability with escalation (*Dibenedetto 2013*). The study of 778 persons on narcotics over time did show statistically significant findings of aberrancy with narcotics. Therefore, it is not clear that narcotics are good for long-term pain. In fact, pain tolerance improves with abstinence (*Wacholtz 2014*).

Once someone has a history of long-term use of opioids he or she has more sensitivity to pain and less tolerance of pain (*Cowan 2005*). Opioids are associated with or cause the following list of additional problems beyond addiction:

Respiratory depression

Dizziness

Delirium

Nausea

Vomit

Aspiration pneumonia

Constipation

Sedation

Depression

Insomnia

Hormone deficiency

Confusion

Fall risk

Hyperalgesia

Allodynia

Increased length of stay at hospitals

Increased costs of operation and supplies

Increased liability and defense costs

The Joint Commission (source of the 5th vital sign...) has stated that opioid adverse events may be caused by administering the wrong dose, monitoring improperly or from simple interactions with other medications. Adverse events cause care to be diminished due to the increased length of stay and treatment of complications associated. Length of stay in particular is related to dosage of opioids and also to pre-operative prescriptions of opioids (*Oderda 2013*).

Physicians are to blame in part. A 2014 survey revealed that less than 10% of prescribers could answer correctly 11 basic questions about opioids (*Gaunt 2014*).

Acute effects of exogenous opioids are cough suppression, analgesia and constipation; these are often sought after. Also, one may develop drowsiness, nausea, vomiting, loss of appetite, reduced body temperature and urinary retention; these are typically not medically useful effects. However, one other acute effect of opioids is mood elevation and euphoria.

40-95% of users will develop constipation. There is now an entire pharmaceutical sub-category industry of treatments for 'narcotic-induced constipation'. In addition to the constipation, people develop reflux, vomiting, bloating, abdominal pain, anorexia, hard dry stool, straining to pass bowel and cramping. Chronic opioid users also may have common bile duct dilation; this is usually only seen with malignant disease in normal populations. Because tolerance to constipation never develops, some believe that co-prescription of laxatives with narcotics is mandatory (*Khademi 2016*). Of course, laxatives have their own side-effects and often aren't effective for narcotic-induced constipation.

Opioid-induced androgen deficiency occurs. In addition, there is damage to the hypothalamic-pituitary-gonadal axis and the hypothalamic-pituitary-adrenal axis. Opioids reduce serum levels of testosterone, estrogen and progesterone as well as other important hormones (anabolic and otherwise). This causes depression, decreased energy levels and sexual dysfunction. ED that is post-traumatic is often simply caused by testosterone deficiency due to too many opioids. Opioids also worsen diabetes and metabolic syndrome as well as cause osteoporosis.

Opioids reduce the function of the immune system as well. Cytokine release is directly altered. For example, people with HIV that utilize opioids have had an increase in viral load and exacerbation of the infection (*Peterson 1990*). Opioids also have associations with a number of cancers.

Opioids also cause cardiac effects. One such effect is prolonged QT interval; this is particularly true with methadone. EKG studies should be done periodically on those with chronic methadone use. Those with reduced liver function are at more risk. Chronic opioid use also causes reduced liver function.

The list goes on and on. As there is no clear evidence that chronic use of opioids improves pain scores or function, then there is no clear evidence that they work. There is evidence of abundant and detrimental side-effects. The only beneficial side-effect seems to be euphoria. Unfortunately, euphoria causes a host of social and family problems and is the source of psychological addiction. In my opinion, the long-term use of opioids should be seriously reconsidered.

There are a variety of medications available for all of the secondary effects of opioids, however it should be considered that reducing or stopping opioid use may be the best solution.

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Peterson