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Editorial

How Do Long Term Oral Pain Killers Enhance Pain and Promote Chronic Pain?

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Abstract

Oral pain medicines are routinely used to treat pain and chronic pain. Recent evidence shows that many of these medicines actually increase chronic pain when used over several weeks. Patients should be encouraged to find alternative pain treatments and avoid oral medicines for pain.

Keywords

Opioids; nonsteroidal anti-inflammatory drugs; pain; chronic pain; chemokines; skin

Chronic pain such as chronic low back pain, whiplash and fibromyalgia affects thousands of patients and can last for several years. Many patients use nonsteroidal anti-inflammatory agents (NSAIDs) or opioids to treat acute and chronic pain. Acetaminophen inhibits cyclo-oxygenase 1 and 2 at the peroxidase site [1] and is therefore an NSAID, although its anti-inflammatory activity is low.

A meta-analysis of 9000 patients found that opioids, NSAIDs, baclofen and duloxetine are effective pain treatments in chronic low back pain [2]. In contrast, a recent study found that long term use of NSAIDs increases pain and promotes the onset of chronic pain [3]. It has been known for sometime that long term use of opioids increases pain, opioid hyperalgesia, and promotes

chronic pain [4]. This is especially true of fentanyl and fentanyl patches that can cause hyperalgesia within a few hours of administration [5]. Acetaminophen is not recommended for the treatment of chronic pain [6]. There has been some speculation that neutrophil associated inflammation may be involved in chronic pain induction by NSAIDs [3].

Pain is sensed in the skin by transient receptor potential cation (TRP) channels and other receptors [7, 8]. The skin is abundantly endowed with these receptors which makes it exquisitely sensitive to pain. Oral pain killers do not penetrate adequately into the skin to treat severe pain. Oral pain killers poison the body after oral administration, induce respiratory depression, strokes, heart attacks and ulcers that may kill 155,000 people in the US every year [7].

An initial painful insult activates skin sensory neuronal TRP channels, many of which respond to mechanical insults [8]. This damage causes the release of chemokines that attract neutrophils and macrophages. The initial insult may also damage keratinocytes that release bradykinin [9]. Pain, swelling, inflammation and chemokine receptor synthesis are induced by bradykinin. Neutrophils release leukotrienes that activate TRP channels and cause long term pain [7]. Macrophages contain cyclo-oxygense 2 and release prostaglandins that enhance pain and activate TRP channels [7].

Chronic pain is generated in the skin [7]. Chemokines released in the skin activate resident T cells that produce IL-17, which causes bradykinin and chemokine release [10]. This produces more TRP activation, pain and chemokine release. A pain chemokine cycle may be established in the skin, which is the basis of chronic pain.

Opioids induce chronic pain by increasing chemokine synthesis [11]. The synthesis of chemokines in the skin during opioid therapy has not been examined. NSAIDs also increase chemokine synthesis and cause chronic pain. Acetaminophen induced damage to hepatocytes increases chemokine release with the attraction of neutrophils and macrophages [12, 13]. Whether this happens in the skin or not has not been examined. Aspirin can induce the synthesis of chemoattractant cytokines, similar to chemokines, in lung tissue [14]. Ibuprofen increases chemokine synthesis and gene expression [15]. NSAID effects on skin chemokines are not yet known. Therapies that inhibit chemokine production [7] are useful in chronic pain.

Author Contributions

The author did all the research work of this study.

Competing Interests

The author has declared that no competing interests exist.

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