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Commentary

Osteoarthritis Pain and Persistent Opioid Use

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Introduction

Osteoarthritis, a widespread arthritic condition associated with enormous individual, social and economic ramifications in our aging society remains incurable despite years of research [1, 2]. Principally due to localized structural and enzymatic disruptions of the articular cartilage lining of freely moving joints such as the knee, these destructive changes and others that commonly co-occur in the surrounding joint tissues, such as the ligaments, bone, and muscles can interact to produce the symptom of most concern to patients, namely pain [See Box 1]. This pain experience, which is often unrelenting, may not only be experienced locally, but is commonly associated with symptoms of widespread pain that tends to greatly limit mobility, the motivation to move, and functional ability. Since the ability to move is very crucial to a person's well-being, most treatments for this condition aim to reduce the pain experience, to prevent excess or further pain, or to increase pain coping and self-efficacy skills [3,4].

*Aberrant biomechanics [5]
*Anxiety
*Cartilage damage
*Depression
*Comorbid conditions e.g. diabetes
*Fear
*Subchondral and cancellous bone damage [6]
*Ligament damage and joint instability
*Joint malalignment
*Synovial inflammation
*Joint effusion
*Muscle inhibition
*Muscle atrophy
*Obesity and adipokines [7]
*Poor proprioception
*Low self-efficacy
*Sleep disturbances [8]
*Surgery[ies]

Box 1: *Key Independent and Oftentimes Overlapping Sources of Osteoarthritic Pain.*

**Disease manifestations or situations that cannot be altered positively by opioids*

Unfortunately, while useful in reducing inflammation that often accompanies the disease, anti-inflammatory medications often advocated for treating this population may fail to alleviate central nervous system pain associated factors, and may even be contra-indicated for a given patient due to their adverse cardiovascular effects. Other analgesics may result in unwarranted side-effects such as gastro intestinal problems, and even if not, can impact cartilage viability negatively. Exercising, often touted as key to the maintenance of joint integrity and life quality, may be impossible to carry out alone if pain is exacerbated by the slightest movement, or if pain is not attributable to musculoskeletal factors.

Moreover, restoring function and ameliorating pain in severe cases of the disease through surgery may not be indicated or successful in relieving pain, especially if multiple joint sites are affected. In addition, even if surgery of a single joint is undertaken, pain may not abate to the degree expected or desired.

With few interventions that can reduce osteoarthritic pain effectively, the use of addictive opioids may consequently be forthcoming, especially in those cases resistant to safer forms of analgesic medication and non-steroidal anti-inflammatory drugs [2].

However, the use of opioids, a class of drugs also called narcotic painkillers, has recently become an epidemic of significant proportions in the United States, in general, with many premature deaths attributable to this type of drug.

Among users are clearly those suffering from one or more forms of chronic pain, and although no study exists to delineate how many osteoarthritis users are being fatally affected by these drugs, clearly opioids are frequently prescribed for arthritic pain in the hip and knee, and other joints, even though no truly well-designed randomized controlled trial can be located in the current literature to support this strategy [9], despite a favorable review in 2007 [10].

Moreover, even if deaths of osteoarthritis sufferers are not yet problematic as a result of opioids, their usage on a prolonged basis appears highly disadvantageous with little benefit in the context of attenuating the disease process, except to alter the perception of pain. Moreover, it is now clear that many cases of osteoarthritis suffer from centralized pain syndromes or pain hypersensitivity, rather than simply experiencing only localized pain, and one of the dangers of excess opioid usage is that it causes the nervous system to become overly sensitive to painful, as well as no- painful stimuli [11].

In absence of pain relief or any strategy to reduce the factors that heighten osteoarthritis pain that are amenable to intervention, more opioid usage rather than less opioid will likely be required.

This brief is derived from PUBMED data on this topic and that has been published in 2017. No specific study design was sought and all 50 publications found on the topic using the key words ‘osteoarthritis and opioids’ were reviewed to highlight the issue and encourage a more focused conversation about this topic.

Search Results

Opioid use and osteoarthritis

As outlined above, one of the dangers of excess opioid use is not only that it often leads to tolerance, a situation where more pain relieving substance is required to produce the original effect, and where withdrawal symptoms can increase muscle pain and anxiety, but both these factors are key correlates of osteoarthritis pathology. As well, opioids are not effective for intervening in centrally mediated pain problems or mixed pain states [11]. They can also increase obesity levels, which contribute to both mechanical and inflammatory categories of pain, and possibly depression.

Moreover, opioid use among older adults is highly risky in general, and elderly osteoarthritis patients who abuse opioids, especially those with comorbid conditions, are at high risk as regards their general wellbeing [12], as well as injurious situations including falls, recurrent falls, and fractures.

In addition, since joints are susceptible to both insufficient or excessive loading activities [13], and both can lead to joint degeneration [14], even if opioids provide extreme pain relief or relief that reduces pain perception, the ultimate effect of prolonged high dose opioid use on the osteoarthritic joint[s] may be especially deleterious if this permits the subject to place excess stress or abnormal loads on the diseased joint, as shown in studies of neuropathic joints where insensitivity to pain produces a heightened risk for fostering or exacerbating joint degeneration processes [15,16]. In addition, if excess drug use fosters sedentary habits or obesity or both, the potential harm to the joint architecture and structure that leads to a worsening of pain should not be underestimated [17]. Ultimately, the ensuing result might be a heightening rather than any lessening of overall pain levels and dysfunction, or a spreading of the disease from one joint to others.

Yet, according to one study, osteoarthritis-related opioid dispensing and associated costs [which may not have factored in excess disability costs] are set to increase substantially over the next 15 years as populations age. Hence the risk of exacerbating the chronicity of the disease, along with the risk of direct adverse events, particularly among older people [18] is likely to rise over time, rather than abate, if alternate solutions are not forthcoming.

Yu., *et al.* [19] determined recent trends in the rate and management of new cases of osteoarthritis presenting to primary healthcare using United Kingdom nationally representative data, and reported rising rates of clinical osteoarthritis, and a shift towards opioid analgesic prescription as a major concern.

Namba., *et al*. [20] who studied a total of 24,105 post-operative osteoarthritis patients found that even after the initial 90-day post-operative period, 41.5% (N = 9914) continued to use opioids. Also, 155 (0.6%) revisions occurred within 1 year and 377 (1.6%) within 5 years. Compared to patients not taking any opioids, patients using medium-low to high opioid use after the initial 90-day period had a higher adjusted risk of 1-year revision, depending on the type of medication used and time period.

DeMik., *et al*. [21] found that despite increasing evidence calling proposed benefits of opioids into question and the increasing awareness of the risks of opioids, prescription rates remained stable between 2007 and 2014. As reported by DeMik., *et al*. [21], the United States is in the midst of an opioid epidemic, yet these medications continue to be used to manage pain associated with osteoarthritis, despite mounting evidence questioning their benefits.

According to a prior report, strong opioids actually only reduce severe osteoarthritis pain by approximately 24%, while weak opioids reduce mild to moderate osteoarthritis by approximately 40%. As well, even though they are as effective as non-steroidal anti-inflammatory drugs for ameliorating osteoarthritis pain, both weak and strong opioids are found to have unpleasant adverse effects, including constipation, fatigue, dizziness, nausea and vomiting in more than 50% of cases [22].

Reasons for excess opioid usage

The use of opioids as first-round therapy for pain has been driven by several factors, including the health care providers' lack of understanding that anti-inflammatory medications are at least as effective as opioids, a patient's expectation of complete pain relief on presentation to the emergency room or doctor's office, and increasing importance placed on patient satisfaction [9].

Myths about osteoarthritis such as the fact not much can be done to impact the disease, treatments other than surgery are of little help, and articular cartilage has no reparative properties and is irreversible are other possible reasons. The belief osteoarthritis is a local degenerative disease, rather than a highly complex disease with multiple central as well as peripheral pain correlates is another factor [23].

Clearly, consumer demand, successful pharmaceutical marketing efforts, economic factors, policy factors, magical thinking, the desire for instant gratification, the glorification of drugs, designer drug demands, and exposure to emotionally compelling marketing messages are also possible interrelated factors.

However, even though this topic has been examined since 1980, and 716 related papers on the present topic have subsequently been published in PUBMED; 472 in last 10 years; 241 in recent 5 years; and 50 for 2017, very few, if any, have examined why this is often the drug of choice for osteoarthritis pain relief.

The specific use of this drug spectrum to alleviate osteoarthritis pain is also puzzling in light of what is known about osteoarthritis pathology and its key determinants, along with a plethora of evidence-based non-pharmacologic approaches and pharmacologic approaches that can produce pain relief commensurate with that achieved by opioids, but without serious long-term consequences.

In addition, even when surgery is undertaken, it is obvious that this alone does not ameliorate osteoarthritic pain to a sufficient degree in some cases, especially when opioids are prescribed. Indeed, not only may the same dosage be required to quell pain, but a higher dosage may be required, and their harmful effects can be duly observed with long-term use leading to worse results than those of control patients who do not take opioids after joint replacement [9].

Also noteworthy in the context of treating the older osteoarthritis patient with well construed pain reduction approaches, is the recent finding by LoCiganic., *et al*. [24] that participants with osteoarthritis or at risk for knee osteoarthritis who used opioids and antidepressants with/without other analgesics/nutraceuticals tended to have an increased risk of recurrent falls after adjusting for potential confounders. Falls, are a major determinant of osteoarthritis disability, and it is shocking to think patients with osteoarthritis or unrelenting unclassified pain can incur this risk, due to the recommendations of a provider unfamiliar with the risks of palliating severe pain with opioids, or a patient who is not clearly informed of the risks or both.

Unfortunately, although Lambova [25] discussed multiple interventions for treating osteoarthritis conservatively, no in-depth attempt has been made to undertake any well-designed comparative study to compare non-drug related interventions versus opioid related interventions for ameliorating osteoarthritis pain relief. Nor is any recently conducted level 1 placebo-controlled study discernable to support the widespread use of opioids to the extent observed by epidemiologists.

Discussion and Recommendations

In terms of addressing pain, the causes of osteoarthritis pain, while complex, unstable and non-linear in character [23] can clearly be attenuated to some degree by careful efforts to prevent excess joint damage, such as those due to falls injury, uncontrolled diabetes, and obesity among other factors, and acknowledging the role of psychological disease correlates that heighten pain.

In addition, Knoop., *et al*. [26] recommended the prescription of analgesics be guided more dominantly by clinical symptoms and needs, and a thorough shared decision-making process between patient and physician than is currently evidenced in general practice. Appropriately tailored and personalized multi-pronged approaches to alleviating pain through joint protection and exercise strategies that are low impact, as others shown in Box 2 may be helpful as well.

In particular, educating patients about safe treatment options and highlighting the dangers of opioid use and possibility of more pathology rather than less, is clearly paramount. In addition, helping patients to understand that adding morphine to periarticular injections is ineffective for relieving local pain, reducing swelling, and improving the postoperative range of motion is also desirable [27].

Smith., *et al*. [28] found patients who used opioids prior to total knee arthroplasy actually obtained less rather than more pain relief from the operation. Hence, decreasing the amount of opioids used before surgery, if this is needed at all, appears likely to yield more favorable, rather than less favorable, surgical results [9].

Kim., *et al*. [29] concluded that over 7% of patients will persistently use opioids in the first year after hip or knee arthroplasty. Among patients who used opioids 80% time for more than 4 months after replacement surgery, this group also noted 72.1% became persistent users. However, given the adverse health effects of persistent opioid use, they clearly implied a safer more efficacious set of pain relieving strategies needs to be developed to prevent persistent opioid use after this common form of surgery.

As outlined by Ruiz Iban., *et al*. [30], usage of strong opioids may indeed be safe and effective in the short-term management of osteoarthritis with moderate to severe pain, when other pharmacological treatments are inadequate and surgery is contraindicated, provided their use adheres to existing guidelines. At the same time though, since osteoarthritis at one joint can lead to osteoarthritis at another joint and patients may clearly continue to use addictive opioids to relieve their pain even if they undergo surgery, efforts to effectively minimize the presence of pain among people with painful disabling osteoarthritis in a timely way is crucial. Alternately rather than discontinuation of opioid treatments [31] safer types of pain remedies should be especially sought if the patient is depressed or obese with multiple comorbid diseases or neurological symptoms who show tendencies to persistence.

In this regard, and according to some recent research, the concomitant use of well controlled exercise and vitamin D supplementation could provide an interesting alternative treatment for osteoarthritis pain [32]. Cibrian [33] too discussed various non-drug interventions to reduce pain and opioid use after total knee arthroplasty surgery. Podder., *et al*. [34] further suggest future studies to examine how to individualize treatment options based on patient phenotype and genotype may hold promise. Tedesko., *et al*. [35] meantime found electrotherapy and acupuncture after total knee arthroplasty effectively reduced and delayed opioid consumption.

Cognitive behavioural therapy, and consulting pharmacists and pain experts is also recommended [12] and may be more helpful than not. However, bearing in mind, patients especially, may not be sufficiently enthused towards applying the principles of disease self-management implied in this approach if their providers do not mention the importance of this, providers might want to spend time educating their osteoarthritic patients about their personal responsibilities for managing their condition to offset pain and unwarranted side effects. While short-acting opioid medications may also provide a safer and cheaper alternative to long-acting opioid therapies in the treatment of chronic osteoarthritis [36], to optimize the use of opioids in older adults, where there is no other choice, clinicians are advised to commence this using the lowest dosage of a product that has been studied clinically in the context of an elderly cohort or population [12]. As well, considering non-drug interventions [33], tailoring the treatment in light of the individual's personal profile can be expected to enhance its therapeutic efficacy. Those with high comorbidity scores, and those who have been knee arthroplasty candidates, or have been treated for anxiety or depression should be targeted especially carefully, however [29,46,47], and reviewed regularly to examine treatment responses and identify any negative treatment effects [45].

- Therapeutic education
- Provider education
- Better evidence based guidelines for osteoarthritis management
- Cognitive behavioral therapy and pain coping skills training [37]
- Media advocacy campaigns against opioids
- Individualized treatment and proactive pain monitoring [38,46]
- Research to validate non-pharmacologic pain reduction approaches
- Physical interventions that potentially alter natural history favorably [5]
- Self-management programs [39,45]
- Strengthening or aerobic exercises [40]
- Weight loss/anti-obesity strategies
- Sleep hygiene promotion

Box 2: *Potential Strategies for Alleviating Osteoarthritis Pain.*

Concluding Remarks

There is increasing evidence that the high rates of disability produced by osteoarthritis are not inevitable, but that lifestyles and behaviours have powerful influences over the outcome and manifestation of pain in this condition [see Box 1]. Other evidence shows more efforts to understand the chief characteristics of this non-fatal health condition, especially those aspects of pain that might be positively affected by one or more non-pharmacologic strategies can markedly improve life quality and possibly health costs of this condition.

By contrast, the widespread use of opioid analgesics should be a matter of concern not only due to their inability to alter the disease process favourably, but due to their ability to irrevocably alter the course of this non-fatal disease by raising the risk for premature death, especially among those who are unable to have surgery, and/or are younger surgical candidates with excess comorbidity [19,41].

In contrast, a well-conceived conservative prescription for managing osteoarthritis pain, based on the most important causes of pain and risks involved in excess analgesic intake of drugs such as opioids and selecting therapies that cannot only prevent tangible disease costs, but the severe human costs currently being uncovered, while favourably promoting regenerative processes, are highly indicated [42,45].

To this end, more educational programs for both osteoarthritis patients as well as their physicians or caregivers along with further research to uncover the most optimal approaches for treating chronic osteoarthritis pain with and without opioids for periods longer than one year [12] that takes into account osteoarthritis pain specific pathophysiological mechanisms should be implemented to better discern their adverse or beneficial effects and to improve care quality.

To reduce the chances of acute flare ups due to joint overuse [13,14], especially in the presence of neuropathic pain [43], minimizing or obviating the use of opioids, avoiding those that have not been studied, and starting with the lowest dosage [12] can minimize any chances of adverse drug effects and/or excess disease progression. In the meantime, regardless of whether or not surgical strategies are indicated or undertaken, to avoid risks below and others, less rather than more opioid intake is highly recommended in efforts to minimize osteoarthritis pain.

These include:

- Tolerance and an increased desire for more of the product
- Physiological withdrawal including sleep problems, anxiety, muscle pain
- Death
- More rather than less joint pathology and dysfunction
- Heightened obesity risk [44].

In sum, opioids, which are of little benefit to people with osteoarthritis, and carry a substantial risk [45], should be used judiciously or avoided where possible and more appropriate safer evidence-based pain relief interventions should be considered, reimbursed favorably, mandated into medical guidelines, and examined empirically to prevent the enormous associated human and social costs of this disease, including centralization of pain and obesity [19,44,45]. Even though opioid analgesics were strongly recommended previously for patients either not willing to undergo or with contraindications for total joint arthroplasty after having failed medical therapy according to a review conducted in 2012 [48], opioids are not recommended for osteoarthritis pain relief as their benefits are palliative and are outweighed by an increased risk for serious adverse events, regardless of joint site affected [45,49].

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