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Opioids for Chronic Pain

Prescription narcotics among Canada's deadliest drugs. Medically induced opioid addiction reaching alarming levels. Expect OxyContin Health Crisis. The dramatic headlines are frightening. As the debate on preventing opioid misuse and the practicalities of using opioids safely continues to rage on, it is all too easy to be overwhelmed by the noise. The following themes and resources provide a good starting point for all health care decision-makers seeking to make sense of the debate — that includes policy-makers, clinicians, or program managers.

Opioid basics

Opioids are the most potent analgesic available and are well established to manage severe short-term pain, surgical pain, and cancer pain.[1] The benefit of these drugs — lack of an analgesic ceiling in full agonists — outweigh the potential adverse events, such as respiratory depression, increased sensitivity to pain, endocrine dysfunction, drowsiness, constipation, tolerance, dependence, and addiction. Use of opioids to address other types of chronic pain — osteoarthritis, low back pain, neuropathic pain, and fibromyalgia — is more controversial. Chronic pain persists for longer than three months, and affects between 15% to 30% of Canadians.[2]

Little data available

The greatest challenge in answering basic questions on the efficacy and safety of opioids in chronic pain is the lack of data. Expertly documented by Dalhousie University's Academic Detailing Service, of the 65 randomized controlled trials found to inform Canadian guidelines on opioid use in chronic pain, half of the studies were of six weeks' duration or shorter.[3] The longest study was just 16 weeks. Importantly, 51 studies had placebo for a control group rather than first-line treatments such as acetaminophen, NSAIDs, COX-2 inhibitors, or exercise.

In essence, most recommendations within the Canadian guidelines on opioid use for chronic pain are based on consensus opinion and

supported by observational studies, as the expert panel making the recommendations found themselves in the unenviable position of providing advice on clinically necessary topics, with little evidence to guide them.[1]

Irfan Dhalla and colleagues argue that physicians are unaware of the lack of randomized controlled trial (RCT) evidence to support the popular assertion that the benefits of long-term opioid therapy outweigh the risks.[4] The authors recommend further marketing restrictions, physician education, and FDA-mandated long-term trials to better understand the circumstances in which the benefits of opioids justify the potential risks.

Guidelines produced by the American Society of Interventional Pain Physicians also highlight the lack of evidence to support the use of opioids for chronic non-cancer pain.[5]

Acknowledging that there is a paucity of high-quality data to be had, what does the available evidence tell us?

Partial pain relief

Opioids have demonstrated a moderate effect on pain relief (a reduction of 10% to 20% on the pain scale), *compared with placebo*, in patients with non-cancer chronic pain.[3] Opioids have not been shown to be superior to other drugs (with weak evidence that morphine and oxycodone may provide a small effect compared to other drugs). In improving function, opioids have a small average effect *compared with placebo* and have not been shown to be superior to other drugs.[3]

In their examination of comparative efficacy, the US Drug Effectiveness Review Project suggests that trial withdrawal rates may be the most reliable efficacy outcome, due to inconsistencies in the reporting of other outcomes across different opioid trials. High withdrawal rates likely indicate a combination of poor tolerability and ineffectiveness in reducing pain. Seven of the ten opioid RCTs reviewed had more than 30% of participants drop out.[6] Within the RCTs used to inform the Canadian guidelines, patient withdrawal rates were also high, with 51% of studies having more than 30% of participants drop out.[3]

Physicians are encouraged to fully explain the limited benefits patients can reasonably expect with opioids, in addition to the treatment risks.[7]

No safest opioid

Wouldn't it be easy if one opioid or formulation of opioid was known to be safer or more effective than the others? Unfortunately, there is very little evidence to support this.

Codeine can be habit-forming and can cause serious side effects such as slow heart rate, weak pulse, confusion, hallucinations, and seizures. Opioid withdrawal is common following chronic tramadol use, and it has been linked to apnea and death. Clinical trial data alone do not demonstrate that any weak opioid (e.g., codeine, tramadol, buprenorphine) is more efficacious or associated with fewer adverse events than other weak opioids.[3]

The same is also true of strong opioids versus other strong opioids and of long-acting opioids versus short-acting preparations.[3] The Physicians for Responsible Opioid Prescribing highlight that extended-release opioids have not been proved to be safer or more effective than short-acting opioids.[8]

If a decision to prescribe opioids has been made, the 2010 Canadian guidelines suggest codeine or tramadol as first-line opioid options for mild to moderate pain; morphine, oxycodone, and hydromorphone as second-line. For severe pain, morphine, oxycodone, and hydromorphone are suggested as first-line opioid options; fentanyl as second-line; and methadone as third-line. It is important to note that this is based upon consensus opinion.[9]

Potential for misuse and addiction

Addiction to prescription opioids is not rare. As many as one in three patients being treated for chronic pain with opioids could meet the criteria for an opioid use disorder.[2] Physical dependence and tolerance of opioids can develop in days or weeks with daily use.[8]

Opioid misusers rank controlled-release oxycodone, immediate-release hydromorphone, and immediate-release oxycodone as the most desirable of opioid formulations. Hydrocodone and oxycodone pills are most frequently taken orally but can be crushed and snorted. Crushing the pills negates the time-release features, so the user experiences effects all at once. Tramadol is most commonly abused by narcotic addicts, chronic pain patients, and health professionals.[10] Most opioids that are used illicitly are obtained via prescription.[11]

The Canadian Centre on Substance Abuse report that opioid-related deaths have nearly tripled in a decade: from 168 in 2002 to 494 in 2010, in Ontario alone. Of the 3,222 opioid-related deaths in Ontario during this period, deaths related to oxycodone were most prevalent, followed by morphine and methadone.[2]

In response to the growing problems associated with prescription drug misuse, a 10-year national strategy developed by the National Advisory Council on Prescription Drug Misuse

was recently released (March 2013). [2] Immediate, short-term measures are identified to deal with existing problems and a foundation is set for longer-term collaborative action focusing on prevention, education, treatment, monitoring, and enforcement.

Try alternatives first

All resources are unanimous: Physicians are encouraged to prescribe non-opioid medications for pain management where clinically indicated and to be aware of a full range of drug and non-drug options so that opioids are not considered as first-line therapy.[8,9,11]

A good place to start is the Saskatchewan RxFiles on chronic non-malignant pain, which emphasizes behavioural, psychosocial, and physical therapies as essential for long-term management; and which recommends adequate trial of suitable non-opioid analgesics and/or adjunct agents before considering opioids.[12] A similar approach is recommended in the Low Back Pain Guidelines produced by Alberta's Institute of Health Economics in 2011.[13]

Avoid the slide into long-term use

Physicians for Responsible Opioid Prescribing suggest setting benchmarks for stopping chronic opioid therapy and warn against continuation of therapy with patients who show no progress toward treatment goals (consensus-based). The Canadian guidelines support this approach, recommending physicians take steps to ensure that long-term therapy is warranted (consensus-based). Switching or discontinuing therapy is recommended for patients experiencing unacceptable adverse effects or insufficient opioid effectiveness.[9]

CADTH supports evidence-based decision-making

The Canadian Agency for Drugs and Technologies in Health (CADTH) understands that Canadian health care providers need to know what evidence exists, or doesn't, to make informed decisions. To that end, CADTH has recently prepared several evidence-based Rapid Response reports addressing specific questions posed by Canadian health care decision-makers on the topics of effective opioid prescribing practices to prevent misuse, and management of opioid addiction. Visit www.cadth.ca for more information.

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