Health
Hunter New England
Local Health District

Reconsidering Opioids

Health Professional Resources
September 2020

Hunter Integrated Pain Service Position Statement

Prescriber support
Staff at Hunter Integrated Pain Service are available to discuss opioid strategy and offer support to clinicians in the Hunter New England region of NSW, Australia.

Email: HNELHD-HIPS@health.nsw.gov.au
Telephone: 02 49223435

Background
There is substantial variation in opioid prescribing for chronic non-cancer pain despite scientific evidence demonstrating lack of efficacy and safety with long-term opioid use.

Policy and Regulation
In Australia regulatory authorities including Therapeutic Goods Administration (TGA), Pharmaceutical Benefits Scheme and State and Territory bodies are seeking greater alignment of practice with the evidence base and reduction in unwarranted clinical variation. Recent changes aim to improve patient outcomes and safety.

Indications
The TGA states that opioids are no longer indicated for chronic non-cancer pain other than in exceptional circumstances.

Scientific evidence supports the following indications for opioid prescription:

i. Acute pain (generally for 3 days or less)
ii. Cancer pain (active disease)
iii. Palliative or “comfort” care at end-of-life
iv. Opioid dependency / addiction (maintenance)

Current scientific evidence does not support opioid prescription for chronic non-cancer pain. There is a consistent body of evidence demonstrating lack of long-term analgesic efficacy, lack of improvement in function or quality of life and substantial risk of harm to both individuals and society.

If a clinician is considering opioid prescription for chronic non-cancer pain then discussion with a pain medicine physician is worth considering to explore treatment options.

Future research may define exceptional circumstances in which the benefits of long-term opioid prescription (short or long acting formulations) for chronic non-cancer pain outweigh harms. Such circumstances should be defined under double blind

research conditions given the inherent difficulty of assessing opioid responsiveness in unblinded clinical practice settings.

Efficacy

The efficacy of opioids is supported by evidence from systematic reviews for use in acute pain[1, 2], cancer pain[3], palliative care[4] and dependency/addiction[5].

A 2018 systematic review of chronic non-cancer pain[6] showed clinically insignificant benefit for pain and physical function. Opioids were associated with less pain relief during longer trials. There was no difference in response between nociceptive, neuropathic and nociplastic pain types. A systematic review of opioids for chronic neuropathic pain found short term moderate benefit in selected patients compared to placebo[7]. However, the quality of studies was low to moderate with enriched trial designs and industry sponsorship introducing potential bias.

Reduction in analgesic benefit over time due to tolerance and/or opioid-induced hyperalgesia[8] is a major limiting factor with longer term use.

Population studies show that patients on long term opioids describe relatively more troublesome pain and functional interference[9]. A 2013 chronic pain dose response study showed no correlation between marked increases or decreases in opioid dose and change in pain intensity[10].

The lack of well-designed, long-term opioid trials was addressed in 2018 with publication of a 12-month pragmatic randomised controlled trial that compared opioid initiation to non-opioid therapy for chronic back, hip, or knee pain[11]. The opioid group reported greater pain intensity and more adverse effects throughout the study period. Another pivotal 2018 study demonstrated that following discontinuation of long-term opioids, pain intensity remained unchanged or in some cases slightly improved, even without the application of active self-management strategies[12].

Harms

There is strong evidence of harm from long-term opioid use. The problems of constipation, dizziness, drowsiness, fatigue, hot flushes, increased sweating, nausea, pruritus, and vomiting are well known[13]. There is increased risk of death, especially with co-prescription of benzodiazepines and other psychoactive agents[14,15]. Endocrine and sexual dysfunction is common. Hypogonadism occurs in more than half of male chronic opioid users and hypocortisolism in approximately 1 in 5[16]. Additional problems include immunosuppression[17], inflammatory effects involving nitric oxide and neuroinflammation[18], driving impairment[19-23], overdose, misuse, addiction and diversion[24].

Opioids work on neural networks associated with pain and pleasure and also modulate psychological distress ("chemical coping")[25]. This capacity to dampen troubling emotions is hypothesised to relate to the high density of opioid receptors in the limbic system[26]. However, resolution of troubling emotions requires the capacity for awareness and expression of those emotions, which relates to prefrontal cortex functionality and inhibitory GABAergic connections with the limbic system. These inhibitory pathways are impaired by opioids. Thus, opioid use often brings the perception of reducing disturbing emotions whilst simultaneously interfering with the potential resolution of those emotional conflicts[27].

Patients with mental health and substance abuse problems are more likely to be prescribed opioids (adverse selection) and at higher doses than people without those risk factors[28, 29]. Opioid-related changes to cognitions and affect make it hard to wean

and cease established opioids regardless of worsening outcomes. In addition, a focus on opioid prescription can distract both patient and prescriber from evidence based active treatment strategies.

Assessment

i. Multidimensional assessment is recommended for all types of pain. This leads to a broad, whole person treatment approach[30].
ii. Consider standardised measurement of pain and functional outcomes (e.g. Pain, Enjoyment, General activity: PEG[31]).
iii. A drug and alcohol history helps estimate risk of negative opioid outcomes. Contact with the Australian Prescription Shopping Information Service (1800 631181) is recommended. Real time opioid monitoring programs are available in several Australian states and prescribers must comply with regulations which vary between States and Territories[32].

Opioids for acute pain

When opioids are used for acute pain (e.g. post-operative or post trauma) the time limited nature of treatment needs to be highlighted.

i. Case discussion and co-ordination between hospital and primary care is recommended if early treatment occurs in hospital.
ii. Opioids should generally be ceased within several days or up to 1 week after surgery or injury[33]. Those prescribed opioid analgesics for longer than one week or at high doses are far more likely to remain on them at one year[34]. In exceptional cases where opioids have been prescribed for longer, tapering to cessation should be undertaken within **90 days**.
iii. A daily oral morphine equivalent dose of **60mg** should not be exceeded in primary care without specialist support (See Faculty of Pain Medicine ANZCA website[35] or Opioid App at http://www.opioidcalculator.com.au/)
iv. Variation from these recommendations should be discussed with a pain medicine or addiction physician.

Opioids for cancer pain

Opioids have an established place in the treatment of pain associated with active cancer. It is suggested that a daily oral morphine equivalent dose of **300mg** not be exceeded unless discussed with a palliative care, pain medicine or cancer physician. If cancer therapy is successful and remission occurs then tapering and cessation of opioids is recommended. A cancer diagnosis does not preclude direct or indirect opioid-related harms and appropriate opioid prescribing and dispensing boundaries are still required.

Opioids for palliation or comfort care

This approach involves acceptance of the patient's transition to end-of-life care where there is no curative treatment and no prospect of functional recovery. The aim is to reduce suffering and distress rather than improve physical and cognitive function. In an elderly and/or frail cohort the increased risk of falls and cognitive impairment with opioids are of particular concern and the balance of benefit and harm needs careful consideration. In some cases, opioid use may shorten life expectancy. It is suggested that a daily oral morphine equivalent dose of **60mg** for non-cancer pain or **300mg** for cancer related pain is not exceeded unless discussed with an appropriate specialist.

Opioids for dependency / addiction

Opioid Agonist Therapy (OAT) incorporates therapeutic boundaries which may include no early prescriptions; no replacement of lost prescriptions or medications; single prescriber; single pharmacy; daily dispensing and possible urine drug testing.

In addition to regular methadone or buprenorphine, depot buprenorphine is now available for weekly or monthly injection. OAT is appropriate where there are concerns about opioid risks. Opioid dose and duration of therapy are guided by a doctor with training in addiction medicine. The general practitioner remains pivotal to whole person care in treating opioid dependency[36]. Although opioid cessation and abstinence is a common desire for those on maintenance therapy[37] the risk of relapse or overdose is high.

Redirecting prescription opioids for chronic non-cancer pain

Across the developed world, many people with chronic non-cancer pain have been maintained on long term opioids, due in part to inappropriate extrapolation of evidence from acute pain and palliative care contexts. The chronic pain evidence base has become clearer in recent years and a change in therapeutic direction is required. An evidence informed approach now involves non-initiation of opioids for chronic non-cancer pain and opioid tapering and discontinuation for people already taking opioids.

The following steps are recommended to redirect the treatment of patients on long term opioids for chronic non-cancer pain:

i. Have a conversation about opioid deprescribing. Discuss the evidence of potential harms and limited benefits for this particular person. Use an empathic manner combined with therapeutic boundaries and motivational techniques. Ask what advantages the patient sees in opioid reduction.
ii. Declare the medical intention to work toward opioid cessation along with a willingness to provide ongoing non-pharmacological supportive care. Opioid reduction does not mean abandoning the patient. Abandoning the liberal provision of opioids facilitates patient safety and pivots to more effective approaches.
iii. Shift the focus to a multimodal, active, non-pharmacological approach (www.hnehealth.nsw.gov.au/pain)[38]. This requires allocated time.
iv. Share decision making about the time frame to cessation. Negotiate when to start and rate of opioid weaning. The aims are to limit withdrawal symptoms and avoid escalation of patient distress while maintaining appropriate prescribing boundaries. A typical plan reduces the opioid by 10-25% of the starting dose each month. This may achieve cessation in 3-9 months.
v. If there has been a previous unsuccessful attempt at weaning then slow the rate of reduction for the next attempt while continuing to offer support and prescribing boundaries.
vi. Opioids should not be co-prescribed with benzodiazepines. If a patient is taking both then a decision needs to be made about which to taper first[39].
vii. The involvement of a pain medicine physician and multidisciplinary pain management team may be helpful in select cases.
viii. If opioid use disorder emerges as the primary issue during the course of opioid reduction then introduce more opioid maintenance strategies such as used for dependency care and consider consulting with a clinician trained in addiction medicine. For some patients the only access to medically prescribed opioids should be via OAT.

Opioid rotation

Opioid rotation involves switching from one agent to another with the aim of improving efficacy or reducing adverse effects. Rotation is mainly used in acute pain, cancer pain[40] and palliative care settings. A typical rotation involves changing to a relatively lower dose equivalence, as direct switch at the equivalent dose may cause an overdose. In chronic non-cancer pain the standard approach, as described above, is to taper the opioid to cessation rather than switch to a new agent.

Driving

The majority of studies of driving performance show no significant psychomotor or cognitive impairment in patients on stable long-term prescription opioids. However, the combination of long-term opioid use with benzodiazepines or other psychoactive medication can produce significant driving impairment[20-23]. In addition, the use of any opioids by opioid naïve patients is likely to cause impairment. The following suggestions aim to reduce the risk of driving related harms:

i. Opioid naïve patients should not drive if exposed to opioids.
ii. Patients on stable long-term opioids are unlikely to be significantly impaired in driving performance. However, for at risk patients (oral morphine equivalent daily dose >60mg, frail, co-morbid or co-prescription of psychoactive medications) on-road testing or assessment in a driving simulator is recommended.
iii. Patients taking both long term opioids and benzodiazepines should not drive.
iv. Patients taking long term opioids should not drive if they feel sedated for any reason (e.g. dose increase, sleep deprivation) or have consumed illicit drugs or alcohol.

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Additional Resources:

Brainman video series

Brainman stops his opioids
Brainman chooses
Understanding pain and what to do about it

Pain Management Network. Agency for Clinical Innovation, NSW Health

NPS Medicinewise resources

Prescribing wellness

Working Group

Hunter Integrated Pain Service: Drs Chris Hayes, Andrew Powell, Hema Rajappa (Specialist Pain Medicine Physicians); Ruth White (Pain Physiotherapist); Sarah Campbell (Clinical Psychologist), Fiona Hodson (Clinical Nurse Consultant), Kathie Nickerson, Belinda Mikaelian (Clinical Nurse Specialists), Gena Lieschke (Research Fellow/Clinical Academic). External consultant Dr Simon Holliday (General Practitioner and Addiction Consultant).

Disclosures

Fiona Hodson is Vice-President of the consumer organisation Chronic Pain Australia. Dr Hayes is a Board member of Painaustralia and has provided advice about opioid policy to multiple groups including the Faculty of Pain Medicine ANZCA, Therapeutic Goods Administration, National Prescribing Service and the Agency for Clinical Innovation NSW Health. The other authors of this document declare no conflicts of interest.