Something For the Pain: Chronic Non-Malignant Pain

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1989

Harry's Hurt

In 1989, Harry sustained a significant right knee injury at work, at the age of 38.

He underwent three knee surgeries in 1990, 1991, and 1994. Afterwards, he continued to experience constant, sharp, aching pain in the knee, with frequent superimposed sharp stabs.

Non-opioid analgesia and co-analgesics proved ineffective.

Opioid therapy in non-malignant pain has come to the fore in recent years, providing both a revolution in treatment and the establishment of chronic pain clinics. New narcotic analgesic products are part of that revolution, allowing physicians to control non-malignant pain as never before.

The opium poppy, with its legacy of euphoria, addiction, and death, has evolved into modern pharmacologic therapy (Table 1).

1995

In 1995, a weak opioid medication, Percocet®, every four to six hours as needed, was eventually prescribed. Harry's daily activities were still severely limited. He also had long periods off work because of his knee pain.

By 2001, Harry had yet to ever be completely pain-free. He was referred to a pain specialist, where his pain was deemed to be a result of advanced degenerative arthritis, compounded by recurrent meniscal tears and past surgery.

Harry subsequently lost his job due to poor attendance. Screening was completed for his suitability for long-term opioid use.

Table 1

Opium-based medications

- Traditional narcotic tablets
- Immediate-release tablets
- Controlled-release tablets
- Dermal patches
- Opioid suppositories
- Parenteral medications

Where do I start with opioids?

Opioid therapy can be considered in chronic non-malignant pain when:

- the underlying pain is unrelieved,
- the quality of the patient's life is decreased, and
- usual methods of treatment have failed.

Table 2 outlines the three protocols available for starting opioid therapy. While the first protocol is the fastest, it also has more initial side-effects. The second is slower, but allows more time for tolerance of side-effects. The third needs to be assessed weekly.

Table 2

Protocols for starting opioid therapy

1. Use an IR drug and titrate to effect. Once stable, the transfer to a CR drug is appropriate
2. Start with a CR opioid with an upwards titration for the ensuing three days
3. Start with a low-dose CR opioid and then an IR opioid to titrate to effect

IR: Immediate release
CR: Controlled release

What are the objectives?

One goal for opioid use should be to balance the risk against the benefit. While non-steroidal anti-inflammatory drugs (NSAIDs) have been the therapy of choice for patients with chronic, non-malignant pain (CNMP), they are linked to side-effects associated with morbidity.[1]

According to the Canadian Arthritis Society, an estimated 1,900 Canadians die annually due to the gastrointestinal (GI)-related adverse side-effects of NSAIDs.

For every 3,800 patients > 65 on regular NSAID therapy, 50 will be admitted to hospital. Of these:

- 18 will sustain an upper GI bleed,
- 22 will have an exacerbation of congestive heart failure, and
- 10 will ultimately develop renal failure.

In contrast, when taken correctly in accordance with professional advice, opioids have never been shown to cause organ damage.[2]

When assessing chronic pain, the goal is always to treat the pain itself. In 2002, the College of Physicians and Surgeons of Ontario released evidence-based recommendations on the management of CNMP, stating significant pain relief could be achieved with a low risk of psychologic dependence or addiction in the absence of a history of substance abuse.

2002

In January 2002, Percocet was replaced by OxyContin®, titrated to 50 mg every 12 hours, which was found to be vastly superior for pain relief.

In May 2002, Harry commented to his family physician that he was very happy with the pain relief; his knee pain was controlled virtually all the time, he felt better than he had in 10 years, and he wanted to return to gainful employment.

Once back at work, Harry experienced some breakthrough pain. A small dose of Oxycodone, 5 mg every eight hours, as needed, helped settle his discomfort.

Harry kept scheduled appointments and did not abuse his prescription.

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Table 3

Opioid tapering protocols

1. 50% of the previous daily dose for two days, then reduce the dose by 25% every two days until the equivalent of 30 mg/day of oral morphine (0.6 mg/kg/day in a child), then stop
2. 10% reduction per day, daily dispensing
3. Methadone (or soon buprenorphine) taper

Table 4

Opioids and metabolites

Opioids	Active metabolites
Codeine	C6G, morphine
Fentanyl	None
Hydromorphone	H3G
Meperidine	Normeperidine
Methadone	None
Morphine	M6G, M3G
Oxycodone	Oxymorphone

Take-home message

- Learn to switch opioids to attain the best balance of analgesia against side-effects.
- Opioids work very well when correctly dosed to effect.
- Consider using controlled release or long-acting opioids.
- Twice daily medications have better patient compliance.
- In the treatment of CNMP, start opioids at low doses and go up slowly.

What about precautions?

High-risk patients need to be screened with established tools (*i.e.*, CAGE questionnaire, SISAP). Also consider patient agreements, framed around various requirements, including:

- patients keeping booked appointments;
- compliance with the dose and frequency of the prescribed medication;
- securing the possession of prescription analgesic drugs;
- attachment to a named physician and one known pharmacy;
- willingness to be reviewed by the physician; and
- awareness of the liability to terminate care if analgesic abuse arises.

All physicians want to avoid being fooled by a drug abuser. In 2000, the Canadian Society of Addiction Medicine issued a policy statement saying physicians using reasonable professional medical judgement in prescribing opioids should not be held responsible for the willful and deceptive behaviour of patients who successfully obtained opioids for non-medical purposes.

2004 In 2004, Harry continues to work in an active job, has not had any change in prescription for two years, is fully compliant, and has agreed to a slow reduction of his controlled release opioid.

How do I reduce opioids?

Table 3 lists how to effectively reduce opioid doses.[3]

What role do metabolites play?

Metabolites are important in the efficacy of opioids. Some drugs have active metabolites of varying potency (Table 4).

Of particular note are morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G). The former is an effective analgesic component of morphine, while the latter may have a role in the unwanted excitatory effects of morphine (mainly nausea). A preponderance of M6G in

Frequently Asked Questions

1. Is respiratory depression a risk in high-dose opioid use?

No, it is very rare with titrated oral dosing. Start low, go slow, and take care in patients with chronic obstructive pulmonary disease or renal failure.

2. Does sedation pose a problem when starting opioids?

Mild sedation can occur with early doses of stronger opioids, but this effect usually decreases within 14 days if the dose is correct. Advice on driving and operating machinery is prudent.

3. Are there any endocrine effects with opioids?

Yes, affecting the hypothalamic-pituitary axis may result in sex hormone changes in both sexes, with temporary amenorrhea and erectile dysfunction in women and men, respectively.

4. Do benzodiazepines have any role in concurrent pain control with opioid use?

No.

5. How do I know which opioid to substitute if one form is not tolerated?

Check tables of equipotent opioid comparables; commence at 50% of the former medication and titrate upwards with your new choice.

an opioid formulation is desirable, while those with excessive M3G should be avoided. CME

References

1. Wolfe MM, Lichtenstein DR, Singh G: Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs. N Engl J Med1999: 340(24);1888-99.
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3. Brands B, Kahan M, Selby P: Management of alcohol, tobacco and other drug problems. A physician's manual. Centre for Addiction and Mental Health (Toronto) 2000.

Net Readings

1. International Association for the Study of Pain®
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2. International Association for the Study of Pain Press®
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