Safe use of Essential Narcotic Drugs in acute and long term pain

NCG PALLIATIVE CARE COMMITTEE

COMPILED BY
NANDINI VALLATH, NAVEEN SALINS

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Background

Opioids have not been adequately available even for severe pain relief in India due to stringent regulations imposed to prevent their misuse and diversion. Whereas in western countries, opioids have been available for decades and were used liberally for all pains including prolonged use when started for acute severe pain, and for non-malignant chronic pains. The accumulated information especially from USA on their liberal long-term use, is suggestive of additional adverse effects, addiction potential, especially when on unmonitored long-term opioid therapy.

As the availability for medical use improves in India, it is our collective responsibility to ensure that these prescription-only-drugs are not misused or abused. It is for this reason that many statutory requirements for procuring, stocking, record keeping, annual reporting as well as mandatory training for prescribers are woven into the medical use of these drugs. The readers are requested refer to the section discussing 'Guidelines for stocking and dispensing opioids in India' for details.

Besides the statutory requirements, we need to develop our own sensibilities and competence to evaluate pain and the person in pain, learn to utilise essential narcotics when needed; but not in excess of what may be needed, and know when to discontinue them, when the drug is no longer serving the intended purpose.

The objective of this section is to provide some guidance in preventing misuse of opioids when utilized for controlling acute pain and for treating pain in long-term conditions.

What are the best practices for using opioids in acute pain?

Due diligence entails the following practices while using ENDs for managing acute pain.

1. Know when to choose opioids for pain relief and when to transition to other drugs.
2. Ensure opioids are used for short term, only to control the brief period of 'severe' pain.
3. Prescribe immediate release [IR] preparations only - for that day and next day.
4. AVOID Sustained Release /Transdermal preparations in managing pains that are transient – for example – post-operative pains.
5. Cover side effects prophylactically even in short-term treatments.
6. Maintain synchronous use of step 1 medications such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and adjuvant medications.
7. Utilize multimodal pain interventions such as epidural analgesia or nerve blocks when indicated, to maintain effective analgesia.
8. Review severity of pain, impact of medicines, and need for further opioid prescriptions.
9. Ensure smooth monitored transition from parenteral formulations to oral immediate release Morphine formulations and then to non-opioid analgesics. This would be required during the transfer from ICU setting to in-patient setting and then during home discharge.
10. When converting to oral medicines, explain the prescription and the rationale of PRN doses for breakthrough pains, with the patient and the person who is administering the medicine and ensure comprehension.
11. Step down early - to non-opioid analgesics. Use the lowest effective dose for the shortest period, ensuring satisfactory pain relief until healing and recovery.

When managing pain in long term conditions, how do we select the right patient for opioid therapy?

Please refer to 'Best practices for using step 3 analgesics' for more details.

The goal of opioid therapy is to reduce the suffering due to pain, improve functionality and the quality of life. The *Lowest dose that achieves analgesia with maximum function and minimum side effects* is used *only* for *the duration of clinical need.* For this to happen, evaluating the nature of pain and the person with pain – both are important. We need to be satisfied with the following aspects of evaluation;

1. Is this pain opioid sensitive?
2. Based on the cause of pain, which drug would be appropriate for this patient, and for how long?
3. Are there major psychological contributors to this pain?
4. Are there negative thoughts and emotions that need to be addressed?
5. Are there non-pharmacological inputs that can help in this situation?
6. How can I follow up this patient?

Opioids are safe, effective and economical analgesics for cancer patients with advanced, rapidly progressive disease, with 'moderate to severe' pain and should be considered early. However, in a patient with chronic, slowly progressive conditions, where analgesia is required for decades, it is a much more deliberated decision. If the pain is indeed persisting and severe, and the non-pharmacologic and non-opioid therapies have been inadequate, the patient may be considered for opioid therapy after thorough evaluation of the type of pain.

The detailed consent and written contract as practiced in western countries for long-term opioid therapy add to the safety and prevents misuse and diversion; but may not be practical for day to day practice in India.

How can addiction potential be detected?

Addiction is compulsive use of a drug despite physical harm. There is craving, drug seeking behavior with instances of unsanctioned increase in dosage, even when not experiencing pain.

It is important to realize that patients are reluctant to disclose a history of substance abuse. A history of substance abuse indicates greater risk of opioid addiction but getting an accurate

Check the box if the item applies. A score of 0-3 indicates low risk, a score of 4-7 indicates moderate risk, and a score of 8 or higher indicates high risk

ITEM	WOMEN	MEN
1. Family history of substance abuse:		
• alcohol	[ ] 1 point	[ ] 3 points
• illegal drugs	[ ] 2 points	[ ] 3 points
• prescription drugs	[ ] 4 points	[ ] 4 points
2. Personal history of substance abuse:		
• alcohol	[ ] 3 points	[ ] 3 points
• illegal drugs	[ ] 4 points	[ ] 4 points
• prescription drugs	[ ] 5 points	[ ] 5 points
3. Age between 16 and 45 years	[ ] 1 point	[ ] 1 point
4. History of preadolescent sexual abuse	[ ] 3 points	[ ] 0 points
5. Psychological disease:		
• attention deficit disorder, obsessive-compulsive disorder, bipolar disorder, or schizophrenia	[ ] 2 points	[ ] 2 points
• depression	[ ] 1 point	[ ] 1 point
TOTAL		

Figure 1: Assessing the Risk for Addiction Behavior[1]

picture of past and current drug use can be difficult. Recommendation is to *"trust but verify"* through standardized screening procedures for addiction potential in a clinical situation.

Can we score addiction potential?

Greater care is exercised in patient population where the therapy may be required for decades, unlike in cancer population where the duration of therapy is months to years.

Higher than usual risk may be suspected when the patient;

1. has current or previous history of substance abuse disorder – nicotine / alcohol/ others;
2. is adolescent, young adult
3. has family history of drug abuse;
4. or is depressed, have other psychological concerns.

The score suggested by Freynhagen in 2013, is given in Figure 1. A **score of 4 or more**, indicates moderate to high risk for addiction.

[1] Ref: Rainer Freynhagen et al. BMJ 2013;346:bmj.f2937

What are the Best Practices when using opioids long term?

1. Always start with immediate-release opioids and NOT the extended-release/modified release (ER/SR/ MR) opioids.
2. Carefully reassess individual benefits and risks when increasing dosage to ≥50 Morphine Milligram Equivalents (MME)/day
3. Prescribe the lowest effective dosage. Justify any decision to titrate dosage to ≥90 MME/day.
4. Titrate over a week with close follow up of functions, analgesia and adverse effects, and stabilize the daily dose as per the patient's preferred goal of pain relief[2].
5. Evaluate benefits and harms with patients within 1 - 4 weeks of stabilised opioid therapy and then every 2 months.
6. If benefits do not outweigh harms, optimize other therapies and taper and discontinue opioids.

Aware	The aim of opioid therapy is improvement in function and quality of life through adequate analgesia. Bringing pain score to zero is not the goal.
Assess	It is irresponsible to prescribe opioids without detailed evaluation of the pain and person with pain; or in a situation where follow up is deemed impossible.
Agree	Before starting opioid therapy, discuss the known risks and realistic benefits of long-term therapy, establish treatment goals and mutually agree on how to use the prescribed medicines.

[2] The pattern of titration and follow up would be very different for Methadone.

Advise	Use opioids by mouth, by clock, by the ladder; maintain non-opioid, non-pharmacological inputs; address psycho-social concerns; and pay attention to individual details.
Appraise	Opioid therapy is continued only if clinically meaningful improvement in pain and function outweighs risks to patient safety.

How do we monitor a patient on long term opioid therapy?

Even after the initial titration is done, planned clinical reviews are done to monitor adherence and to ensure that the opioids in the prescribed dose is indeed the right treatment to be continued for that patient. The follow-ups may be done using the care giver, the family doctor or through home –based care, if the patient is very sick to travel. The best policy is "trust but verify". It is the prescribers' responsibility to ensure that the medicine is used by the intended person for the intended reason and in the prescribed dose and duration.

The clarifications we seek during these clinical reviews are the 4 **A**s.

1. Is the **A**nalgesia satisfactory?
2. Is the pain relief improving patient's **A**ctivity?
3. Have we achieved the right balance between Pain relief and **A**dverse effects??
4. Is there an abuse potential? **A**berrant behaviour

Opioid prescription is a very responsible decision, done with due diligence, only after careful patient evaluation, risks and realistic expectations of benefits, and with clear explanation and written instructions ensuring ground rules for safe use.

How do we assess patient's adherence to prescription?

Adherence monitoring practices followed to check aberrant usage of prescription medications are[3];

1. One prescribing doctor and one designated Pharmacy.
2. Prescription monitoring programs e.g. pill counts – patient presents the empty strips during each visit
3. Double check on reports of lost or stolen medicines
4. Urine analysis during follow up

All the above, except urine analysis for drug levels, are feasible and should be applied on every visit even within the Indian scenario.

Which are the aberrant behaviours that should alert the clinician[4]?

Craving - The Focus of patient in getting opioids into the prescription more than any other requirement

1. The person always asks about opioids, is unwilling to try non-opioid modalities, requests for the medicine and is unduly upset when denied opioids
2. Unsanctioned escalations - Opioid overuse
3. The person visits the emergency unit for getting medicines for pain and repeatedly uses up own supply very fast. Alternatively, she/he may 'lose' prescriptions and approach other doctors for repeat prescriptions.
4. History of using other addictive substances – smoking, alcohol, benzodiazepine or other drugs
5. Vagueness/ inconsistencies/ exaggerations- in symptom descriptions - Poor functional status with unclear etiology of pain which exacerbates with minor stimuli.

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[3] Opioids in the Management of Chronic Non-Cancer Pain: An Update of American Society of the Interventional Pain Physicians' (ASIPP) Guidelines, 2008

[4] Atluri SL et al. Pain Physician 2004; 7:333-338

Are there additional and different adverse effects when a patient is on long term opioids?

Yes, besides constipation, nausea and vomiting commonly seen with short term use, long term opioid usage comes with additional adverse effects. These include;

1. Chronic constipation with fecal impaction causing obstipation
2. Chronic dry mouth which can lead to tooth decay
3. Unintentional overdose leading to respiratory depression. This is higher when using sustained release preparations.
4. Increased incidence of falls due to dizziness
5. Hypogonadism
6. Increased pain sensitivity
7. Sleep-disordered breathing

What are the common misconceptions when prescribing opioids long term?

Table 1 - Common misconceptions amongst professionals and provides explanatory facts.

Myths	Facts
Since sudden withdrawal of opioids cause a variety of symptoms, all patients on opioid therapy get addicted to the drug. The presumption is that 'physical dependence' is same as addiction	In physical dependence, the body adapts to the drug, which leads to drug-specific physical or psychological symptoms when the drug use is abruptly ceased. This may be managed easily with gradual weaning of the drug over days to weeks. Addiction is psychological dependence, where the drug becomes central to existence.
Physical dependence happens only with high dosage over very long periods of time	With daily opioid use, physical dependence can develop in days or weeks
In patients who develop physical Dependence, opioids can easily be tapered off and stopped.	Successfully tapering of chronic pain patients from opioids can be difficult, withdrawal symptoms can be prolonged and disturbing.
Opioid overdoses only occur among drug abusers and patients who attempt suicide	Patients using prescription opioids long term are at risk of unintentional overdose. Risk increases with dose and when combined with other CNS depressants like benzodiazepines and alcohol.

DOs and DON'T's when considering long term opioids

DOs	DON'Ts
1. Choose opioids when evaluated to be absolutely essential for pain relief	1. DON't start opioids when review is not feasible
2. Reconsider possibilities for disease management, non-pharmacological inputs, physical therapy, non-opioid analgesics and psychological support through appropriate referrals	2. DON'T continue opioids in patients who show no progress toward treatment goals defined by increased function, quality of life and reduced pain.
3. Explain that discontinuing opioids may be difficult after prolonged usage e.g. increased pain, insomnia, or anxiety and withdrawal symptoms	3. DON'T assume patients know how to use opioids. Risks increase with higher dose and are greater for extended-release preparations[5].
4. Take time to talk clearly and empathetically with patients about how they are using opioids. Ask patients about their problems and concerns	4. DON'T assume patients use opioids as you intend. Many patients vary their dose and use combinations of other CNS depressant drugs or alcohol. Hence *trust but verify*.
5. Screen patients for depression and other psychiatric disorders; they may be better served by mental health treatment	5. DON'T abandon patients with a prescription drug problem. Offer help or refer to someone who can treat their substance abuse, while the pain is safely managed with opioids if so indicated.

[5] Patients may mistakenly take extended-release opioids "as-needed" for pain.

Take home message

Every drug has its share of therapeutic benefits and adverse effects. Physician must balance the medical need for long term opioids especially in a non-cancer pain situation, with the possibility of abuse and diversion. Kerala is one of the earliest states in India, to have used opioids in pain management in cancer and other diseases and hence has had extensive experience. A study published in The Lancet, in 2001, describes the follow up of 1723 patients in Calicut, India, who were being treated for pain with oral morphine on an outpatient home-care basis. Over the 2 years of the study, the investigators did not identify any instances of misuse or diversion[6].

The above study, concluded that diligence in selection of patients, regular follow-up, adherence monitoring, and committed record keeping were all important to prevent misuse.

The result of this study published in Lancet suggest that, after establishing medical necessity by a trained professional, along with systematic record keeping and regular review, oral morphine can be dispensed safely to patients with pain, for use at home without fear of misuse or diversion.

We may conclude that essential narcotic medications are safe and effective in managing pain. It is our responsibility to follow the statutory procedures and documentation as per the NDPS regulations, for stocking and dispensing them. It is also our responsibility to enhance our own professional competence and undertake the necessary training to identify patients who would benefit, apply ground rules for safety and ensure that relief of pain and suffering is achieved while possibilities for diversion and abuse of these prescribed medications are prevented.

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[6] Medical use, misuse, and diversion of opioids in India, M R Rajagopal, David E Joranson, Aaron M Gilson; THE LANCET • Vol 358 • July 14, 2001

Test your Knowledge

True / False

1. For acute pains it is best to start with sustained release medications or transdermal patch to ensure safe and adequate pain relief. [False]
2. Opioid therapy may be combined with multimodal pain interventions, to reduce the total dose used while maintaining effective analgesia. [True]
3. For acute pains, prescribe opioid preparations for minimum 5 days. [False]
4. Patients readily disclose their history of substance abuse [False]
5. The aim of therapy in chronic pain is to improve functions [True]
6. Increasing requirement of opioids with progressively increasing disease is not addiction [True]

Choose the Best answer among the choices

1. When deciding on using opioids for treating long term pain the following evaluation is essential to prevent overuse, misuse
    a. Is the pain opioid sensitive?
    b. Are there major psychological contributors to this pain?
    c. Is there a non-pharmacological input that can help in this situation?
    d. How can I follow up this patient's progress?
    e. All of the above
2. The following behavior is NOT suggestive of addiction
    a. Craving and drug seeking behavior
    b. Request for a dose once the duration of drug action is over
    c. instances of unsanctioned increase in dosage
    d. repeated loss of prescription
3. Addiction potential is taken as higher than usual in all EXCEPT;
    a. In elderly with malignant disease
    b. In patients with history of smoking, alcohol intake
    c. In patients with psychological disorders such as depression
    d. Adolescent patient