



Best Practices for medical use of strong opioids

NCG Palliative Care Committee
Collated by Dr. Nandini Vallath

Best Practices for medical use of strong opioids

NCG Palliative Care Committee
Collated by Dr. Nandini Vallath

Step 3 opioids are also known as strong opioids OR opioids for moderate to severe pain.

Overview

- Indications, ground rules and best practices
- Individualization in special populations
 - Geriatrics, Patients with kidney disease
- Exercises on prescribing for patients with Persistent moderate to severe Pain

This presentation **does not** cover the following aspects about pain management using step3 opioids.

1. Pharmacology of opioids
2. Differences of chronic pain from acute pain
3. Pathophysiological classification of pains and pathophysiology of chronic pain
4. Pain assessment and documentation
5. Non-pharmacological inputs for managing pain
6. Interventional pain management techniques

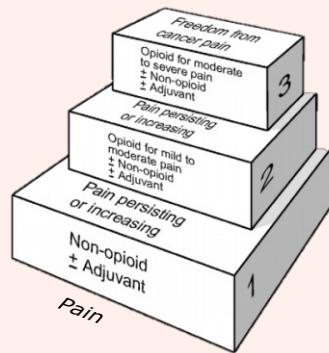
Indications

- Moderate to severe pain
 - Nociceptive, neuropathic or mixed
 - Acute or chronic
- Let the choice be based on intensity and type of pain and not on the stage of disease

We have Morphine, Fentanyl and Methadone available in the Step 3 category in India.

This presentation would emphasize most on usage of Oral Morphine for chronic persistent severe pain.

WHO Analgesic Ladder - 1986



- By Mouth
- By the Clock
- By the Ladder
- Attention to details
- Individualize

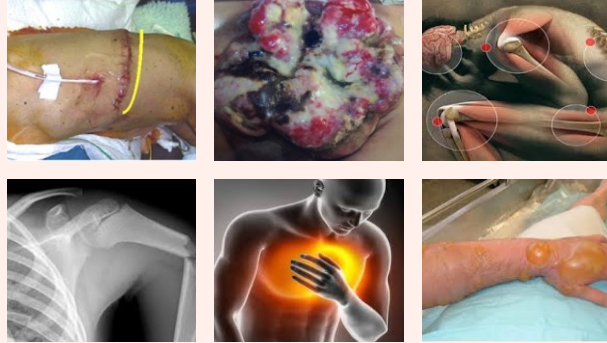
WHO recommended the analgesic ladder for a structured approach to managing pain seen in patients with cancer. The aim was to recommend simple method of utilising analgesics that are safe, economical and titrate them for effectiveness. It was meant to empower health professionals across the globe to approach pain with empathy and handle its management, to relieve the needless suffering due to pain in cancer patients.

BY MOUTH – Ease of drug administration, Manageable by family at home without need for health care professionals – as the drug is needed as long as the pain lasts – which could be life long..

BY THE CLOCK – continuous pain requires continuous analgesia. If prescribed only when patient screams with pain – Pain relief is unsatisfactory AND also, the total analgesic requirement shoots up.

BY THE LADDER – Move up and down the ladder and use the recommended class of drugs based on severity of pain and NOT on poor prognosis or terminality of illness.

Opioids in Acute & Chronic Pain



How can we improve our sensitivity to persistent pain suffered by our patients?

An important way is to acknowledge, document and respond to the pain when the patients complaints.

In acute pain states - the patient is seen to be obviously in pain with tachycardia, sweating, higher BP, and distinct emotional expressions such as crying, moaning etc.

Chronic pain patients may not exhibit the typical sweating, tachycardia, crying etc. seen with acute pain. Instead - they move less, sleep less, speak less, eat less. Their ADLs are affected. These aspects can only be elicited through empathetic conversations and not by objective measurements.

Best Practices: Managing Acute Pain with step-3 opioids

- Control severity until healing brings down the pain -Prescribe for the day and next day only
- Use IR preparations, AVOID SR/TD preparations
- Cover side effects prophylactically
- Review the pain frequently and decide on the need for further opioid prescriptions
- Step down to non-opioid analgesics EARLY

IR – Immediate Release

SR/TD – Sustained Release, Transdermal

Step-3 Opioids for persistent severe pain

Recognize that:

1. Chronic pain is NOT just a long-standing pain. It self-exacerbates, with neuro-plastic changes of Peripheral NS and Central NS with exhaustion of the modulating mechanisms. The frequency and intensity of discharge along the tracts flares up over time and worsens the experience and distress of the patient.
2. Chronic Pain has NO protective role. It is our job to do the best to relieve it.

Ground Rules

E	Evaluate	Evaluate the pain and the person with pain
E	Explain	Communicate goals, benefits, side effects, listen
M	Manage	Establish Ground rules for prescription. Be mindful of comorbidities
M	Monitor	Ensure Follow up Use dosage that maximises QOL.
A	Attention to details	The dose required is lower when there is good rapport, confidence in is self controllability, and access to P-S support for better coping with the situation.

EEMMA is the slogan for controlling pain.

Rule One Evaluate

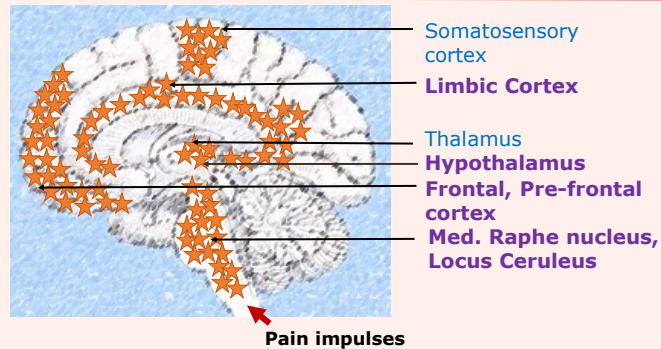
- Opioid prescription is a very responsible decision taken after careful evaluation of the pain and the person in pain
- Is the pain opioid sensitive?
- Is there a non-pharmacological input that would help?
- Are there negative thoughts and emotions? What is the meaning of the pain to the patient?
- How can I follow up this patient?

If psychological morbidity is suspected – manage it through Multi-disciplinary approach including MSW, psychologist, psychiatrist.

Depression lowers the threshold to pain - Mental calm and good sleep brings down the dose of opioids in managing the pain.

The Emotional Experience

Role of psycho-social care influencing appraisal of pain



Reference: Unpleasant Subjective Emotional Experiencing of Pain (A review), Nandini Vallath, Manoj Kumar, Naveen Salins, Indian Journal of Palliative Care 19 (1), 12-19 (2013).

It may be noted that pain pathway is projected beyond the thalamus and sensory cortex - into several regions of the brain dealing with affect and emotions.

Pathways also involve Brain stem regions for descending modulatory pathways, dealing with modulation of perceived pain.

The Pain felt by the person is a product of many complex factors influencing perception and modulation.

Evaluation - Best practices

- Factors affecting appraisal of pain by the person
 - The context
 - Feeling believed, responded to...
 - Confidence of being taken care of – trust, confidence
 - Controllability, self management

Reference: Unpleasant Subjective Emotional Experiencing of Pain (A review), Nandini Vallath, Manoj Kumar, Naveen Salins, Indian Journal of Palliative Care 19 (1), 12-19 (2013).

Individuals differ in their appraisal of pain.

Context

The situation in which pain is experienced also affects the severity – e.g. Pain of major trauma in a war front – with immediate possibility of return to safety, is observed to be less severely experienced by the soldier; than when a person is diagnosed with a life-threatening illness like cancer.

Controllability

By acknowledging, validating their experience and responding to it early - we are contributing to raising their pain threshold.

Rule Two - Explain

- The pains noted possible contributors as relevant
- Communicate therapeutic goals, realistic benefits
- Transient and long-term side effects
- Invite questions and clarify

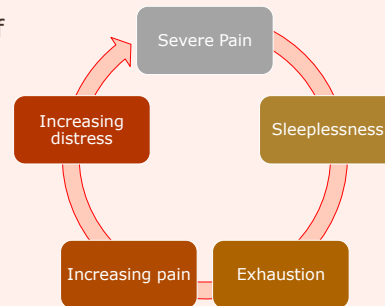
Elicit and respond to questions by the patient and family

Compliance is possible only when we understand details, explain situation and how the medicine would help, elicit fears in the patient and family in starting the opioid medications and respond to them satisfactorily.

Refer to the Frequently Asked Questions in the Palliative Care section on the NCG website. This includes FAQs by patients as well as professionals.

Explanation - Best practices

- The aim is to **improve functions**
- The aim is **NOT** Complete Pain relief
- Goals
 1. First step is to allow a good night's sleep by breaking the vicious cycle of pain
 2. Next step is to achieve Activities of Daily Living - ADL
- Elicit patient's pain goal



Complete pain relief may lead to unacceptable levels of adverse effects.

The adverse effects can make the patient non-compliant- e.g. patient may refuse medications due to severe nausea / vomiting. Such a patient may prefer tolerable reduction in pain with minimal side effects.

Patient's Pain Goal is the best guide to plan our dose and titration.

Explanation - Best practices

- Pro-actively ensure compliance through questions, clarifications
 - Waking dose – in empty stomach?
 - Will she be drowsy? confused? delirious?
 - Will it harm kidney?
 - Questions about addiction?

Explanation that waking up dose means not having to wait until breakfast. That it can be taken in empty stomach without harm.

Many patients generalize pain killers into one group as toxic to kidney – this needs explanation that opioids do not harm kidney function.

Differentiate addiction seen for the euphoric effect with peak CNS plasma levels of parenteral opioids in prone personalities Vs. the gradual plateau levels of the Morphine 3 or Morphine 6 Glucuronide released after liver metabolism of the orally taken drug.

Refer to the Frequently Asked Questions in the Palliative Care section on the NCG website. This includes FAQs by patients as well as professionals.

Rule Three - Manage

- Prescribe appropriately, safely
- Clear prescription - continuous pain relief for continuous pain - SOS dose

Oral Morphine – it is safe, economical and effective. It is available in most formats –immediate and sustained release tablets, oral solutions, injections. It may be administered by most routes used for giving medicines – oral, parenteral – IV, SC, epidural, intrathecal, topical, intraarticular etc.

It is effective per rectum. We should request manufacturers for PR formats too. This formulation would be useful in very sick patients and in small children.

Morphine is not calculated according to mg / Kg body weight. It is gradually titrated based on the severity of pain and relief experienced.

In an adult without comorbidities who has persisting pain despite appropriate prescription of step – 2 medications and multi-disciplinary inputs, we may start with 10 mg of immediate release Morphine 4 hourly. Extra SOS doses would be required for covering breakthrough pains and this needs to be explained clearly.

The number of regular doses and the extra doses used is best recorded in a book - for adjusting the total dose during the next review.

Best practices


- Continue step I drugs when indicated
- Long acting preparations [SR tab, Transdermal] are NOT SUITABLE as 1st line therapy
- Prescribe Prophylactically for known Side Effects
- Provide written Precautions

Always prescribe stimulant laxatives for constipation that occurs in 99% of patients. Do not wait for constipation to happen.

Nausea/ vomiting is seen in 1/3rd of patients only. Providing antiemetic - haloperidol / metoclopramide and instructing to take it if required adds to compliance to prescription by the patient.

Sedation is a self-limiting effect. Patient may also sleep more in the first few days to compensate for the lost sleep of weeks/months spent with severe pain. It would be important to advice on not using machinery [including driving] during this period.

If sedation continues after the 1st week, it is important to review the patient, look for other drugs /contributory factors, and reduce the dose when appropriate.

Date	Medicine	On waking	10 AM	12 PM	2 PM	6 PM	Bed time	SOS	What for	Review Date	Sign.
15 th Aug	T PARACETAMOL 650 MG		1		1		1		Pain Relief		
	T. METOCLOPRAMIDE 10 MG							1	Vomiting		
	T. MORPHINE 10 MG	1	1		1	1	2	1	Pain relief		
	T. BISACODYL 5 MG						2		Motion		
										17 th Aug	

This is a sample of prescription of strong opioids. The timing and explanation for each drug is clearly indicated.

Instead of time – we can use face of the clock too

Avoid using formulations which contain drug combinations. As it hampers individual drug titrations. They are also costlier.

The early morning and night doses ARE NOT TIMED specifically as 6 am or 10 pm – so that patients are not unnecessarily disturbed from sleep just to give medications. Disturbed sleep can lower the pain threshold.

The night dose may be doubled – so that patient need not wake up with pain in the middle of the night. The drowsiness due to the extra dose may be advantageous.

The review date – to ensure clarity in review and for record for the nurse in charge to follow up if the patient does not show up.

Prescribing - Best practices

Instructions on the backside of Prescription

1. Medications such as Morphine are effective only if taken in the prescribed dosage at the prescribed time intervals
2. If there is excessive sleepiness, irrelevant talking, or if there are difficulties with passing urine, vomiting etc. please stop the medications and contact the clinic at the earliest.

Prescribing - Best practices

Instructions on the backside of Prescription

3. If for any reason, the tablets are unused, they have to be returned to the clinic
4. Store them safely in closed containers without moisture
5. Do not share these drugs with anyone else
6. Keep the tablets strictly away from children

Patients and family care givers should be aware of the strength of the medicines they hold.

Prescribing - Best practices

- Documentation
 - Maintain daily update of prescriptions in a Register as per the NDPS Rules
- If personal/ family history indicates abuse potential
 - One or max. two prescribers,
 - Maintain pill count
 - Trust but Verify

Ensure there is a person committed to daily record keeping. The registers are maintained meticulously. This is very important requirement as per the NDPS Rules. The guidelines are available at the NCG site.

Risk of abuse in a patient is discussed in more detail in the document on Safe Usage of Opioids.

Refer to the Palliative Care section on the NCG website.

Sample of daily record keeping

Authority	Serial No.	Supplier	Quantity	Unit	Price	Total	Stock
	04-5853	P. Chandrakala	10	Box	18236		
	01-9095	Shri. Anand Bai	40	Box	18196		
	07-6250	R. Laxmi Bai	40	Box	18156		
	09-7450	Ameera Begum	50	Box	18106		
	07-6581	S. Jayatha	50	Box	18056		
	10-3457	A. Chandramma	20	Box	18036		
	08-1964	K. Shanti	30	Box	18006		
	07-7886	M. Rajkumar	50	Box	17956		
	10-5634	P. Sankar	20	Box	17936		
	07-6097	H. Rajeshwari	60	Box	17876		
	09-3914	L. Sureshbabu	20	Box	17856		

The number on the right-end column indicates the reducing number of stock of tablets of Morphine Sulphate. The next day's register begins with the end stock of the previous day.

Interruptions in supply leads to needless suffering. The doctor in charge of the stocks should stay mindful of the quantity of opioids in the institution. Application for fresh stock early would prevent interruptions in the supply to patients who require the medicine for their pain relief.

Rule Four Monitor

- Review, review, review
- Do not start if review is impossible
- If direct review is difficult, use family carer, general practitioner or community volunteer

Monitoring – Best Practices

- Is the Analgesia satisfactory?
- Oral Immediate Release [IR] Morphine - Dose is usually modified after 36 hours.
- This allows steady blood levels to be achieved as per the T $\frac{1}{2}$ life of the drug before escalating the dose.

Frequency for upscaling daily dose

- Approximate duration for steady state blood levels = 5 times T-half life
- For oral IR Morphine - $5 \times \text{half life} = 5 \times 6 \text{ hours} = 30 \text{ hours}$
 - Hence - wait for at least 36 hours before stepping up the dose by 25-50%
 - Exception – escalating uncontrolled pain
- For SR Morphine- $5 \times 16 - 20 \text{ hours} = 80 - 100 \text{ hours}$
 - Step up not earlier than 4-5 days

Difficulty with titration is another reason why Fentanyl patch is not a good 1st line Step -3 drug.

Monitoring – Best Practices

- Is the **A**nalgesia satisfactory?
- Is the pain relief improving patient's **A**ctivity?
- Pain relief and **A**dverse effects -Right balance??
- Is there an **A**buse potential?
 - **A**berrant behaviour
 - Trust but verify

The 4 As guide the decision to continue opioids as well as the dose.

The most important factor is that the relieved pain improves prioritized functions of the patient.

Goal of opioid therapy

Lowest dose that achieves analgesia with **maximum function** and **minimum side effects**

Aim of therapy is NOT complete pain relief; it is enhancing function due to satisfactory pain relief. Hence it is important to elicit patient's pain goal.

Rule Five Attention to Details

- **Individualize:** understand meaning attributed to the pain, psycho-social contributors, patient's pain goal, abuse potential to attain the right dose
- Understand and foster dignity → maximise QOL
- Progress of disease, function of systems
e.g. kidney

Often the meaning attributed by the patient for his/her suffering contribute to unrelieved pain. There may be guilt and pain is seen as a punishment. This needs to be elicited and addressed

Dignity Question

What is it that I should know about you, that would help me care for you better?

If Pain persists?

- Is there compliance to the medicine?
- Is it reaching the site of action?
 - Alimentary absorption – nausea, vomiting?
 - Edema / poor circulation affecting subcutaneous injection?
- Under-dosing? improper choice?
- Have we missed major distress?

Despite impeccable assessment and rational and adequate prescriptions –
Rule out 1st - Poor compliance with medication or a new pain

Consider emotional contributors - fear, anxiety, depression.

Pain will not be adequately managed unless patients feel heard and participates to control their situation.

If Pain disappears? Weaning - Best Practices

- Opioids given for even = or > 1 week needs weaning
- Wean when pain-free for > 4 weeks on a regular unchanged dose, OR post intervention
- Decrease by 25–50% and observe for a week.
- If pain relief continues, decrease by 25% or 10% [when long term] every 1-2 weeks - until it is stopped, or until the pain recurs.
- If pain recurs, increase to the previously satisfactory dose.

Patient on long term opioids may have total relief of pain through an intervention e.g. radiotherapy for bone pain / interventional Nerve Block.

Opioids should not be stopped suddenly, unless used for very short duration of < 4 days.

Ground Rules

E	Evaluate	Evaluate the pain and the person with pain
E	Explain	Communicate goals, benefits, side effects, listen
M	Manage	Establish Ground rules for prescription. Be mindful of comorbidities
M	Monitor	Ensure Follow up Use dosage that maximises QOL.
A	Attention to details	The dose required is lower when there is good rapport, confidence in is self controllability, and access to P-S support for better coping with the situation.

EEMMA is the slogan for controlling pain.

Best Practices for Older Patients

Best practices - older patient

- Pain may masquerade as abrupt changes in behavior and function
 - Instability; Incontinence; Immobility
 - Confusion, restlessness, aggression, anorexia, and fatigue
- Patient may not complain – Assess carefully

Older patient do not always complain of pain even as they suffer. It may surface as changes in routines.

Step 1 Drugs

- PCM not > 2 g/D – [liver dysfn, alcohol]
- Avoid - Nonselective NSAIDs and COX-2 Inhibitor
 - Gastrointestinal and renal toxicity, hypertension, heart failure
 - Naproxen, Ibuprofen safer with CAD / CVD

AUGUST 2009–VOL. 57, NO. 8 PHARMACOLOGICAL MANAGEMENT OF PERSISTENT PAIN IN OLDER PERSONS - **American Geriatric Society**

PCM- Paracetamol

CAD – Coronary Artery Disease

CVD – Cerebrovascular Disease

COX-2 – CycloOxygenase 2 Inhibitor

Step 1 Drugs

- Avoid Diclofenac Na
- Avoid taking NSAIDs with
 1. Aspirin
if necessary, take 20 min before
 2. Steroids

AUGUST 2009–VOL. 57, NO. 8 PHARMACOLOGICAL MANAGEMENT OF PERSISTENT PAIN
IN OLDER PERSONS - **American Geriatric Society**

PCM- Paracetamol

CAD – Coronary Artery Disease

CVD – Cerebrovascular Disease

COX-2 – CycloOxygenase -2 Inhibitor

Using Step 3 Drug

- Morphine has slower onset and takes longer for peak levels
 - Start with 2.5 mg – then titrate ...
- TD Fentanyl – onset -18-24 hours; duration 72-96 hours

Using Opioids in elderly

- **Prefer Immediate Release preparations**
- Evaluate Hydration, malnutrition
- Look for co-morbidity, other medications
- **Care - with administration of medicine**
- Simplest regime, bunch medicines together, check understanding
- Cognitive dysfunction, depression
- Who is the personal care giver? Is the patient alone?
- **Gradual and slower titration to the right dose**

Cockcroft-Gault Equation

82 year old male with serum creatinine of 1.2

$$\frac{140 - 82 \times 62(\text{Weight})}{72 \times 1.2(\text{S. Creat})}$$

Estimated GFR = 41.6
(moderate to severe renal failure)

22 year old male with serum creatinine of 1.2

$$\frac{140 - 22 \times 62(\text{Weight})}{72 \times 1.2(\text{S. Creat})}$$

Estimated GFR = 84.6
(mild renal failure)

Alteration in the estimated GFR in two patients of different ages, with the same creatinine levels.

FACTOR IS 1 IN MALES AND 0.85 IN FEMALES. Hence value to be multiplied by 0.85 in females

Opioids in renal impairment

Drug	Effect	Comments
Fentanyl*	Drug may accumulate Not removed by dialysis	Not significant with bolus dose. Caution with infusion. RECOMMENDED
Methadone*	No accumulation Not removed by dialysis	Usual caution. 50% reduction. Learned vigilance. RECOMMENDED

*Ref: OTPM & PCF-5th

OTPM – Oxford Text Book of Palliative Medicine

PCF 5th – Palliative Drug Formulary – 5th edition

Opioids in renal impairment

Drug	Effect	Comments
Codeine* Morphine	M3G and M6G accumulates Removed by dialysis	M3G – neurotoxic Prolonged narcolepsy NOT RECOMMENDED ↓ dose, ↑ interval
Tramadol* MAY USE	Parent and metabolite accumulates	↑ Epileptogenicity NOT RECOMMENDED Not > 50 mg BD

*Ref: OTPM & PCF-5th

Fentanyl Citrate TD Patch

TD – Transdermal system

Fentanyl Citrate TD Patch

- Specific indications
 - Difficulty with oral intake, Tablet phobia / poor compliance, Renal failure
 - Intolerable side effects - nausea, vomiting, severe constipation, hallucinations
- The dose may need to be adjusted in patients with fever or has high core body temperature
- It is costly

Fentanyl is very expensive.

As the medications are required for long periods, cost is a very important consideration.

The cost involved long term is an important consideration. If the prescription is given to the patient, without this consideration, we may be contributing to the poverty of the family. As the meagre earnings would get used up for pain medications as crisis expenditure. Children may be pulled out of schools and the family may compromise on food – so that the suffering patient gets relief.

Oral Morphine is cheap and there is always a dose for most pain patients – that may be arrived at with meticulous evaluation of pain and titration of medications.

Exercises

Answers are given below each exercise

True or False?

96% of patients have “satisfactory” pain relief with the WHO 3 step analgesic ladder.

- Ventafridda, [Tamburini M](#), [Caraceni A](#), [De Conno F](#), [Naldi F](#). A validation study of the WHO method of pain relief. *Cancer* 1987; 59:850-856.
- [Zech DF](#), [Grond S](#), [Lynch J](#), [Hertel D](#), [Lehmann KA](#). Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. *Pain*. 1995.63(1):65-76.

Answer - 71-76%

Which is the appropriate Step 1 analgesic here?

1. Diabetic, Hypertensive patient
2. Bronchial asthma?
3. Neonate?
4. Pregnant woman?
5. Bleeding polyps?
6. Coronary artery disease?
7. Musculoskeletal pain?

1. Acetaminophen, Paracetamol
2. Acetaminophen, Paracetamol
3. Acetaminophen, Paracetamol, Ibuprofen
4. Acetaminophen, Paracetamol
5. COX 2 Inhibitors may be considered here – if there are no contra-indications
6. Acetaminophen, Paracetamol. Amongst NSAIDs - Ibuprofen has best evidence for safety in CAD [Fosbol]. Diclofenac is as dangerous as COX 2 Inhibitors
7. Non-pharmacological interventions, physical therapy, Acetaminophen, Paracetamol

True or False?

1. Step II opioids have prescription advantage
2. Step II opioids do not have a ceiling dose

1. True – Step 2 opioids are available with chemists across the counter
2. False – Tramadol – 400 mg/D; Codeine – 360mg / D

True or False?

1. The maximum dose of Codeine if combined with PCM is 240mg /D
2. The maximum dose of Morphine in a patient weighing 60 Kgs is 120 mg/Day
3. Morphine at ≤ 30 mg/D is a useful Step II opioid

1. True
2. False

Step 3 drugs are not given according to body weight. It is started at a low dose and gradually titrated to effect according to the response of the pain and patient's pain goal decided by discussion.

3. True

In small doses Morphine is useful as step 2 drug. It is also much cheaper than Tramadol

Prescription errors?

- T Ibuprofen 400mg BD
- T Tramadol 50 mg OD and SOS
- T Wysolone 30 mg OD
- C Omez 10mg OD
- Syp Looz 2 tsf HS

1. Under dose of Ibuprofen
2. Underdoses of Tramadol
3. Steroid + NSAID – avoidable combination
4. Underdoses of gastric protection
5. Patient may need stimulant laxative as constipation due to opioids slows bowel movements
6. Trade names avoidable
7. Provide clarity of when to take the medicines, e.g. before or after food etc.

52 year old 62 Kg cirrhotic patient with S. Creatinine 1.2 mg% - has nausea, occasional vomiting, abdominal pain with inadequate pain relief with the following prescription.

- T Dolo 650 mg 1-1-1
- T Acabel SP - 1-1-1
- T Pan - D 1-1
- T Cyclopam 1-1-1
- Inj Voveran IM SOS
- T Ultracet 1-1-1
- PCM **650**
- PCM **500**, Aceclofenac, Serratiopeptidase
- Pantaprazole + Domperidone
- Dicycloverine + PCM **500**
- Diclofenac Na
- Tramadol + PCM **325**

Is Step 3 analgesic indicated here?

Overdose of total Paracetamol – avoid combination preparations in managing chronic pain

Domperidone and Dicycloverine – have opposing effects - irrational to use together in the same patient

IM drugs are best avoided in patients with persistent pain – especially when the same drug is available in oral format.

Step 2 medicine is under-dosed.

Answer – No.

This patient's prescription needs to be optimized first at Step 2. Only if that does not work – then we may consider stepping up to Step - 3

Opioids induce constipation by all the following mechanisms EXCEPT

- A. Relaxing the circular smooth muscles of the large intestine
- B. Increased tone of anal sphincter
- C. Suppressing forward propulsive movement of colonic smooth muscles
- D. Impaired defecation reflex

Answer - A

Patient in severe pain with following prescription. Is step 3 opioid indicated here?

- T. Tramadol 50 mg QDS and SOS
- T. Ibuprofen 400 mg TDS
- Paracetamol 650 TDS
- Omez 20mg / D, Dulcolax 10mg HS

Yes

Patient seems to have had a good trial of Step 2 medications, if the pain is nociceptive in origin.

For someone on 30 mg Sustained Release Morphine tablets twice daily, the rescue dose of immediate release P.O. Morphine for break through pain is...

- 5 mg
- 7.5 mg
- 10 mg
- 30 mg

Answer – 10 mg

Dose for breakthrough pain is $1/6^{\text{th}}$ of the daily dose of the same route.

$$60\text{mg} / 6 = 10 \text{ mg}$$

Oral morphine may be needed less frequently in patients with

- A. Respiratory alkalosis
- B. Opioid tolerance
- C. Renal failure
- D. Past history of drug abuse

Answer – C

The unexcreted Morphine and its active metabolites maintain the pharmacodynamic action for longer periods.

Primary indications for morphine in advanced cancer include all EXCEPT

- A. Pain
- B. Dyspnea
- C. Diarrhea
- D. Sedation

Answer – D

Morphine is used only if analgesia is required in the patient who requires sedation.

All the following are morphine non-responsive pain EXCEPT

- A. Tension head ache
- B. Pain of Cancer of the stomach
- C. Biliary colic
- D. Muscle spasm(cramp)

Answer - B

A patient getting oral morphine 4th hourly has satisfactory relief but complains of pain half hour before every dose. The next logical step is to

- A. Increase the frequency of morphine
- B. Increase the dose by 25%
- C. Add a sedative
- D. Assess for addiction potential

Answer – B

This is an end of dose pain, which means that blood levels are not maintained even for 4 hours.

When oral morphine is to be converted to continuous subcutaneous infusion, the 24 hour dose would be...

- A. Halved
- B. Quartered
- C. Maintained same
- D. Doubled

Answer - A

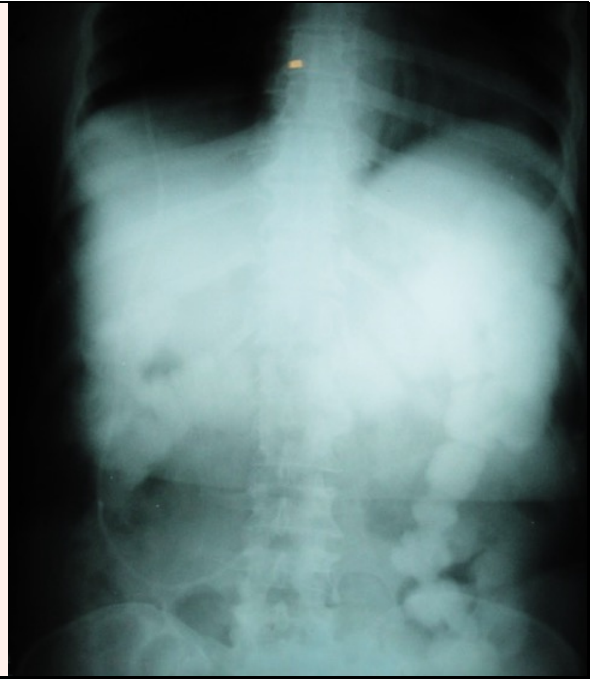
Ms. Garewal – Ca lung, and metastasis to 8th Rib.

- Comes in distress with no relief from chest pain and an additional pain, 2 weeks after starting the following treatment.
 - Oxa Forte [Diclofenac + codeine], Ultracet [tramadol + PCM]
 - Syp Corex [Codeine] for cough
- She has
 - Continuous dull aching pain 7/10 over the right side of the upper back – which she already had earlier
 - Intermittent severe 10/10 pain over the upper abdomen that affected her sleep last night
 - Foul smelling leaking of stools since few days

Please note the high content of Codeine in the prescription and there is no laxative given during the last 2 weeks. She has developed severe constipation. The pain is due to the colic of constipation.

Bacterial action on parts of the impacted dry stools over time leads to its disintegration into a foul-smelling fluid that descends around the faecal balls and leaks out –as spurious diarrhoea. Please see next slide.

X-Ray Abdomen of Ms. Garewal



Note the fecal balls impacted along the descending colon.

This patient required High up enema [with the enema solution placed into sigmoid colon, through a lubricated catheter, passed up gently PR.

After evacuation of stools - his pain prescription was modified and rationalized by incorporating right doses of step 2 drugs along with stimulant laxative to prevent constipation and saline nebulization for the dry irritant cough.

The most unsuitable group of laxatives to relieve morphine induced constipation is..

- A. Stimulant
- B. Bulk forming
- C. Osmotic
- D. Stool softener

Answer – B

As the overall colonic movement is slowed by opioids, bulk forming laxatives would form larger fecal balls which may worsen constipation

Case continued..

- Ms. Garewal 's pain on the chest is unrelieved with step 2 full dose medications. As it was a cancer related pain, she was advised to use 25 µg/hr Fentanyl transdermal patch.
- It has been 5 hours after application, but, pain is severe and unrelieved. What should be done?

Fentanyl is NOT a 1st line opioid from step 3. We should first start him on immediate release Morphine, understand the daily requirement by review over a week or so. Details of use are explained earlier.

Also, it takes > 12 hours for the drug in the TD patch to saturate the subcutaneous reservoir, which then transfers the prescribed dose per hour and maintains blood levels. Hence, we need to supplement the pain relief with oral IR Morphine until it is time for TD Fentanyl to act.

Patient receiving Morphine 10 mg 6 hourly. Double dose at night. She experiences pain before the next dose. Why?

Prescription exercise

- She is asking for Fentanyl patch as she wants definite pain relief.
- What is the dose of Fentanyl Patch in your prescription?

Answer– Patient is having End-of-dose pain here. This means inadequate dosing of Morphine. The dose has not been optimized.

Fentanyl is not a 1st line opioid. The dose of TD Patch to be used for this patient may be found - only after stable pain relief using IR preparations of oral Morphine.

Patient needs to be explained about:

1. The Morphine dose needs to be titrated to achieve stable pain relief before switching over to TD fentanyl
2. Pain not controlled by Morphine is unlikely to be controlled by Fentanyl
3. The cost for a week of therapy can be prohibitively expensive.

Which of the following statements about indications for use of fentanyl patches is correct?

- A. It is indicated for acute, severe pain
- B. It is indicated after stable pain relief has been achieved with daily oral Morphine in patients titrated for relief for continuous severe pain.
- C. It is the best opioid to start for opioid-naive patients
- D. It is indicated only when patients have uncontrolled pain despite titrated Morphine dosing

Answer - B

Further Reading

- **Managing pain in children - WHO**
http://apps.who.int/iris/bitstream/10665/44540/1/9789241548120_Guidelines.pdf
- **Cancer Pain Relief - WHO**
<http://apps.who.int/iris/bitstream/10665/37896/1/9241544821.pdf>

Why is there so much needless suffering due to persistent unrelieved pain?

1. Lack of knowledge, experience with using opioids beyond institutionalized patients. This has led to misconceptions, and opiophobia amongst professionals. There is fear to prescribe. This can be overcome only by learning practically - more about pain and about using opioids by doing brief courses from palliative care training institutions. The list of training centres are available in the NCG website.
2. Very poor availability of strong opioids within pharmacies / chemists due to the NDPS regulatory language. Now it is amended – details of guidelines for stocking are available in NCG website.
3. Unfounded fear of addiction, respiratory depression when used in titrated doses
4. Most important reason – we have got away with it!! Due to poor accountability on quality of care.