

Basic Certificate in Palliative Care
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Week-07
Lecture 04: Safe Use of ENDS

This is week 7 lecture number 4. Namaste (Hindi word meaning greetings). In, in this week we also studied about how to prescribe ENDS essential narcotic drugs.

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Safe Use of Essential Narcotic Drugs

DEPARTMENT OF PALLIATIVE MEDICINE
GUJARAT CANCER & RESEARCH INSTITUTE
AHMEDABAD



Again we are emphasizing this subject because safe prescription of essential narcotic drug is our moral responsibility and if it is prescribed safely your patients also will be benefited with good pain relief without causing any adverse effect or side effect of the drug. So, few of the slides may be repetition or content may be repetition of the previous subject, but this is we want to emphasize that how to use ENDS safely.

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Purpose

1. To lay down guidelines for Opioid prescription

- Cancer pain Mx / Breakthrough pain
- Opioid rotation from one opioid to another opioid
- Conversion from oral to transdermal opioid
- To manage opioid induced side effects

2. Make clinician aware of NDPS amendment



First and foremost the purpose of this lecture is to lay down guidelines for opioid prescription. There are each and every department should lay down a guideline whenever you are prescribing ENDS or opioids to your patient the certain guideline needs to be followed.

So, this guidelines is for the cancer pain management and breakthrough pain management, how to do opioid rotation from one opioid to another opioid, how to convert from oral to the transdermal opioids and how to manage opioid induced side effects. So, the guidelines should contain all these points in detail. Secondly, the purpose is also to make clinician aware about the NDPS amendment. NDPS act it is a narcotic drug and psychotropic substance act.

It was introduced in India in 1985 and then amended in 2015 which is a very important amendment as far as palliative care physicians are concerned. And all clinicians who are practicing palliative care or who are going to subscribe narcotic drugs to the patient should know about this NDPS act and its amendments.

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Scope

- To standardize prescription of Opioids across the hospital service
- To prevent and actively manage the opioid related side effects



The scope of this guideline is also to standardize prescription of opioids across the hospital service. It is not only restricted to your department, but even other department who prescribes opioid should follow this guideline and to prevent and actively manage the opioid related side effect. The main focus of the guideline can be extended by even management of its side effect and prevention of the side effects.

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

- Goal: Reduce the suffering due to pain
 - Improve Functionality
 - Improve the quality of life
- 

So, when you are managing pain in long term, long term pain means chronic pain usually observed in cancer pain, HIV patients and few of the non cancer patient have also has a chronic pain like low back pain, shoulder pain, cervical pain etcetera. Here the goal is to reduce the suffering due to pain, improve the functionality of the patient and improve the quality of life of the patient.

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What are the best practices when using Opioids long term?

For Patients with mild to moderate pain whose pain is not controlled by Non opioids given orally & regularly, low dose step III opioid

- Oral morphine ≤ 30 mg/ day may be used alternatively instead of Codeine or Tramadol
- Immediate-release and slow-release oral formulations of morphine, oxycodone, and hydromorphone can be used for dose titration.
- The titration schedules for both types of formulation should be supplemented with oral immediate-release opioids given as needed
- Transdermal fentanyl and buprenorphine are alternatives to oral opioids.
- Either drug may be the preferred step III opioid for some patients.
- For patients unable to swallow they are an effective, non-invasive means of opioid delivery

So, whenever you are using opioids for long term for many months or even years many of our patients are on morphine or other opioids for 1 year 1 and half year.

So, what are the best practices? For patient with mild to moderate pain whose pain is not controlled by non opioids given orally and regularly low dose step 3 opioids should be started. So, oral morphine less than 30 milligram per day may be used alternatively instead of codeine or tramadol.

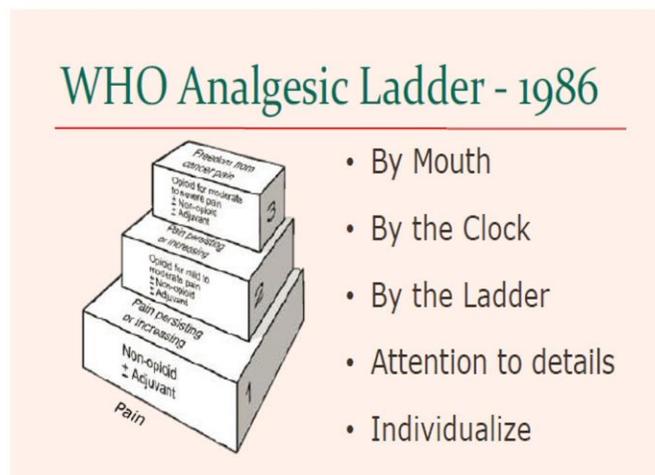
Sometimes step 2 drug like codeine and tramadol. Codeine is a very good analgesic, but severe constipation is noted with codeine and nowadays it is not available except in the syrup form for cough syrup and all that too they are misusing for addictive purpose. Tramadol available across the counter, but it does have side effects like irritation, gastritis, nausea, vomiting. So, you can use instead of these you can start morphine less

than 30 milligram per day. Immediate release and slow release oral formulation of morphine, oxycodone and hydromorphone can be used for dose titration.

Other these 2 drugs are not available in our setup. The titration schedules for both types of formulation should be supplemented with oral immediate release opioids given as needed and transdermal fentanyl and buprenorphine are alternative to overall opioid. As I said patients who cannot swallow we can put them on transdermal fentanyl of course, it is very costly drug cannot be afford can many of our patient cannot afford. In tablet buprenorphine is alternative which is available in Indian market. It has its own limitation after certain dose you cannot increase the dose because it will not be effective in giving pain relief to patient.

So, it has got a ceiling effect because it is partially agonist and partially antagonist against the morphine receptor after certain dose it will not be effective. Secondly, incidence of nausea vomiting is also reported of course, it does not have constipation with whenever you are using buprenorphine. Either drug may be preferred step 3 appeared for some patients. For patient unable to swallow they are they are an effective non invasive method of opioid delivery. For patient who are not able to swallow you can give transdermal fentanyl or buprenorphine can be given sublingually.

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This we discuss in previous lecture on WHO ladder always to be drugs to be given by mouth, by clock, by ladder, attention to detail and individualized treatment.

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How does one start oral morphine?

➤ **Oral preparations: 2**

- Quick release or immediately acting
- Sustained release/ Constant release

➤ **Initial titration** : Immediate release preparations

➤ **Start at 5mg** every 4 hours

➤ **If pain relief inadequate** - increase dose gradually (5 mg increments)

➤ **Rescue doses** for BTP (SOS)

How does one start oral morphine? Start with immediate release, quick release then switch over to constant release. One thing about constant release tablet means morphine SR tablet you should remember that it should not be crushed. Most of our head and neck cancer patients are with ryles tube. So, we give immediate release tablet which can be crushed mix into the water and give it through the ryles tube.

But this sustained release tablet cannot be crushed it will lose its effectiveness. So, patient who are on ryles tube and who are given tablet in crushed form they should not be given sustained release tablet they are always put on the immediate release tablet. So, initially you can start with a immediate release tablet every 4 hour and increase the dose 5 milligram at a time till the pain is relieved and rescue dose means keep for breakthrough pain intermittently patient get sudden pain you can give extra dose of morphine.

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How to take your medicines?



Bring the remaining stock of medicines and wrappers

- ✓ Take the medicines round the clock
- ✓ Do not take all tabs at a time
- ✓ Instructions about tabs on empty / full stomach
- ✓ Increase / decrease the dose

Again we discuss this that counseling of the patient explain each and every medicine properly with timings with its side effect and what are the changes patient should bring in the diet and lifestyle when they are on morphine.

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How to start Sustained Released Morphine?

4-hourly dose of oral morphine	12-hourly dose of Morphine SR
5 mg	15 mg ✗
10 mg	30 mg
20 mg	60 mg
30 mg	90 mg
45 mg	120 mg
60 mg	180 mg
90 mg	270 mg

Once the patients' pain is controlled on a regular 4-hourly dose, then change to the equivalent dose of Morphine SR given every 12 hours.

Breakthrough dose is 4-hourly dose of morphine

How to start sustained release is like converting immediate release dose multiplied by 3 is the sustained release dose.

So, breakthrough pain dose is 4 hourly dose of the morphine. So, if patient is on 10 milligram 4 hourly and he gets intermittently very severe pain one extra tablet of 10 milligram he take take he can take during that time whenever he is getting a pain episode intermittently.

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Cancer Pain

4. Principles of opioid maintenance therapy
 - a. Extended release or long-acting preparations on a regular schedule to provide background analgesia once dose requirements are stable
 - b. Rescue doses (1/6th of the 24 hr dose of morphine) in the form of an immediate acting/ short acting opioid preparation should be prescribed for breakthrough pain or acute exacerbations related to activity
 - c. The same opioid, if possible, should be used for breakthrough and "around-the-clock" dosing
 - d. Increase the dose of the "around-the-clock" preparation if patient requires more than 3 breakthrough analgesic doses
 - e. Dose increase, if necessary
 - i. Immediate release preparation: after every 24 hours
 - ii. Controlled release or extended release preparations: after 48 hours
 - f. Each dose increment can be set at 33-50% of the pre-existing dose and should be accompanied by a proportionate increase in the rescue dose.
 - g. Transmucosal fentanyl should be used only in opioid tolerant patients and initiated with the lowest dose
 - h. For patients who experience inadequate pain relief or unacceptable side effects : Consider Opioid rotation

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Principles of opioid maintenance therapy. So, maintenance you can switch over to extended release, rescue dose is always prescribed, rescue dose is always immediate release tablet because it has to act very fast. Patient just got up from the back and he strain his back bed he got up from the bed and he had sudden pain in the back because of the vertebral metastasis that time he can again sit down take one immediate release tablet one extra tablet of morphine and his pain will be relived within 20 to 30 minutes.

So, anytime when you want to increase the dose it should be 33 to 50 percent increase from the previous dose and fentanyl should be should be used only in opioid tolerant patients means patient who are tolerating opioids properly they will tolerate fentanyl otherwise fentanyl also causes lots of nausea vomiting.

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6. Principles for prescription of Transdermal fentanyl
 - a. Pain should be well controlled on a short acting opioid prior to starting a Transdermal fentanyl patch.
 - b. Should be used only in opioid tolerant patients
 - c. Not recommended for unstable or poorly controlled pain
 - d. Fever and use of warming devices (warming blankets etc) accelerate absorption from the patch, hence are contraindications for its use.
 - e. Analgesic duration is usually 72 hours, but some patients require replacement every 48 hours

Before prescribing fentanyl one should keep in mind that patients pain should be adequately treated or controlled by morphine then the same dose can be converted into fentanyl patch. If the pain is poorly controlled it is given for the stable pain, if pain is poorly controlled fentanyl will not act. So, if patients pain increases day by day the fentanyl patch will not act because once you apply the patch it will act for 72 hours and you cannot change the dose in that case intermittently again you have to give morphine along with fentanyl patch to relieve the pain.

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Fentanyl Patch

➤ Specific indication:

Difficulty with oral intake/ Poor compliance/ Renal failure

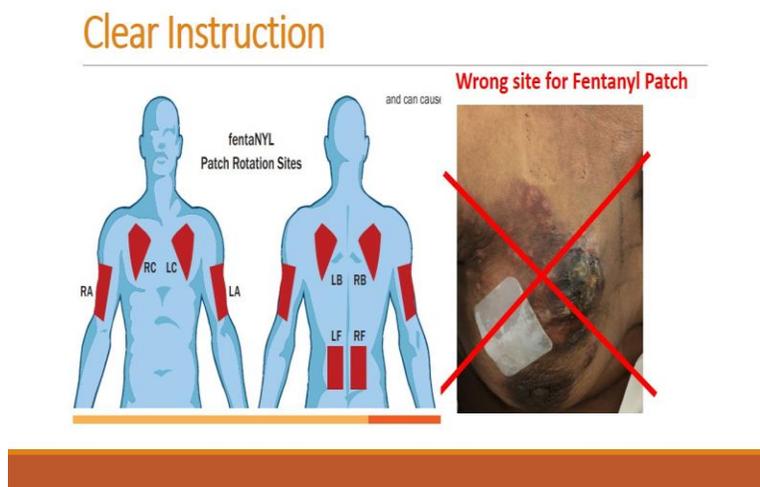
Intolerable side effects- Nausea, vomiting, severe constipation , hallucination

- Too costly
- Can give prescription only for three patches
- Needs Patient's presence – MAA

Specific indications for the fentanyl patch are the patient who cannot swallow who has got poor compliance to the tablets many of the patient does not like to swallow tablet.

So, in or they have many plenty of tablet to swallow then by giving patch you can reduce few tablets which spare few tablets which he does not have to swallow. So, poor compliance patient, patient with renal failure in which morphine action can be prolonged you can prescribe fentanyl patch. Then patient having severe constipation with morphine or severe nausea vomiting hallucination. In this patient you can switch over to fentanyl patch. It is too costly about a 125 microgram patch cost about 550 rupees, but of course, it action last for 72 hours means for 3 days.

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Where you should apply fentanyl patch? This is the training it should be given to the all nurses in our setup wherever in whatever hospital we are using fentanyl patch all nurses and all doctors, paramedical staff should be given how to apply fentanyl patch because they feel the patch should be applied on the area where there is a pain here it is wrongly applied on the nipple.

So, it should always be applied on the flat skin, dry skin and skin without hair. It need not be applied to the area where it is pain it can be applied any other way like on the front of the chest, on the side of the arm, back of the chest or back of the lumbar region in the back on on back side of the lumbar region. So, this is the way you should apply the patch.

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Tramadol & Morphine

- Small margin of demarcation between weak and strong opioid
- Act on μ Receptor
- Potency : Oral (1:5)
IV (1:10)

Cancer pain Management From molecules to suffering : IASP 2011

Robert Twycross. Symptoms management : Introduction to palliative care 2008



Tramadol and morphine there is no comparison, tramadol is a weak opioid, morphine is a strong opioid definitely more potent and very highly effective in cancer pain management.

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

1. Is the analgesia satisfactory?
2. Is the pain relief improving patient's activity?
3. Have we achieved the balance between pain relief and adverse effects?
4. Is there an **abuse potential**? Aberrant behavior?



Whenever a patient is given morphine how you will monitor them? First of all is analgesia satisfactory means you are giving adequate dose of the morphine, does after pain relief patients activity has increased, have we achieved the balance between pain relief and adverse effect, his adverse effect are under control like constipation is manageable, nausea, vomiting is manageable, he is not too sleepy, he is able to do his routine and all or whether is there any abuse potential.

So, every time he comes you check how much morphine he has taken, has he taken extra dose of morphine, are there any missing pills, has his pain is stable or is he taking morphine from some other prescriber all these things you have to evaluate to check on the abuse potential of the patient.

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How can addiction potential be detected?

How you can detect the potential addiction potential be detected?

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Opioid check list

Name (Full Name):	Age/Sex:	Address
Mobile Number:	Education:	Occupation:

Stage of disease/ Type of cancer:

H/o Addiction: Pan Masala/Gutkha/Tobacco/Bidi/ Cigarrates/other

H/o Opioids/Drug addiction/Alcohol

Willing to stop using? Yes/No / Has tried quitting Tobacco?

Family History --Married/ staying alone

Name & No of caregiver..... Relation

Who will give medicine...Self administration/care giver

H/o Psychiatric illness.....Depression/Psychosis/Major psychiatric illness

Any other illness.....Hypertension/ Diabetes/CAD/Hypothyroidism/Renal/Liver

Prescription of Opioids from other source

Can we score addiction potential?

Check the box if the item applies : A score of 0-3 low risk, 4-7 moderate risk, ≥ 8 high risk		
ITEM	WOMEN	MEN
1. Family history of substance abuse:		
• alcohol	<input type="checkbox"/> 1 point	<input type="checkbox"/> 3 points
• Illegal drugs	<input type="checkbox"/> 2 points	<input type="checkbox"/> 3 points
• Prescription drugs	<input type="checkbox"/> 4 points	<input type="checkbox"/> 4 points
2. Personal history of substance abuse:		
• alcohol	<input type="checkbox"/> 3 point	<input type="checkbox"/> 3 points
• Illegal drugs	<input type="checkbox"/> 4 points	<input type="checkbox"/> 4 points
• Prescription drugs	<input type="checkbox"/> 5 points	<input type="checkbox"/> 5 points
3. Age between 16 and 45 years	<input type="checkbox"/> 1 point	<input type="checkbox"/> 1 points
4. History of preadolescent sexual abuse	<input type="checkbox"/> 3 point	<input type="checkbox"/> 0 points
5. Psychological disease:		
• Attention deficit disorder, obsessive-compulsive disorder, bipolar disorder, or schizophrenia	<input type="checkbox"/> 2 points	<input type="checkbox"/> 2 points
• Depression	<input type="checkbox"/> 1 points	<input type="checkbox"/> 13 points
TOTAL		

First of all opioid checklist which is this is filled up during the first visit of the patient and by tools as I had said in previous lecture that by using the tools and this questionnaire where there is a history of family addiction in family alcoholism, illegal drugs, prescription drugs, alcohol abuse, illegal drugs all this history needs to be taken and given a score.

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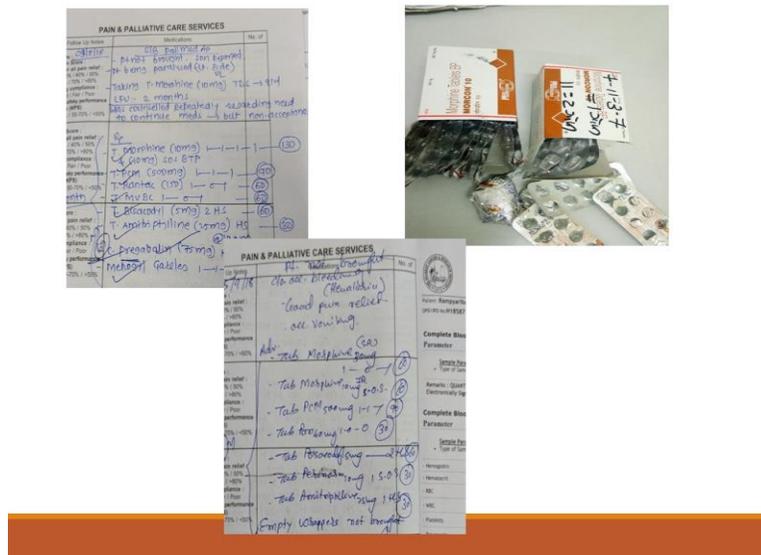
How do we assess patient's adherence to prescription?

1. One prescribing doctor and one designated pharmacy
2. Prescription monitoring program – pill count, checking empty strips during each visit
3. Double check on reports of lost or stolen medicine
4. Urine analysis during follow up

How we how do we assess the patient's adherence to prescription? First check whether patient is taking morphine from only one doctor and one designated pharmacy and not from the multiple prescription. Monitoring program where you have to pill count you have given 100 tablets row of morphine to the patient when he comes back exactly how many he should suppose he comes back after 15 minutes 15 days how many tablet he should have used, how many should be remaining with him with where are the empty wrappers and also things are the it is called prescription monitoring program. Double check on the stolen medicine if the pills are missing check with the relatives check with the patient check with the patients family doctors or any friend in the in in his group.

Lastly urine analysis can be taken up which will measure the morphine into the urine if he has taken very large dose it can be detected in the urine test.

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This is how we write the prescription of the morphine like tablet morphine 10 milligram immediate release 1 tablet 4 hourly right. Then we write 1-1-1-1 and night 2 dose the middle night middle of the night dose is combined over here and the last dose here we write timings 7 AM, 11 AM, 3 PM, 7 PM and 11 PM. Then if suppose we are giving it for 15 days here we write the number of tablets like for 15 days it will be 90 tablets. This is the complete and with this you have to write tablet bisacodyl 5 milligram 2 tablet at

night suppose for 15 days means 30 tablets. This is the way we write the morphine prescription. So, number of tablet has to be written. So, the pharmacist also counts the tablet and give it to the patient.

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Which are the aberrant behaviors that should alert the clinician?

1. Always ask about opioids, *unwilling to try non opioid*, request for medicine and undue response when denied medicine
2. Unsanctioned escalations- *Opioid overuse*
3. *Repeated visit to emergency dept. for pain killer*
4. *Approach other doctors for repeat prescription*
5. History of using other addictive substance
6. *Vagueness/inconsistencies/exaggeration- in symptom description- poor functional status*



Which are the aberrant behavior patient keeps on asking for morphine frequently frequent visit to you then there is suddenly he instead of 1 tablet he takes 4 tablets 4 hourly, repeated visit approach to other doctor we come to know from the pharmacist. We come to note that he has come very frequently to take the medicine and all such thing. So, these are the symptoms which causes shows aberrant behavior.

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What are the different adverse effects when a patient is on long term Opioids?

1. Chronic constipation and serious fecal impaction
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

On long term adverse effect very few adverse effect has been noted which which can be severe constipation with fecal impaction, dryness of mouth, tooth decay, increase incidence of fall and dizziness hypogonadism, increase pain sensitivity and sleep or disorder breathing can be detected in this patient.

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Do's and DON't's when considering long term opioid- Dos

1. Choose opioids when evaluated absolutely essential for pain relief
2. Consider alternatives such as primary disease management, appropriate referrals, non-pharmacological inputs, physical therapy, non-opioid analgesics and exercise
3. Explain that discontinuing opioids may be difficult after prolonged usage e.g. increased pain, insomnia, or anxiety and withdrawal symptoms
4. Take time to talk clearly and empathetically with patients about how they using opioids
5. Screen patients for depression and other psychiatric disorders; they may be better served by mental health treatment

So, again we are emphasizing on evaluation of the patient consider alternative whenever you are in suspicious of that patient is not using their morphine properly discontinuing

opioids may be difficult. Explain to the patient then you have to taper off over a period of 10-15 days then it can be discontinued take time to talk clearly and screen patient for depression and other psychiatry disorder before starting opioids.

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Don'T's

1. DON't start opioids when review is not feasible
2. DON't continue opioids in patients who show no progress toward treatment goals- Opioid rotation
3. DON't assume patients know how to use opioids
4. DON't assume patients use opioids as you intend. Hence *trust but verify*.
5. DON't abandon patients with a prescription drug problem. Offer help or refer to someone who can treat their substance abuse



Do not give opioid to relatives first time at least patient should be seen by you evaluate the patient and just do not give away with any other person. So, evaluation of the patient dont start opioid without evaluation. Opioid rotation you should have some alternative opioid available. Otherwise, don't continue opioid in patients who show no progress toward treatment and goal is opioid rotation. Do not assume that patient knows how to use opioid. You have to tell them each and every steps. Always trust the patient, but always verify in your own way whether he is using morphine properly.

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No Morphine SR/CR tablets thro' Ryle's
Tube feeding. Do not crush SR/CR Tablets



So, here we talked about CR and SR tablet should not be crushed.

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Narcotic Drug and Psychotropic Substance Amendment - 2014

- Training in Pain and Palliative care for prescription of Essential Narcotic Drugs
- Opioid substitution therapy for prescription of Essential Narcotic Drugs for treatment of opioid dependence

This was amended in 2014 and there and in this amendment it was in as an introduced essential narcotic drugs which has got uniform law central law as far as prescription procurement and sale of this END's is concerned throughout India.

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Conclusion

- Essential narcotics are safe and effective in managing pain.
- Every drug has its share of therapeutic benefits and adverse effect. Physician must balance the medical need for long term use of opioid
- Care and diligence in selection of patients, regular follow up, adherence monitoring and committed record keeping are all important to prevent misuse of medication

So, if you have proper guideline it is safe to use narcotics you should have knowledge of NDPS act and you should have knowledge of how patient behaves when they are on morphine and it is responsibility of all treating doctor or prescribing doctors to check repeatedly that the morphine is used properly for pain management and not misuse or abuse by patient.

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Responsibility

- As per NDPS regulation – It is our responsibility to follow statutory procedure for **stoking and dispensing drug**
- Also it is our responsibility to **enhance competence and undertake necessary training** to understand indications, identify patients who would benefit, apply ground rules for safety.
- **Possibility of diversion and abuse of medication should be prevented**

So, it should not be misuse by patient and should be used properly by for pain management only. Thank you very much.