

## RELIEF FROM CHRONIC PAIN WHEN RESOURCES ARE LIMITED.

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The Indian health care scene has a curious mix of paradoxes. Advances in Cardiovascular surgery or high-tech investigative facilities in India are on par with any advanced country at least in some cities. But across the road from a high tech hospital, it will be easy to find hundreds denied of primary health care. Pain relief is a case in point. At least a million people in India suffer unrelieved cancer pain. The number of people suffering other chronic pain conditions is anyone's guess. India is not alone. The situation is common to most of the developing world.

For any medical advance to occur, the initiative has to come from either the professionals or from the executive. Neither happens in the field of pain. Unlike high-tech medicine, pain treatment lacks glamour. So it does not attract the professional. The executive does not consider this a priority. Control of infectious diseases is a priority item; pain control is not.

**But it should be. The extent of suffering in the community is enormous. And unnecessary. Most of chronic pain can be effectively treated by simple measures. And it is up to us professionals to point this out to the administrators and to generate some interest.**

For this, the first requirement is that pain relief centres should be able to demonstrate efficacy and cost effectiveness. Unfortunately, even interested professionals or institutions often lack a sense of direction. Many professionals attempt to treat pain single-handedly, employing those treatment modalities with which they are most familiar and in which they are most skilled. The anaesthetist uses nerve blocks, the acupuncturist attempts to treat every pain with acupuncture and the physiatrist relies on physical measures alone. This approach is doomed to fail.

The hardest part in pain treatment is that it requires multi-disciplinary approach. In an ideal world, every specialist's opinion should be pooled with those of the nurse and the psychologist, and the perfect treatment decided on, of course with the involvement of the patient and the relatives. But this theoretical ideal can never be reached. Several professionals sitting around one table to look after a patient is a Utopian dream which can never be practiced, considering how busy professionals are.

The answer is for the pain therapist to understand the importance of the multidisciplinary approach. He must be prepared to take on the role of the general practitioner and to look at the problem from the patient's point of view. He will have to assess the pain and the degree of emotional involvement in the pain experience and then consider various therapeutic options. And when necessary seek the help of other specialists.

### Management of Pain

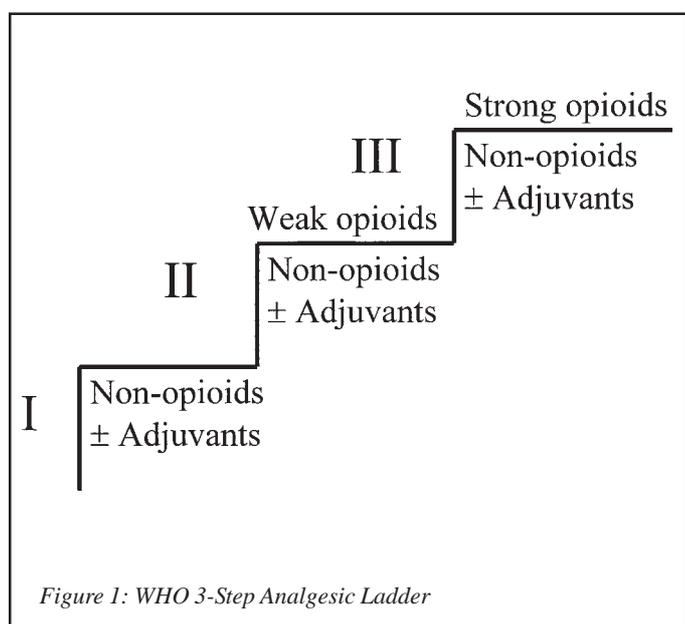
Assessment of pain need be no more difficult in the developing world than in more advanced countries, because (with some exceptions) evaluation is clinical. What is needed is only the expertise - the ability to distinguish between a nociceptive pain and a neuropathic pain, for example. It is also important to remember the concept of total pain: pain is not just a sensation. It is "*a sensory and emotional experience*"<sup>1</sup>. Physical pain will inevitably be modified by social, emotional and spiritual factors. Therefore attempts to treat chronic pain only as a physical entity are bound to be ineffective. Every pain therapist will need to learn the fundamentals of counseling and communication skills. And the patient must be believed about the pain. "*Pain is what the patient says, hurts*"<sup>2</sup>.

### The World Health Organisation (WHO) analgesic ladder

The World Health Organisation (WHO) Three-step Analgesic Ladder<sup>3</sup> (Figure 1) has revolutionized treatment of cancer pain all over the world. It involves the use of oral drug therapy by the clock, depending on the duration of action of the drug. In step I, non-opioids like paracetamol or NSAIDs are used. When they are inadequate to control pain, weak opioids like codeine or dextro-propoxyphene are added. If this fails to control the pain, the weak opioid is stopped and a strong opioid like morphine is substituted. The most important principle in practicing the ladder are:

- Give drugs **by mouth** whenever possible. Injections are impractical in the long term and add to discomfort.
- Allergic manifestations, including bronchospasm, which is uncommon with oral therapy.

As these drugs are usually effective only if given round the clock, the following recommendations for the frequency of administration may be helpful.



- Give the drugs **by the clock** depending on the duration of action of each individual drug.

### Step I

For a mild pain of the obvious nociceptive nature, it is amazing how much benefit a simple drug like paracetamol can give if used by the clock - say, 4-6hourly. No other analgesic has less of side effects; and it is quite safe to use it in the long term even in doses as high as 4-6g/day. Even if it is not enough to give a reasonable degree of pain relief, it can reduce the dose of more potent drugs.

Most non-steroidal anti-inflammatory drugs (NSAIDs) are used in the long term by mouth to treat cancer pain. They can be used safely if we remember the most important side-effects namely,

- Gastritis (If this happens, a concurrent H<sub>2</sub> blocker may be needed).
- Platelet dysfunction
- Possibility of renal failure in the patient who is predisposed to it.

Drug	Frequency in hours
Aspirin	4-6 hourly
Ibuprofen	6-8 hourly
Diclofenac	8-12 hourly
Ketorolac	6-8 hourly
Some COX-2 selective NSAIDs are relatively inexpensive in India	
Meloxicam	24 hourly
Rofecoxib	24 hourly

### Step II

If step I by itself is inadequate to control the pain, step II involves the addition of a weak opioid. The commonly available drugs in India, the recommended dose and the required frequency of administration are:

Drug	Frequency in hours
Codeine 30 - 60mg	4 hourly
Dextropropoxyphene 65mg (This is usually available only in combination with paracetamol).	6-8 hourly
Tramadol 50-100mg	6-8 hourly
Buprenorphine (0.2-0.4mg sublingual) (Many would include buprenorphine among strong opioids)	6-8 hourly

Dextropropoxyphene is the least expensive among the lot. Tramadol is more potent; but expensive. Pentazocine is available for oral use, but is not recommended because it causes dysphoria and has too short a duration of action<sup>4</sup>. Weak opioids have a special place in our country because of limited availability of oral morphine. But unfortunately they all seem to have a ceiling effect. This means that their dose can be increased only up to a point. This limits their use in severe pain.

### Step III

When step II drugs are inadequate to treat pain, step III involves continuing the step I drugs, stopping the weak opioids and adding a strong opioid.

**Oral morphine** is the mainstay of treatment of severe cancer pain. Contrary to popular belief, oral morphine (when used for opioid-sensitive pain, with dose titrated to the degree of pain relief) **does not cause addiction or respiratory depression**<sup>4</sup>. An overdose causes side effects like drowsiness, delirium and myoclonus, which serve as warning signs.

The usual starting dose is 5-10mg. As required, the dose is increased by 50% every 1-2 days, till the desired effect is reached. The following are the common side effects:

- Constipation can be troublesome, and almost all patients on opioids require laxatives. The choice in this case would be a stimulant laxative like bisacodyl or senna. It can be usefully combined with a softener/lubricant like docusate or liquid paraffin.
- Up to one third of patients get vomiting in the first few days of therapy and require anti-emetics.
- Up to one third of patients feel tired especially in the first few days of therapy. A few may also have anorexia.
- Urinary hesitancy is a relatively rare side effect.
- A few may have pruritus. This usually disappears with a few days of antihistaminics.

### Bypassing steps I and II

Pain clinics in India being few and far between, we often see patients in long-standing excruciating pain. The concept of WHO analgesic ladder, obviously, needs to be modified in such pain emergencies. One possibility is to use titrated intravenous bolus doses of 1.5mg of morphine every ten minutes till eventually the patient either gets pain relief or becomes drowsy<sup>5</sup>. If the patient gets drowsy while still in pain, it indicates that the patient has at least some opioid-insensitive pain. An alternative in cancer pain emergencies is to start the patient on 10mg oral morphine every hour till pain relief is achieved<sup>6</sup>. The point to be emphasised here is that in severe cancer pain, there is a case for bypassing the first two steps of the ladder.

### Availability of oral morphine

India has the paradoxical situation of supplying the rest of the world with opium for medical purposes, while our own patients are denied pain relief. Stringent and unrealistic narcotic regulations are responsible for this situation. Efforts are under way to simplify narcotic regulations. Seven states in India now

have simplified narcotic regulations that make availability of oral morphine easier<sup>7</sup>. A complicated licensing system is necessary in the other states.

### Adjuvant Analgesics in Opioid-Resistant Pain

Adjuvant analgesics are drugs that have no analgesic action per se, but in a particular context confer pain relief. Not all pains respond to opioids. Some of them respond only partially. Administration of morphine to such a patient will make him more miserable by causing drowsiness, tiredness, delirium or myoclonus. The following types of pains are examples of relatively opioid-resistant pains.

- **Muscular pains.** (Should be treated by muscle relaxants and injection of myofascial trigger points in some cases).
- **Colicky pain.** (This responds to antispasmodics like hyoscine butylbromide or dicyclomine).
- **Bone pain.** (Here, opioids need to be combined with NSAIDs, and in some cases, with corticosteroids).
- **Pain in constipation.**
- **Neuropathic pain.**

### General Principles of Management of Neuropathic Pain

The mainstay in the treatment of neuropathic pain is the use of two groups of drugs, **anticonvulsants and antidepressants**<sup>8</sup>. Either could be the first-line drug. Antidepressants are better tolerated and for many centers, they form the first line drug. When one alone fails, combinations of the two might work. Usual doses of these drugs are:

<b><i>Anticonvulsants</i></b>	
Carbamazepine	200 - 400 mg 8 hourly
Phenytoin	200 - 400 mg daily
Sodium valproate	Up to 1200 mg nocte.
<b><i>Tricyclic antidepressants</i></b>	
Amitriptylene	25 - 75 mg at bed-time
Doxepin	25 - 75 mg at bed-time

As they all cause significant side effects, the starting dose should be low, and the dose should be increased gradually. And side effects should be looked for and treated.

Anticonvulsants act by membrane stabilization. It is possible that sodium valproate also works by GABA enhancement<sup>4</sup>. Tricyclic antidepressants act on the descending inhibitory pathways by preventing re-uptake of serotonin and norepinephrine and thus increasing the concentration of these inhibitory neurotransmitters at the synapses.

When these two first-line drugs are inadequate to control neuropathic pain, there are several other options. One is the oral administration of local anaesthetic agents like **mexiletine**. An intravenous dose of **lignocaine**, 1mg/Kg can be used as a

therapeutic trial. If it succeeds in achieving analgesia for more than 20 minutes (a short-lived analgesia could be because of placebo effect) then the patient can be started on oral mexiletine on a regular basis<sup>9</sup>.

**Ketamine** hydrochloride, an anaesthetic agent that acts on the NMDA receptor also has been successfully used orally in the relief of intractable neuropathic pain<sup>10</sup>. It can be started in a dose of 0.5mg/Kg six-hourly, and gradually increased. However, there can be significant side effects like delirium and hallucinations. **Amantidine**, an anti-parkinsonism drug, also has been shown to cause NMDA -antagonism and has been seen to be of help in nerve injury type of pain. It is used in doses of 50 - 100mg daily<sup>11</sup>.

**Corticosteroids** are of particular value in nerve compression pain and in pain of elevated intracranial tension. They may be administered systemically, but when feasible, local drug delivery (such as epidural) has advantages. Dexamethasone is the preferred agent for systemic administration and triamcinolone for epidural injection.

Some local measures can be of help. When there is significant cutaneous hyperalgesia, a topical agent like **capsaicin** may help. When there is accessible normal nerve proximal to the lesion, **Transcutaneous Electrical Nerve Stimulation (TENS)** can be helpful. **Repeated stellate ganglion local anaesthetic blocks** are recommended for complex regional pain syndrome (CRPS) of the upper limb.

When oral drug therapy fails, central measures **like continuous epidural analgesia or neurolytic procedures** may be indicated. Coeliac plexus blockade in upper abdominal malignancy is an example. These have particular relevance when the patient comes from too far away for review and for titration of drug doses. When facilities like image intensifier are unavailable, other practical solutions may have to be sought, like thoracic epidural alcohol injection for pain of thoracic and upper abdominal malignancy<sup>12</sup>.

### General Principles of Pain Management

The following general principles may be useful for people who venture to the field of pain relief.

- Identification of the type of pain is key to successful treatment of pain. Therapeutic modalities to be followed in neuropathic pain, say, are significantly different from those needed in bone pain.
- Remember that any pain, if long-standing, can become centrally established. Neural tissue can develop anatomical and even genetic alterations. Once a pain is centrally established, peripheral attempts at treating them (like peripheral nerve blocks) are bound to be ineffective
- Somatisation: When negative feelings like fear or anger are brought out as physical symptoms like pain, it is called "somatisation". It is common for doctors to feel irritated about it. But we should remember that somatisation is not the patient's fault. There may be emotional reasons behind the pain. It is up to the doctor to identify it and to deal with it.
- While a particular intervention like a nerve block may have its relevance in a particular case, drug therapy is usually the ideal basic therapeutic modality in a large number of patients.

- The obviously perfect form of therapy (from the physician's point of view) may be totally unsuitable if it is unaffordable to the patient. The patient's financial status must be taken into consideration when planning treatment.

### Development of a Pain Relief Service

Any attempt at solving the pain problem in a poor country has to take into account the enormity of numbers and should be realistic. We find that about 80% of patients approaching a pain clinic have cancer pain<sup>13</sup>. Two parallel services have developed in the West - the pain clinics run mostly by anaesthetists and the 'hospice' or palliative care service. Neither is well established in India or in most of developing world. Much of the needs are common in both services, and perhaps an integration of both services is the most practical solution for us.

When we developed a palliative care unit in Calicut<sup>14</sup> we based it on the following principles.

- **The patients' needs should come first.** This may sound obvious; but does not often get practiced. We need to remind ourselves that our efforts can succeed only if the management is based on what the patient needs for improved quality of life.

- **The care delivery system should be realistic.** It has to suit the local cultural and economic background

- **Doctors need to establish a partnership in care with the family.** The strength in India is in the strong family structure. Empowering relatives to care for the patient can achieve a lot.

- **A partnership in care also needs to be established with the patient.** The average villager is quite capable of making brave and intelligent decisions regarding treatment options. Formal education and intelligence are not synonymous. Doctors have no right to force decisions on the patient.

- **We have to make use of existing resources.** India has the advantage of a network of primary, secondary and tertiary health care centers. These have their advantages and their drawbacks. We need to use whatever the existing machinery has to offer. If we don't, we will end up spending too much.

- **Deficiencies in existing facilities need to be supplemented by NGOs.** We must find ways to supplement all shortcomings in the available machinery. If non-Government organizations (NGOs) can work with the Government machinery, it could prove to be of benefit to the patient.

- **Willing volunteers can be the backbone of the facility.** There are numerous individuals who are kind hearted and are willing to help. This strong work force only needs to be organized and channeled properly.

### The Calicut Experience

In Calicut, a small city in the South Indian state of Kerala, we have developed an organisation that could be represented with the patient at the apex, the relatives and the volunteers next to them and the medical system supporting them. The medical system in this case involves both the Government machinery and an NGO<sup>14</sup>. A clinic works in the Government Medical College Hospital, supported by The Pain and Palliative Care Society, a registered charitable organisation with its headquarters at Calicut.

It finds and trains volunteers and provides essential staff, equipment, and drugs wherever the Government machinery falls short.

The system, over the last eight years, has grown to reach an average of 2000 patients a year in the parent clinic at Calicut. Daily patient attendance now averages 60 and the clinic sees an average of 100 - 130 new patients a month. We work with local doctors and NGOs to establish peripheral centers in neighboring districts. 27 such clinics are operative now in the various parts of Kerala. In some of them there are also home visit programmes to look after those who are too sick to travel to a clinic<sup>15</sup>. We now estimate that 15% of the needy in Kerala have access to pain relief and palliative care.

While it is true that a lot has been achieved in eight years, there are still a million more in India in need of pain relief. To reach out and to ease them, we do not need a lot of expensive gadgetry or sophistication. Morphine manufactured in India out of poppy already grown in India, a few other not-too-expensive drugs, and the realization among administrators and professionals that freedom from pain is a human right, are all that are needed.

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This article on Chronic Pain Management in Difficult Situations was commissioned by the WFSA Committee on Pain Relief for publication in Update in Anaesthesia. Dr Rajagopal is part of a team that started with minimal resources and built an excellent pain and palliative care centre, which is now recognised by WHO as a role model for developing countries and utilised by WHO as their training centre.