

Challenges in the management of cancer pain in elderly population: A review

Akhil Kapoor, Ashok Kalwar, Mukesh Kumar Singhal, Raj Kumar Nirban, Harvindra Singh Kumar

Department of Radiation Oncology, Acharya Tulsi Regional Cancer Treatment and Research Institute, Sardar Patel Medical College and Associated Group of Hospitals, Bikaner, Rajasthan, India

ABSTRACT

Elderly people are more susceptible to the experience of pain than any other sector of the population. Neoplasia is an important cause of pain in the elderly population. The prevalence of persistent pain in older persons living in a care home setting is estimated at 45-80%, thus highlighting that persistent pain in older people is widespread and problematic in these settings. This article reviews the difficulties in the management of pain in the elderly population and the important differences from other population besides describing the various pain assessment tools, pharmacologic and non-drug management of pain.

Key words: Cancer pain, elderly, non-drug management, pain assessment

INTRODUCTION

Pain is defined by the International Association for the Study of Pain as “an unpleasant sensation and emotional experience which is associated with actual or potential tissue damage or is described in terms of such damage.”^[1] This definition recognizes that the pain is a perception and not a sensation. There is an important implication of the concept of pain as perception: It is almost always best to believe that the patient is experiencing what is being reported.^[2] Since there is no objective indicator for pain, experts agree that the best clinical approach in most circumstances is to assume that the patient is reporting a true experience, even in the absence of a clear explanation.

Acute pain is a temporary sensory experience which can be of benefit, warning the individual of possible tissue damage or injury. Persistent pain persists for many weeks, months, and years. It is defined by the International Association for the Study of Pain as “continuous or recurrent pain that

persists past the normal time of healing, most commonly about 3 months’ duration.” It has no beneficial properties, and it is difficult to treat effectively.^[3]

Current evidence implies that older people are more susceptible to the experience of pain than any other sector of the population.^[4] For instance, the prevalence of persistent pain in older persons living in a care home setting is estimated at 45-80%,^[5] thus highlighting that persistent pain in older people is widespread and problematic in these settings. This article reviews the difficulties in the management of pain in the elderly population and the important differences from other population.

PATHOPHYSIOLOGY OF PAIN IN ELDERLY

Tissue injury activates primary afferent neurons called nociceptors, which are small diameter afferent neurons (with A-delta and C-fibers) that respond to noxious stimuli and are found in skin, muscle, joints, and some visceral tissues.^[6] Depolarization of the primary afferent involves a complex neurochemistry, and the role of prostaglandins, bradykinin, protons, nerve growth factor, and other compounds provide opportunities for the development of new analgesic drugs.^[7] Once depolarization occurs, transmission of information proceeds proximally along the axon to the spinal cord and then on to higher centers.

Access this article online

Quick Response Code:



Website:

www.ccij-online.org

DOI:

10.4103/2278-0513.148910

Address for correspondence: Dr. Akhil Kapoor, Room No. 73, PG Boys Hostel, P. B. M. Hospital Campus, Bikaner, Rajasthan - 334 003, India.
E-mail: kapoorakhil1987@gmail.com

The endorphinergic pain modulatory pathways are characterized by multiple endogenous ligands and different types of opioid receptors: Mu, delta, and kappa.^[8] Endorphins are present in the periphery, on nerve endings, immune-related cells, and other tissues, and are widely distributed in the central nervous system. They are involved in many neuro-regulatory processes apart from pain control, including the stress response and motor control systems. Opioid drugs mimic the action of endogenous opioid ligands.^[9] Most of the drugs used for pain are full mu receptor agonists.

Neuropathic pain has a different pathophysiology. Injury to a peripheral nerve axon can result in abnormal nerve morphology. The damaged axon may grow multiple nerve sprouts, some of which form neuromas.^[6] These nerve sprouts, including those forming neuromas, can generate spontaneous activity, which peaks in intensity several weeks after injury. These areas of increased sensitivity are associated with a change in sodium receptor concentration, and other molecular processes, and also can occur at sites of demyelination or nerve fiber injury not associated with the severing of axons.^[10] Unlike normal nerve, these injured regions are more sensitive to physical stimuli, which is clinically associated with tenderness and the appearance of Tinel's sign (i.e. pain or tingling when the area over a nerve is tapped).^[11]

Gibson reported that over 50 studies have examined age differences in sensitivity to experimentally induced pain and that the majority of these studies have focused on pain threshold.^[12] When all results were examined meta-analytically, the effect size is 0.74 ($P = 0.0005$), indicating that there is definite evidence of an increase in pain threshold with advancing age.^[12] Lasch *et al.* examined the effect of intraesophageal balloon dilatation in healthy young and older adults.^[13] The volume of air inflated into the balloon before report of pain was measured. The volume was significantly higher in the older subjects with many of the elderly subjects failing to report pain even after maximal balloon inflation, in marked contrast to the younger patients.^[13] This unique experimental technique certainly proves that pain threshold increases with age. This may point toward the possibility that a larger volume within a hollow viscus is required an elderly patient before pain is experienced as compared to younger subjects, thus, the discomfort caused by an obstructive lesion in the bowel, for example, may take longer to become symptomatic in elderly leading to poor prognosis of the disease.

One factor that is of practical concern is that of analgesic tolerance when opioid drugs are being used. Buntin-Mushock *et al.* performed a retrospective chart review of 206 patients who had been prescribed strong opioids.^[14] They found

that younger patients reached a maximum dose of around 450 mg of oral morphine over a 15-month period while the older patients achieved a maximum dose of around 210 mg over 14 months. Homeostatic changes increase the risk of gastric irritation and bleeding following exposure to nonsteroidal antiinflammatory drugs (NSAIDs) and figures would suggest that the risk of gastric bleeding is 4 times higher in older individuals when compared to younger adults.^[15]

Differences in the neuroanatomy, physiology and biochemistry of the nociceptive pathways may cause alterations in pain perception while differences in the pharmacology of drugs in the elderly may alter expected responses to these drugs.^[16] There have been four studies on age-related changes in endogenous pain inhibition tested in a conditioned pain modulation paradigm, all of which came to similar conclusions.^[17-20] Their findings showed that this kind of pain inhibition is not only functioning poorly in the elderly but sometimes is even reversed into a facilitatory function.^[20] In other words, the first pain does not reduce the sensitivity for a second pain in elderly as it does in young individuals, but instead it may enhance it. These data suggest an increase in pain threshold and a decrease in tolerance threshold, which both are dependent on the physical nature of the stressor, as well as a developing deficiency in endogenous pain inhibition, which might be paralleled by an enhanced disposition to central sensitization (stronger temporal summation).^[21]

CAUSES OF PAIN IN ELDERLY

Elderly people have a multitude of painful diseases such as arthritis, joint pain, heart diseases, bowel disorders, and cancer. Arthritis is the most common cause of pain in elderly.^[22] It is estimated that >50% 65+ aged person having pain is suffering from arthritis.^[23,24] Pain is often a constant and may be localized to the joint affected. The pain from arthritis is due to inflammation that occurs around the joint, damage to the joint from disease, daily wear and tear of joint, muscle strains caused by forceful movements against stiff painful joints and fatigue.

Research suggests that 70-90% of people with advanced cancer experience persistent pain.^[25] It is estimated that at any 1 time the over-65s will occupy about two-third of hospital beds.^[26] Further statistics indicate that the over-60s are likely to stay more than twice as long in hospital for conditions associated with persistent pain than those aged 59 and under. While pain management has advanced significantly in recent decades, older people remain less likely than younger people to receive good pain management, with older women and being more at risk of under-treatment than older men.^[27] In addition, the proportion of the aged

population is increasing slowly. These statistics highlight pain in older people is an increasingly important health issue needing greater recognition and attention.

CANCER PAIN

Individuals with cancer experience both acute and persistent pain syndromes. Most acute pain problems that these patients encounter are caused by diagnostic or therapeutic interventions. Moreover, many cancer patients with well-controlled persistent pain have transitory “breakthrough” pain.^[28] Persistent pain experienced by cancer patients may be the direct result of the type of cancer that they have, or it may be related to therapies administered to manage the disease or to disorders unrelated to the disease or its treatment. The incidence of cancer rises with age, with one estimate indicating that individuals over 65 are 11 times more likely to develop cancer than younger people.^[29] Pain is, therefore, a priority in the care of older people with cancer. The extent to which cancer pain is relieved during this stage of life has long been understood to have a profound impact on quality-of-life.^[30]

Bone metastasis which is common in advanced cases of prostate, lung, and breast cancer is an important etiology of pain in elderly cancer patients. At autopsy, 84% of those with prostatic adenocarcinoma have skeletal metastases.^[31] Prostate specific antigen is currently the most useful marker for assessing the level of bone involvement in prostate cancer. Treatment with bisphosphonates or denosumab helps to prevent complications related to bone metastases. Painful bone metastases can commonly be treated successfully with external beam radiation therapy. 41% of patients achieve a 50% pain relief within 4 weeks of treatment.^[32]

EFFECTS OF PAIN ON THE LIFE OF AN ELDERLY

Research has shown to increase pain thresholds with older age.^[33] Hence, while the management of pain in older people is a major concern, attention must also be paid to the absence of pain in older persons where under normal circumstances

pain would be present, because neglecting any warning of impending problems in older people could result in greater long-term persistent pain. Further consequences of persistent pain in older people include limited mobility, breathlessness, depressive symptoms, emotional distress, disturbed sleep, social isolation, and suicidal tendencies.^[33] This results in greater responsibility, cost and resource for the caregiver, care-provider, and healthcare system.

Assessment of pain in elderly people

If pain is not recognized, it cannot be treated. Assessment of pain is a prerequisite for successful pain management. Difficulties arise when assessment is inadequate, and also because of the highly subjective nature of pain and the difficulty in defining atypical manifestations of pain. Table 1 highlights the differences between acute and persistent pain. American medical association has issued the following “Initial Pain Assessment Guidelines.”^[34]

Obtain a detailed history, including an assessment of the pain characteristics, impact of the pain on multiple domains (physical, psychosocial, role functioning, work, etc.,) related concerns and co-morbidities (other symptoms, psychiatric disorders including substance use disorder, etc.,) prior work-up and working diagnosis, and prior therapies.

SOCRATES PAIN ASSESSMENT FRAMEWORK

- S – severity: None, mild, moderate, severe
- O – onset: When and how did it start?
- C – characteristic: Is it shooting, burning, aching – ask the patient to describe it
- R – radiation: Does it radiate anywhere else?
- A – additional factors: What makes it better?
- T – time: Is it there all the time, is there a time of day when it is worse?
- E – exacerbating factors: What makes it worse?
- S – site: Where is the pain?

Conduct a physical examination, emphasizing the neurological and musculoskeletal examination. Obtain

Table 1: Differentiating acute pain from persistent pain

Characteristics	Acute pain	Persistent pain
Temporal features	Recent onset and expected to last no longer than days or weeks	Remote, often ill-defined onset; duration unknown
Intensity	Variable	Variable
Associated affect	Anxiety may be prominent when pain is severe or cause is unknown; sometimes irritability	Irritability or depression
Associated pain - related behaviors	Pain behaviors (e.g., moaning, rubbing, splinting) may be prominent when pain is severe	May or may not give any indication of pain; specific behaviors (e.g., assuming a comfortable position) may occur
Associated features	May have signs of sympathetic hyperactivity when pain is severe (e.g., tachycardia, hypertension, sweating, mydriasis)	May or may not have vegetative signs Such as: lassitude, anorexia, weight loss, insomnia, loss of libido; these signs may be difficult to distinguish from other disease-related effects

and review past medical records and diagnostic studies. Develop a formulation including: (1) Working diagnoses for the pain etiology, pain syndrome and inferred pathophysiology, and (2) plan of care including need for additional diagnostic studies and initial treatments for the pain and related concerns.^[34]

Self-reporting is the standard method for identifying pain. Simply worded questions and easy-to-understand tools are designed to assess the sensory and emotional experience of pain and the impact it has on the physical, functional, and psychosocial aspects of the individual's life. However, concerns persist regarding the effectiveness of using any one multi-dimensional tool to assess pain in older people, with a recent systematic review of the literature on the assessment and management of pain in older people by Schofield emphasizing the need for further work to investigate pain and behavioral pain assessment scales.^[35]

NUMERIC RATING SCALE

In the clinical setting, the numeric rating scale (NRS) is simple to use and is one of the most common approaches for quantifying pain.^[36] Patients indicate their pain intensity on a scale of 0-10, with 0 indicating no pain and 10 the worst pain imaginable. The NRS can be used at the bedside by the clinician or at home by the patient as part of a pain diary that serves as a record of pain intensity at fixed times throughout the day.

VISUAL ANALOG SCALE

The visual analog scale (VAS) is another validated approach to pain measurement and is conceptually similar to an NRS.^[37] The most common VAS consists of a 10-cm line with one end labeled "no pain" and the other end labeled "worst pain imaginable." The patient marks the line at the point that best describes the pain intensity. The length of the line to the patient's mark is measured and recorded in millimeters. The main theoretical advantage of the VAS is that it does not limit pain to 10 discrete levels of intensity, permitting a more detailed rating of pain.

FACES PAIN SCALE

This scale presents pictures of 6-8 different facial expressions depicting a range of emotions [Figure 1]. This scale may be useful in patients who have mild to moderate cognitive impairment, or patients with other language barriers.^[38]

In addition, an older person's ability to self-report may become increasingly compromised as a result of impaired cognition and communication. Factors including dementia, some forms of stroke, Parkinson's disease and/or language

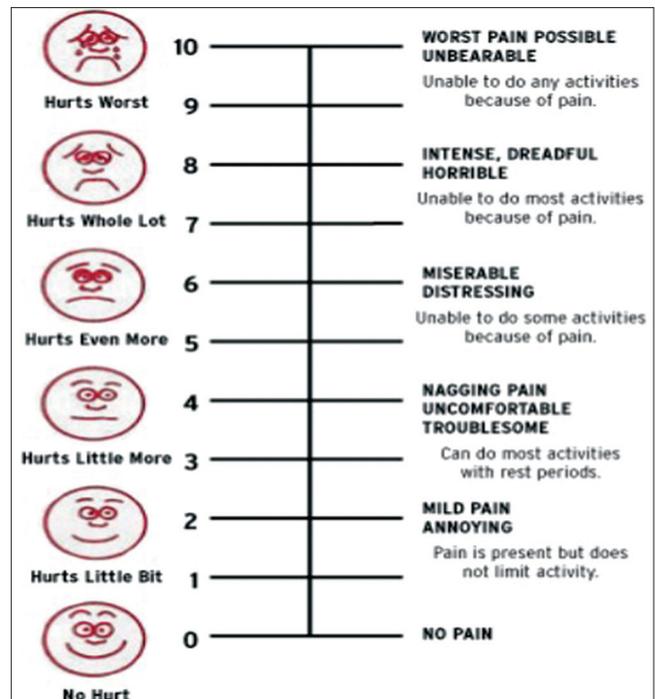


Figure 1: Faces pain scale

and cultural barriers may cause such difficulties.^[35] Greater education and training on this subject are vital to enable healthcare staff to effectively understand and treat the complex sensory and emotional experience an older person in pain suffers.

MANAGEMENT OF PAIN IN ELDERLY

Most of the times, pain can be controlled effectively through a combination of drug and non-drug strategies. Two basic principles should be kept in mind:

- Believe the person you are caring for,
- Every person has the right to good pain control.

Older people are more likely to experience a variety of medical conditions requiring polypharmacy, making them more susceptible to adverse drug reactions. Reduced renal function, altered volume of distribution, and a range of other factors can result in elevated levels of free drugs for older persons and an increased potential for toxicity. Therefore, it is important that the analgesic treatment is tailored for older people, with an eye on co-morbidities. Besides, physiological changes in elderly include increased fat mass, reduced muscle mass and reduced body water which have important implications on drug distribution.^[39] With the reduction in relative fat mass, highly lipophilic drugs, such as fentanyl and lidocaine, can have an increased duration of effect due to lower uptake in fat. At the same time, water soluble drugs, like morphine are less proficiently distributed leading to higher plasma concentrations with equivalent doses causing

increased frequency of side effects. Furthermore, free drug availability is significantly amplified by reduction in serum albumin which is common in cancer patients leading to increased propensity for adverse effects associated with highly protein bound analgesics such as NSAIDs and antiepileptic agents such as valproate, phenytoin, and carbamazepine.^[39] Lipid-soluble drugs such as lidocaine and narcotic analgesics undergo considerable first-pass metabolism while passing from the gastrointestinal tract to the liver. Due to altered pharmacokinetics in elderly, peak plasma concentrations may rise along with the potential side effects. This situation may be further worsened due to associated reduced cardiac output.^[40] Furthermore, it seems that hepatic phase I reactions involving oxidation, hydrolysis and reduction appear more strongly altered by age than phase II conjugation processes (acetylation, glucuronidation, sulfation, and glycine conjugation).^[41] Carbamazepine, lidocaine and fentanyl are subject to reduced metabolism by the same enzyme systems in elderly. Glucuronidation of morphine and glutathione conjugation of acetaminophen are examples of reduced and unaltered phase II reactions respectively. The most important pharmacokinetic effect of age is the reduction in renal clearance.^[42] This can be compounded by illnesses which further reduce renal function. This can lead to drug toxicity at dosing levels appropriate for a younger patient with normal renal function. Drugs with a predominant renal mode of excretion, like gabapentin, can cumulate when kidney function fails.

Inadequate management of pain is the result of various factors, such as deficiencies in the education of physicians and other health professionals in pain control and palliative care; fear among health professionals of drug dependence and addiction that results in underprescription and limited availability of suitable drugs.^[43]

The reluctance to prescribe and administer strong analgesics to alleviate pain at the end of life following the Shipman case is known as the "Shipman effect".^[44] While the exact effect of the Shipman case is debated, the fact remains that if older people do not receive appropriate pain relief at the end of life, they risk dying in pain – which is extremely distressing, not only for the patient but also for any family members who witness the death. Therefore, the educational and emotional needs of the older person, as well as any informal carers, friends, and family need to be taken into consideration in order to maximize the effect of pain management strategies.

The World Health Organization (WHO) analgesic ladder [Figure 2] has been the gold standard in management of pain and has been shown to eliminate pain in 80% of patients.^[45] Additional drugs "adjuvants" are used depending on the nature of the pain experience. Analgesic ladder for neuropathic pain is depicted in Figure 3.

The principles governing analgesic use have been encapsulated in a series of slogans by the WHO:

- By the mouth: The oral route is the preferred one and should always be considered in the first instance
- By the clock: One should not wait for the pain to return to take the next dose of pain killer; instead they should be taken at regular interval to maintain blood level all the time
- By the ladder: If after optimizing the dose a drug fails to give adequate relief, move up the ladder; do not move sideways in the same efficacy group. The goal is to keep the patient pain-free at all times
- Individualized treatment: The right dose is the one which relieves the pain. The dose can be titrated upwards till adverse effects prevent further escalation.

It is important to use an NSAID and an opioid in combination for most cancer pains. Nerve inflammation results in peripheral hyperexcitability which further causes central sensitization. Relief from opioids is limited by this central sensitization. Hence, NSAID can be used to control nerve inflammation which is the root cause of failure of pain to respond to morphine. Other interventions, including spinal analgesics, epidural steroids, spinal cord stimulation, and nerve blocks, may provide further pain relief if drugs are not wholly effective.^[46]

MORPHINE: THE GOLD STANDARD OF PAIN RELIEF

Morphine can be taken by multiple routes including oral, intravenous, sublingual, buccal, rectal, subcutaneous, intrathecal or epidural. Its duration of analgesia is about 3-4 h when administered via the intravenous, subcutaneous, or intramuscular route and 3-6 h when given by mouth.^[47,48] It interacts predominantly with the μ -opioid receptor. Morphine is metabolized primarily in the liver, and approximately 87% of a dose of morphine is excreted in the urine within 72 h of administration.^[47] Table 2 lists the step wise use of commonly prescribed analgesics for somatic pain management. Table 3 lists the adjuvant analgesics required in the routine clinical practice.

TITRATION OF OPIOID DOSE

The titration of opioid dose is an orderly procedure,^[49] requiring following steps:

Step 1

- Start with immediate release opioid (e.g. oral morphine 2.5-10 mg depending on age and intensity of pain) 4 hourly
- Breakthrough analgesia (immediate release) is given at the same dose as a regular dose.

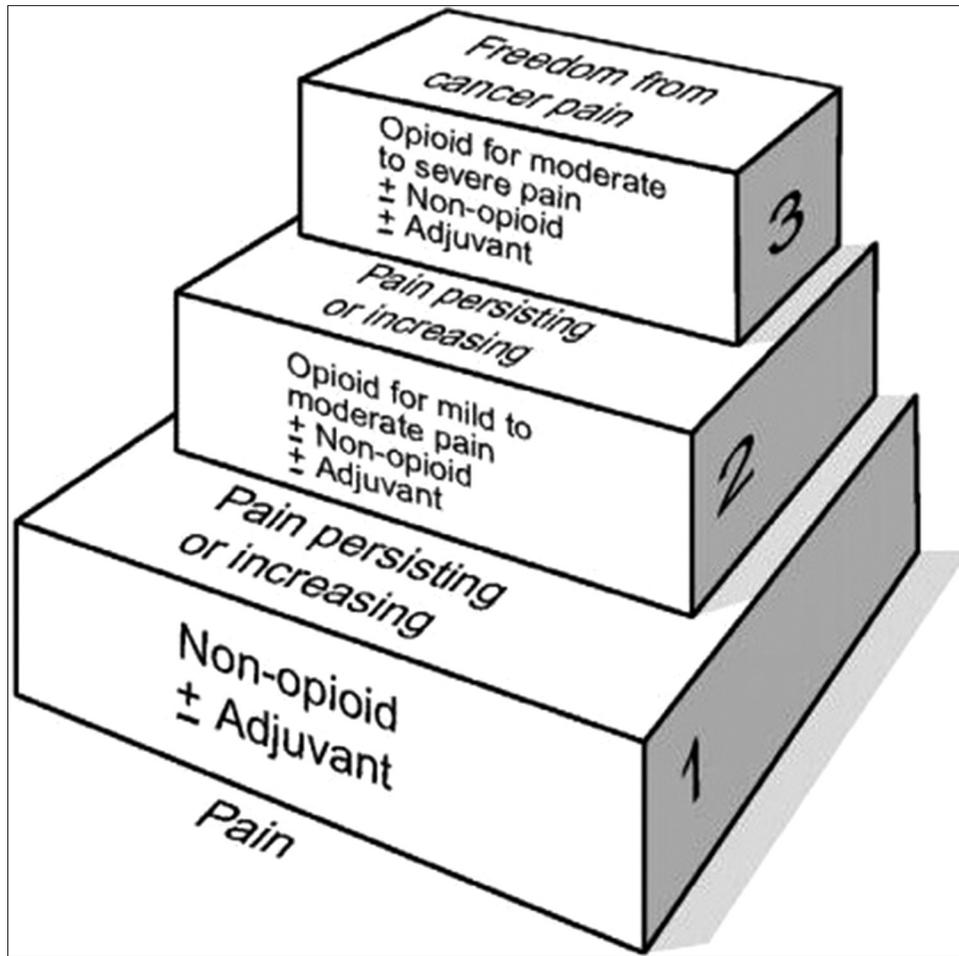


Figure 2: World Health Organization pain ladder for somatic pain

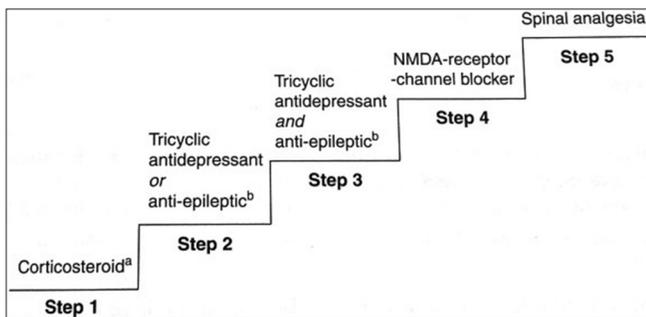


Figure 3: Analgesic ladder for neuropathic pain. ^aA trial of corticosteroid is important when neuropathic pain is associated with limb weakness. ^bSome centers use mexiletene as an alternative to an antiepileptic

Step 2

- Calculate total analgesic requirement (after 48-72 h).

Step 3

- Start controlled release preparation at the equivalent daily dose of immediate release (e.g. if oral morphine requirement is 120 mg/day, morphine sulfate tablet started as 60 mg 12 hourly)
- Breakthrough analgesia is the same analgesia at one-sixth

of the regular total daily dose (e.g. oral morphine 20 mg from the previous example).

Step 4

- If patient needs >4 breakthrough doses per day, the baseline controlled release dose needs to be increased by following steps 2 and 3.

There are some important adverse effects of morphine. All patients experience some degree of drowsiness on starting opioids. This, usually, wears off 3-5 days after being on a stable dose. Constipation is inevitable, and 30-50% patients develop nausea and vomiting.^[50] It acts on the myenteric plexus in the intestinal tract, reducing gut motility, causing constipation. Intolerable side effects necessitate switching to an alternative opioid. Morphine is a potentially highly addictive substance. It can cause psychological dependence and physical dependence as well as tolerance.^[48] In the presence of pain and the other disorders for which morphine is indicated, a combination of psychological and physiological factors tend to prevent true addiction from developing, although physical dependence and tolerance will develop with protracted opioid therapy.

Table 2: Analgesics for somatic pain management

Drug	Dose	Remarks
Step 1		
Paracetamol	650 mg 4 hourly	Hepatotoxicity
Diclofenac	50 mg 4-6 hourly	GI and renal toxicity
Ibuprofen	200 mg 4 hourly	GI and renal toxicity
Step 2		
Codeine	60 mg 4 hourly	Maximum 240 mg daily
Dihydrocodeine	60 mg 4 hourly	Maximum 360 mg daily
Tramadol	50-100 mg 4 hourly	Maximum 400mg daily
Tapentadol	50-100 mg 4 hourly	Confusion in elderly
Step 3		
Oral morphine		
Immediate release	2.5-10 mg 6 hourly	Hallucination, drowsiness
Parenteral morphine		
12-h sustained release (MST)	Starting dose 5-10 mg	Accumulates in renal insufficiency
24-h release (MXT)		
Diamorphine	Subcutaneous at 1/3 rd dose of oral morphine	Less hallucination and confusion compared to morphine
Oxycodone	Starting dose 20 mg oral	
Hydromorphone		
Fentanyl		
Transdermal	Starting dose 8 mg oral	Takes 48-h to reach steady state. Used only for stable pain and relatively safe in renal failure
Transmucosal	12-100 mcg/h over 3 days (12 mcg/h equals to morphine 40 mg/day)	
Buccal		
Nasal		
Buprenorphine		
Oral	0.4 mg	
IV	0.3-0.6 mg	
Transdermal	17.5-35 mcg/h	
Methadone	10 mg	Useful in neuropathic pain. Safe in renal failure

MST: Morphine sulfate tablet, MXT: Methotrexate, IV: Intravenous, GI: Gastrointestinal

Table 3: Adjuvant analgesics

Indication	Drug	Dose
Neuropathic pain	Dexamethasone	8-16 mg daily
	Gabapentin	100-300 mg TDS
	Amitriptyline	Starting dose 25 mg at HS In elderly 10 mg
	Pregabalin	150-600 mg
	Carbamazepine	100 mg BD up to 1200 mg daily in three divided doses
Muscle spasm	Sodium valproate	200-500 mg at HS
	Diazepam	2-10 mg daily
	Baclofen	5 mg TDS titrated to 100 mg max daily
Smooth muscle spasm	Hyoscine butyl bromide	20 mg SC stat. Upto 120 mg in 24 h
	Tenesmus	Nifedipine 5/20 mg BD oral

TDS: Ter Die Sumendum (latin), three times a day, HS: Hora Somni (latin), before sleep, at bedtime, BD: Bis in Die (latin), twice a day, SC: Subcutaneous

Opioid toxicity, usually, manifests as hallucinations (visual and auditory), pseudohallucinations (shadows at the peripheries of the field of vision), myoclonic jerks, and cognitive impairment.^[50] Dehydration is often a precipitant of the toxicity and thus initial management includes adequate hydration, reduction of opioid and haloperidol (1.5-3 mg oral) for cognitive impairment. In cases of persistent toxicity, switching to oxycodone or hydromorphone is required. Naloxone is used intravenously to reverse accidental severe opioid overdose.^[47,50]

There are few relative contraindications for morphine which should be kept in mind. They include acute respiratory

depression, renal failure (due to the accumulation of the metabolites morphine-3-glucuronide and morphine-6-glucuronide), raised intracranial pressure, including head injury (risk of worsening respiratory depression).^[49]

Other nonmorphine opioids commonly used include codeine, tramadol, and pentazocine. Nonopioid pain killers include paracetamol, diclofenac, ibuprofen, nimesulide, and cyclooxygenase-2 inhibitors such as celecoxib and valdecoxib.

MANAGEMENT OF BREAKTHROUGH PAIN

Because of its sudden onset, severity, and brief duration, an analgesic ideal for breakthrough pain should have very rapid onset and brief duration of analgesic effect.^[28] A widely cited approach to manage cancer-related breakthrough pain is the use of oral immediate-release opioids. However, oral immediate-release morphine first appears in the blood close to half an hour after it is ingested.^[50] In fact, in a recent study evaluating the analgesic effectiveness of several breakthrough pain rescue medications among hospice patients taking oral preparations (including morphine, oxycodone, or hydromorphone), the average time to meaningful pain relief was >30 min, whereas the average duration of breakthrough pain in these patients was only 35 min.^[51] Thus, alternative methods of managements have

been studied and offered to the patients. Some agents can be predicted to have more rapid onset of analgesic effect than traditional opioids. For example, an intravenous bolus morphine has an onset of analgesic effect of about 5 min after administration, with a lag of the peak effect beyond 20 min.^[52] The most extensively studied novel route for breakthrough medication is transbuccal, using the oral transmucosal fentanyl citrate lozenge.^[53,54]

USE OF NERVE BLOCKS

Nerve blocks may be used to relieve chronic, recalcitrant pain not responding to other treatments.

Injection of local anesthetics near the stellate ganglion can mitigate the symptoms of sympathetically mediated pain such as complex regional pain syndrome type I (reflex sympathetic dystrophy).^[55] A celiac plexus block by means of fluoroscopically guided injection is indicated to control pain of the epigastric viscera, especially due to primary or metastatic upper abdominal cancers.^[56] The most frequent pathology associated with the use of this block is pancreatic cancer and associated the metastasis. Trigeminal nerve block is indicated for the treatment of trigeminal neuralgia, recalcitrant herpes zoster ophthalmicus and postherpetic neuralgia.^[57]

NONDRUG TREATMENT IN THE MANAGEMENT OF PAIN

The importance of nondrug treatments to alleviate pain in older people must not be underestimated. Although various nondrug treatments still require empirical evidence to support their use, many have been found to help relieve and reduce pain in older people; including moderate exercise, transcutaneous electrical nerve stimulation,^[58,59] acupuncture,^[60] massage therapy,^[61] reflexology,^[62,63] music therapy,^[64] relaxation and holistic techniques. Yet there is limited access to information on complementary and alternative pain management solutions for older people, or their carers, and, as a result, they are not widely used in the community.^[35]

CONCLUSIONS

The management of cancer pain is a complex issue especially in the elderly population with various co-morbidities. Sufficient expertise and knowledge must be obtained prior to prescription of analgesics in this special group of the population.

ACKNOWLEDGMENTS

The authors would like to thank the consultants in the department of Oncology Dr. A Sharma, Dr. N Sharma, Dr. R Bothra and Dr. SL Jakhar. Furthermore, they express gratitude to PG Students

of the department: Dr. Sitaram, Dr. Murali, Dr. Tanya, Dr. Rajesh and Dr. Ramesh Purohit.

REFERENCES

1. Pain terms: A list with definitions and notes on usage. Recommended by the IASP Subcommittee on Taxonomy. *Pain* 1979;6:249.
2. Tracey I, Mantyh PW. The cerebral signature for pain perception and its modulation. *Neuron* 2007;55:377-91.
3. Goucke CR. The management of persistent pain. *Med J Aust* 2003;178:444-7.
4. Melzack R, Casey KL. Sensory, motivational, and central control determinants of pain: A new conceptual model. In: Kenshalo D, editor. *The Skin Senses*. 2nd ed. Springfield, IL: Charles C. Thomas; 1968. p. 423-9.
5. Pickering G. Age differences in clinical pain states. In: Gibson SJ, Weiner DK, editors. *Pain in Older Persons: Progress in Pain Research and Management*. Vol. 35. Seattle: IASP Press; 2005. p. 67-85.
6. Vanderah TW. Pathophysiology of pain. *Med Clin North Am* 2007;91:1-12.
7. Kawabata A. Prostaglandin E2 and pain – an update. *Biol Pharm Bull* 2011;34:1170-3.
8. Cross SA. Pathophysiology of pain. *Mayo Clin Proc* 1994;69:375-83.
9. Trescot AM. Review of the role of opioids in cancer pain. *J Natl Compr Canc Netw* 2010;8:1087-94.
10. Thacker MA, Clark AK, Marchand F, McMahon SB. Pathophysiology of peripheral neuropathic pain: Immune cells and molecules. *Anesth Analg* 2007;105:838-47.
11. Gelmers HJ. The significance of Tinel's sign in the diagnosis of carpal tunnel syndrome. *Acta Neurochir (Wien)* 1979;49:255-8.
12. Gibson SJ. Pain and aging: The pain experience over the adult lifespan. In: *Proceedings of the 10th World Congress on Pain*. Seattle: IASP Press; 2003.
13. Lasch H, Castell DO, Castell JA. Evidence for diminished visceral pain with aging: Studies using graded intraesophageal balloon distension. *Am J Physiol* 1997;272:G1-3.
14. Buntin-Mushock C, Phillip L, Moriyama K, Palmer PP. Age-dependent opioid escalation in chronic pain patients. *Anesth Analg* 2005;100:1740-5.
15. Rahme E, Bernatsky S. NSAIDs and risk of lower gastrointestinal bleeding. *Lancet* 2010;376:146-8.
16. McClean G. Pharmacological pain management in the elderly patient. *Clin Interv Aging* 2007;2:637-43.
17. Larivière M, Goffaux P, Marchand S, Julien N. Changes in pain perception and descending inhibitory controls start at middle age in healthy adults. *Clin J Pain* 2007;23:506-10.
18. Edwards RR, Fillingim RB, Ness TJ. Age-related differences in endogenous pain modulation: A comparison of diffuse noxious inhibitory controls in healthy older and younger adults. *Pain* 2003;101:155-65.
19. Washington LL, Gibson SJ, Helme RD. Age-related differences in the endogenous analgesic response to repeated cold water immersion in human volunteers. *Pain* 2000;89:89-96.
20. Riley JL 3rd, King CD, Wong F, Fillingim RB, Mauderli AP. Lack of endogenous modulation and reduced decay of prolonged heat pain in older adults. *Pain* 2010;150:153-60.
21. Lautenbacher S. Experimental approaches in the study of pain in the elderly. *Pain Med* 2012;13 Suppl 2:S44-50.
22. Fitzcharles MA, Lussier D, Shir Y. Management of chronic arthritis pain in the elderly. *Drugs Aging* 2010;27:471-90.
23. Abell JE, Hootman JM, Zack MM, Moriarty D, Helmick CG.

- Physical activity and health related quality of life among people with arthritis. *J Epidemiol Community Health* 2005;59:380-5.
24. Ferrell BA. Pain evaluation and management in the nursing home. *Ann Intern Med* 1995;123:681-7.
 25. Portenoy RK, Lesage P. Management of cancer pain. *Lancet* 1999;353:1695-700.
 26. Hospital Episode Statistics (HES). Totals Report for Diagnosis 'R522' (Other Chronic Pain) for the All SHAs of Treatment, Year 2005/6; 2007.
 27. McLachlan AJ, Bath S, Naganathan V, Hilmer SN, Le Couteur DG, Gibson SJ, et al. Clinical pharmacology of analgesic medicines in older people: Impact of frailty and cognitive impairment. *Br J Clin Pharmacol* 2011;71:351-64.
 28. Hagen NA, Biondo P, Stiles C. Assessment and management of breakthrough pain in cancer patients: Current approaches and emerging research. *Curr Pain Headache Rep* 2008;12:241-8.
 29. Ashkanani F, Heys SD, Eremin O. The management of cancer in the elderly. *J R Coll Surg Edinb* 1999;44:2-10.
 30. Ferrell BR, Ferrell BA, Ahn C, Tran K. Pain management for elderly patients with cancer at home. *Cancer* 1994;74:2139-46.
 31. Brown JE, Sim S. Evolving role of bone biomarkers in castration-resistant prostate cancer. *Neoplasia* 2010;12:685-96.
 32. Lutz S, Berk L, Chang E, Chow E, Hahn C, Hoskin P, et al. Palliative radiotherapy for bone metastases: An ASTRO evidence-based guideline. *Int J Radiat Oncol Biol Phys* 2011;79:965-76.
 33. McCleane G. Pain and the elderly patient. In: McCleane G, Smith H, editors. *Clinical Management of the Elderly Patient in Pain*. Dartmouth, MA, USA: The Hawthorn Medical Press; 2006. p. 1-9.
 34. American Medical Association: Module1-Pain Management. Available from: http://www.ama-cmeonline.com/pain_mgmt/module01_2012/. [Last accessed on 2014 Jun 12].
 35. Schofield P, editor. *Complementary approaches. The Management of Pain in Older Persons*. 1st ed. New Jersey, USA: John Wiley and Sons; 2007. p. 165-84.
 36. Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, et al. Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: A systematic literature review. *J Pain Symptom Manage* 2011;41:1073-93.
 37. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res (Hoboken)* 2011;63 Suppl 11:S240-52.
 38. Garra G, Singer AJ, Taira BR, Chohan J, Cardoz H, Chisena E, et al. Validation of the Wong-Baker FACES Pain Rating Scale in pediatric emergency department patients. *Acad Emerg Med* 2010;17:50-4.
 39. Turnheim K. When drug therapy gets old: Pharmacokinetics and pharmacodynamics in the elderly. *Exp Gerontol* 2003;38:843-53.
 40. Vuyk J. Pharmacodynamics in the elderly. *Best Pract Res Clin Anaesthesiol* 2003;17:207-18.
 41. Vyskocilová E, Szotáková B, Skálová L, Bártíková H, Hlaváčová J, Boušová I. Age-related changes in hepatic activity and expression of detoxification enzymes in male rats. *Biomed Res Int* 2013;2013:408573.
 42. Weinstein JR, Anderson S. The aging kidney: Physiological changes. *Adv Chronic Kidney Dis* 2010;17:302-7.
 43. World Health Organization (WHO) Expert Committee Report. *Cancer Pain Relief and Palliative Care*. Technical Report Series 804. Geneva: World Health Organization; 1990.
 44. Baker R. Patient-centred care after Shipman. *J R Soc Med* 2004;97:161-5.
 45. Vargas-Schaffer G. Is the WHO analgesic ladder still valid? Twenty-four years of experience. *Can Fam Physician* 2010;56:514-7, e202.
 46. Wiffen PJ, Wee B, Moore RA. Oral morphine for cancer pain. *Cochrane Database Syst Rev* 2013;7:CD003868.
 47. Shepard KV, Bakst AW. Alternate delivery methods for morphine sulfate in cancer pain. *Cleve Clin J Med* 1990;57:48-52.
 48. Gallagher R. Multiple opioids in pain management. *Can Fam Physician* 2007;53:2119-20.
 49. Cherny N, Ripamonti C, Pereira J, Davis C, Fallon M, McQuay H, et al. Strategies to manage the adverse effects of oral morphine: An evidence-based report. *J Clin Oncol* 2001;19:2542-54.
 50. Collins SL, Faura CC, Moore RA, McQuay HJ. Peak plasma concentrations after oral morphine: A systematic review. *J Pain Symptom Manage* 1998;16:388-402.
 51. Zeppetella G. Opioids for cancer breakthrough pain: A pilot study reporting patient assessment of time to meaningful pain relief. *J Pain Symptom Manage* 2008;35:563-7.
 52. Coda B, Tanaka A, Jacobson RC, Donaldson G, Chapman CR. Hydromorphone analgesia after intravenous bolus administration. *Pain* 1997;71:41-8.
 53. Coluzzi PH, Schwartzberg L, Conroy JD, Charapata S, Gay M, Busch MA, et al. Breakthrough cancer pain: A randomized trial comparing oral transmucosal fentanyl citrate (OTFC) and morphine sulfate immediate release (MSIR). *Pain* 2001;91:123-30.
 54. Portenoy RK, Taylor D, Messina J, Tremmel L. A randomized, placebo-controlled study of fentanyl buccal tablet for breakthrough pain in opioid-treated patients with cancer. *Clin J Pain* 2006;22:805-11.
 55. Huygen FJ, De Bruijn AG, De Bruin MT, Groeneweg JG, Klein J, Zijlstra FJ. Evidence for local inflammation in complex regional pain syndrome type 1. *Mediators Inflamm* 2002;11:47-51.
 56. Eisenberg E, Carr DB, Chalmers TC. Neurolytic celiac plexus block for treatment of cancer pain: A meta-analysis. *Anesth Analg* 1995;80:290-5.
 57. Jürgens TP, Müller P, Seedorf H, Regelsberger J, May A. Occipital nerve block is effective in craniofacial neuralgias but not in idiopathic persistent facial pain. *J Headache Pain* 2012;13:199-213.
 58. DeSantana JM, Walsh DM, Vance C, Rakel BA, Sluka KA. Effectiveness of transcutaneous electrical nerve stimulation for treatment of hyperalgesia and pain. *Curr Rheumatol Rep* 2008;10:492-9.
 59. Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. *Cochrane Database Syst Rev* 2012;3:CD006276.
 60. Paley CA, Johnson MI, Tashani OA, Bagnall AM. Acupuncture for cancer pain in adults. *Cochrane Database Syst Rev* 2011:CD007753.
 61. Ernst E. Massage therapy for cancer palliation and supportive care: A systematic review of randomised clinical trials. *Support Care Cancer* 2009;17:333-7.
 62. Ernst E. Is reflexology an effective intervention? A systematic review of randomised controlled trials. *Med J Aust* 2009;191:263-6.
 63. Kim JI, Lee MS, Kang JW, Choi do Y, Ernst E. Reflexology for the symptomatic treatment of breast cancer: A systematic review. *Integr Cancer Ther* 2010;9:326-30.
 64. Bradt J, Dileo C, Grocke D, Magill L. Music interventions for improving psychological and physical outcomes in cancer patients. *Cochrane Database Syst Rev* 2011:CD006911.

Cite this article as: Kapoor A, Kalwar A, Singhal MK, Nirban RK, Kumar HS. Challenges in the management of cancer pain in elderly population: A review. *Clin Cancer Investig J* 2015;4:111-9.

Source of Support: Nil, **Conflict of Interest:** None declared.