Indian Society for Study of Pain, Cancer Pain Special Interest Group Guidelines on Interventional Management for Cancer Pain

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Abstract

The Indian Society for Study of Pain (ISSP), Cancer Pain Special Interest Group guidelines on interventional management for cancer pain in adults provide a structured, stepwise approach which will help to improve the management of cancer pain and to provide the patients with minimally acceptable quality of life. The guidelines have been developed based on the available literature and evidence, to suit the needs, patient population, and situations in India. A questionnaire based on the key elements of each sub draft addressing certain inconclusive areas where evidence was lacking was made available on the ISSP website and circulated by e-mail to all the ISSP and Indian Association of Palliative Care members. We recommend using interventional management when conventional therapy fails to offer adequate benefits or causes undesirable side effects. Vertebroplasty should be offered to patients with uncontrolled bone pain when expertise is available.

Keywords: Cancer pain management guidelines, cancer pain management, cancer pain special interest group, celiac plexus neurolysis, Indian Association of Palliative Care, Indian Society for Study of Pain, interventional cancer pain management

Introduction

Worldwide, low-and middle-income countries are experiencing significant increases in rates of noncommunicable diseases, including cancer.[1] In India, more than one million new cases of cancer are diagnosed each year, and it is estimated that the cancer burden in India will almost double during the coming 20 years.[2] The incidence of pain in advanced stages of cancer approaches 70%–80%.[3] A meta-analysis of epidemiological studies on cancer pain revealed that the pain prevalence rate was 39.3% (95% confidence interval [CI] 33.3–45.3) after curative treatment; 55.0% (95% CI 45.9–64.2) during anticancer treatment; 66.4% (95% CI 58.1–74.7) in advanced, metastatic, or terminal disease; and 50.7% (95% CI 37.2–64.1) in all cancer stages.[4] It was also shown that over 38.0% of all cancer patients experienced moderate-to-severe pain (pain score >4/10).[4] In a study done in four regional cancer centers in India, a total of 88% of patients reported experiencing pain for about 7 days, and approximately 60% reported that their worst pain was severe.[5]

Although pain is often the primary presenting symptom of cancer and despite the presence of guidelines and the availability of opioids, cancer pain still remains undertreated. In a systematic review[6] published in 2014 using the pain

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management index, approximately one-third of patients did not receive appropriate analgesia proportional to their pain intensity (PI), as advised by the World Health Organization (WHO) analgesic ladder.

The WHO states that "drug treatment is the mainstay of cancer pain management."[7] Pain treatment using the WHO guidelines provides pain relief in majority of patients, though effective pain relief may take a long time in the third of the patients. Even in the best hands, the WHO analgesic ladder might leave 12% of patients with inadequately managed pain, which is when interventional techniques should be considered.[8] These guidelines are developed to improve the management of cancer pain and to provide the patients with a minimal acceptable quality of life.

Methods

Literature search [Appendix IV] was carried out using PubMed, Medline, Cochrane Database, Google Scholar, and OVID Search engine. The search included studies published in the English language until November 2018. Where evidence is lacking, recommendations were made by consensus (good clinical practice), following extensive discussion among the committee members and considering the results of the questionnaire [Appendix V] circulated during the meeting, and also were made available on the Indian Society for Study of Pain (ISSP) website and circulated by e-mail to all the ISSP and Indian Association of Palliative Care (IAPC) members.

There is a limited amount of high-quality evidence for interventional pain management techniques to manage cancer pain due to difficulties in performing randomized controlled trials (RCTs) in this therapeutic area. The interventional treatment should be offered when conventional therapy fails to offer adequate benefit and or causes undesirable side effects.

The following are the prerequisites and selection criteria of interventional techniques for pain management:

1. When standard treatments such as systemic drug therapy (oral, transdermal, subcutaneous, etc.) fail to offer adequate pain relief or cause unbearable side effects
2. 2. Adequate counselling of the patient and patient care providers about the procedure (including the benefits, risks, expenses, complications, failure, alternate treatmentavailability, aftercare provisions)
3. Written informed consent
4. 4. After ruling out other causes of incomplete or inadequateanalgesia
5. When expertise in performing the procedure is available
6. There are no contraindications to the planned procedure.

Commonly used interventional procedures

1. Neurodestructive procedures for well-localized pain syndromes
   a. Head and neck: Peripheral nerve block
   b. Upper extremity: Brachial plexus neurolysis, intrathecal neurolysis
   c. Thoracic wall: Epidural neurolysis, intercostal neurolysis, intrathecal neurolysis
   d. Upper abdominal pain (visceral): Celiac plexus block, splanchnic neurolysis
   e. Pelvic pain: Superior hypogastric plexus block
   f. Rectal pain: Intrathecal neurolytic saddle block, superior hypogastric plexus block, ganglion impar block
   g. Unilateral pain syndromes: Cordotomy.
2. Radiological interventions: Percutaneous vertebroplasty/ kyphoplasty, radiofrequency ablation for bone lesions
3. Neurostimulation procedures for cancer-related symptoms (i.e. peripheral neuropathy)
4. Regional infusions (requires spinal intrathecal infusion pump) easy to internalize implanted pump; for infusions of opioids, local anaesthetics, and clonidine.

Commonly used neurolytic agents are absolute alcohol (diluted to 50% alcohol) and 6% aqueous phenol and 6% phenol in glycerine. One retrospective study[9] comparing the effectiveness, duration of benefit, and complication profile of these two agents had shown no difference in pain outcomes, complications, and duration of benefit. Thus, we recommend that the choice of neurolytic agent can be appropriately left to the good clinical judgment and availability of the expertise.

Celiac plexus neurolysis

The celiac plexus neurolysis is utilized for pain arising from cancer of pancreas, liver and biliary tract, kidney, ureter, spleen, bowel up to proximal third of transverse colon. Earlier, most of the neurolysis was done using the landmark-guided or fluoroscopy-guided technique; however, recently, these interventions are done by newer modalities such as endoscopic ultrasound, trans-abdominal ultrasound, or sometimes computerized tomographic guidance also. There is good pain relief and lowering of opioid dose with reduced side effects and improved quality of life after the neurolysis. There are four RCTs comparing fluoroscopic-guided celiac plexus neurolysis with the standard WHO analgesic ladder, while one comparing computed tomography (CT)-guided celiac neurolysis with the WHO analgesic ladder showed good and prolonged relief in pain together with reduced opioid intake and improved quality of life.[10-14] Furthermore, no RCT compared endoscopic or trans-abdominal ultrasound-guided neurolysis with standard treatment. However, there are only observational studies on the ultrasound-guided celiac plexus neurolysis showing positive results.[15-17] Two recent meta-analyses have shown endoscopic-guided celiac ganglion neurolysis is effective in relieving pain in 80% and 72% of cancer patients, respectively.[18,19] Furthermore, the Cochrane review had demonstrated that celiac plexus neurolysis has fewer adverse effects and can be considered for pain relief.[20]

Splanchnic nerve neurolysis

Splanchnic nerve neurolysis, although described in the books as an alternative to celiac plexus neurolysis for relief of pain from abdominal cancers, has limited evidence with only one observational and three retrospective studies.[9,21,22]

The evidence on the radiofrequency splanchnic nerve neurolysis is limited with only one retrospective study.[23] Some clinicians combine radiofrequency lesioning with neurolytic block for enhanced effect.

Superior hypogastric plexus block

The superior hypogastric plexus neurolysis has also been used for the management of pain arising from pelvic organs. One RCT and three observational studies show good and prolonged relief after the neurolysis of the superior hypogastric plexus.[18,19,24,25] The neurolysis can be done under fluoroscopy, CT, or ultrasound guidance,[26,27] with the CT and ultrasonography approach having the advantage of supine position and less chance of vascular injury.

Ganglion impar block

There are few case series or reports on the use of ganglion impar block[28-32] for the relief of pain arising out of perianal structures. The block can be performed with the aid of ultrasound, fluoroscopy, or CT guidance. Furthermore, it can be combined with superior hypogastric block for combined pelvic and perianal pain.

Intercostal neurolysis

Although the intercostal neurolysis or radiofrequency ablation has been used for chest wall pain from cancer, the evidence pertaining to it is limited with observational studies and case series.[33-36]

Brachial plexus neurolysis

The brachial plexus neurolysis has been useful for relieving intractable pain arising from tumour compressing upon it; however, it leads to loss of motor function of the limb and should be attempted very cautiously.[37-39] The use of continuous brachial plexus block with a catheter can be a good alternative and has been described in a few descriptive studies.[40,41] In selected patients, even single-shot injection with local anaesthetics along with corticosteroid or liposomal bupivacaine can be useful.[37,38] Intrathecal selective sensory neurolysis is a preferred option as it does not compromise motor function.

Epidural neurolysis

Evidence on interlaminar or transforaminal epidural neurolysis is limited with few case series only.[42,43] However, these are rarely attempted nowadays as much safer options such as intrathecal delivery of opioids or other agents are available.

Intrathecal neurolysis

Similar to the epidural one, the literature on the intrathecal neurolysis is limited with a few old studies or recent case reports.[44-49] Recently, these are rarely attempted except in specialist centers as much safer options such as intra-intra-thecae delivery of opioids or other agents are available. Most commonly chemical agents such as alcohol with concentrations of 50%–100% and phenol 6%–12% are used for neurolysis. Alcohol is hypobaric, and thus, the affected side is positioned up at 45° angle; phenol is hyperbaric, and thus, the affected side is positioned down at 45° angle. Its limitations include inadequate pain control with the progression of the disease, limited duration of effect, motor weakness of lower limb, and rectal or bladder sphincter dysfunction.[44]

The procedure is helpful in patients with <1-year life expectancy with well-localized intractable pain and also in somatic than visceral pain.[50]

Epidural, intrathecal, or intraventricular opioid infusions

It has been widely accepted that this technique provides good benefits to select group of patients in whom the pain is not controlled by medications given systemically nor have undesirable side effects at doses required to provide the analgesia. However, there is only limited number of high-quality studies on this. There are two randomized trials[51,52] showing both improved analgesia and prolonged survival in patients receiving neuraxial opioids as compared to conventional medical management. Another trial[53] also showed improved analgesia with neuraxial opioids. Furthermore, another high-quality review[54] has found similar efficacy of opioids delivered through intrathecal, epidural, or intraventricular route.

There are different types of pumps, ranging from percutaneous catheters to fully implantable programmable pumps. There is less incidence of infection with the implantable pumps along with lower maintenance. Furthermore, after 3 months, the cost of therapy of implantable pumps is less than nonimplantable devices.

Normally, for patients with a life expectancy of < 3 months, an epidural route is preferred; whereas an intrathecal route is preferred for patients with a life expectancy of more than 3 months. The epidural catheter should be placed percutaneously and fixed at skin or by subcutaneous tunnelling with medication being delivered through a programmable pump or syringe driver. These patients if ambulatory can be managed as outpatients also.

The intrathecal medications can be deceived via an external pump or an internal programmable pump. The programmable pumps need refilling after few weeks or months, and these patients need to in close follow-up with the managing specialists.

Most commonly, opioids such as morphine are used for patients who respond partially to systemic morphine and/or are limited by side effects. For patients, who fail to respond to opioids, other medications such as local anaesthetics, clonidine, and ziconotide can also be used and have shown good results.[55-57]

For pain in the head and face intraventricular opioids can be administered via an implanted pump and catheter.

Finally, these interventions should only be undertaken in centers with expertise in these techniques and with aftercare.[58]

Cementoplasty

Cementoplasty includes the vertebroplasty, kyphoplasty, sacroplasty, acetabuloplasty, and osteoplasty. Cementoplasty

includes the injection of acrylic bone cement into the malignant bone cavities to either relieve the pain or stabile the bone or both. Vertebroplasty is the injection of bone cement into the vertebral body. The injection of cement into the sacrum, acetabulum, and other weight-bearing bones is referred to as sacroplasty, acetabuloplasty, and osteoplasty, respectively. Kyphoplasty involves the restoration of the original height of the vertebrae by inflating a balloon inside the cavity of the vertebrae and filling up of the space created with bone cement. Sometimes, cementoplasty is considered after tumour ablation using radiofrequency techniques.

There is no randomized trial of the cementoplasty procedures; however, there are few observational studies and case series. A recent review of the studies has shown that these procedures have rapidly and significantly reduced the PI reduced the requirement of opioids and functional disabilities.[59] However, these procedures were associated with cement leakage, and most of those are asymptomatic and are less commonly associated with kyphoplasty.[60]

In patients with sacral metastasis, the injection of cement into sacrum or pelvic bones has shown to reduce pain and improve mobility. The evidence for sacroplasty comes from a few case series and retrospective studies.[61-64] The complications rates are similar to vertebroplasty and mostly asymptomatic.[65]

Conclusion

The ISSP Cancer Pain Special Interest Group (SIG) guidelines on interventional pain management for cancer pain in adults emphasize the importance interventional pain management treatment as adjunct therapy for pharmacological cancer pain management [Table 1].

We believe that the ISSP Cancer Pain SIG guidelines on interventional management for cancer pain in adults will help pain specialist, anaesthesiologists, palliative care specialists, and others who are involved in cancer pain care, in the safe management of cancer pain, and provide the patients with a minimally acceptable quality of life.

Table 1: Summary of recommendations

Recommendations	Level of evidence
Choice of neurolytic agent should be based on good clinical judgment and availability of expertise (Grade B, GCP)	IIa
Neurolytic coeliac plexus block should be considered in patients with pain from pancreatic cancer (Grade A)	I
Patients whose pain control is poor despite optimal pharmacological therapy should be referred to specialists trained in interventional pain management (Grade B)	II
Vertebroplasty should be offered to patients with uncontrolled bone pain from malignant vertebral collapse where expertise is available (Grade B)	III
Epidural, Intrathecal or intra-ventricular opioid infusions (Grade A)	I

GCP: Good clinical practice

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Disclaimer

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. These guidelines should neither be construed or serve as a standard of care.

These guidelines do not represent the minimum standard of practice, nor are they a substitution for good clinical judgment. These guidelines need to be used in conjunction with patient assessment and may be individualized as per patient need.

These guidelines were developed in 2018-2019 and may be reviewed again in 2024 or sooner, based on the availability of new evidences.

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Conflicts of interest

There are no conflicts of interest.

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Appendix IV: Literature search

The following terms or MESH terms were used either in combination or single:

"Pain"[Mesh], "Prevalence"[Mesh], "Signs and symptoms"[Mesh], "Syndrome"[Mesh], "Diagnosis"[Mesh], presentation, "Neoplasms"[Mesh], tumours, cancers, physical assessment", "Pain Measurement"[Mesh], "pain scale'', psychosocial, assessment, "cognitively impaired', "psychological distress", distress, "Emotions"[Mesh] "Nursing"[Mesh], "prime assessor", "Palliative Care"[Mesh], "supportive care'', "cancer pain management", "Patient-Centered Care"[Mesh], "Patient Care Team"[Mesh], "Patient Care Management"[Mesh], "Primary Health Care"[Mesh], "Physicians, Family"[Mesh]), interdisciplinary, Education"[Mesh], outcome, barrier, "World Health Organization"[Mesh], "Guideline "[Publication Type], "cancer pain ladder", "World Health Organization three step analgesic ladder"[Mesh], Drug Therapy"[Mesh], "Analgesics, Opioid"[Mesh], "administration and dosage"[Subheading], titration, "breakthrough pain", "Drug Tolerance"[Mesh], "Adjuvants, Pharmaceutic"[Mesh], "adjuvant analgesics", "pregabalin "[Substance Name], "Ketamine"[Mesh], "Dexamethasone"[Mesh], corticosteroid, "opioid rotation", "opioid switching", "alternative opioid", "Bisphosphonates"[Mesh], "Sedation score", "Morphine protocol", "Radiotherapy"[Mesh], "Soft Tissue Neoplasms"[Mesh], "Behaviour Therapy"[Mesh], "Cognitive Therapy"[Mesh], "Physical Therapy Modalities"[Mesh], "Acupuncture"[Mesh], "Massage"[Mesh], "Exercise"[Mesh], "Exercise"[Mesh], "Nerve Block"[Mesh], "Injections, Spinal"[Mesh], "intrathecal therapy", "Vertebroplasty"[Mesh], "follow-up", "Physician's Role "[Mesh], "community care", "home program*", "general practitioner", hospice, "pain clinic", "Outpatients"[Mesh], "Outpatient Clinics, Hospital"[Mesh], "Ambulatory Care"[Mesh]

Appendix V: Cancer pain management questionnaire

1. How many patients of cancer pain do you manage per month?
2. What is the most frequent cancer pain that you encounter in your daily practice?
3. What are the clinical presentations of cancer related pain?
4. What are the methods used for clinical assessment of cancer pain?
5. What are the principles of management of pain in patients with cancer?
6. What is the WHO Analgesic Ladder? What are its principles? How effective is it in clinical practice?
7. Do you follow WHO step ladder approach for cancer pain management?
8. What do you prefer for step II and step III of WHO ladder?
9. What non-pharmacological techniques do you use to manage Cancer Pain
10. Do you screen all patients of substance abuse? If yes, which scale do you use.
11. What medications do you use to manage cancer pain
12. What are the major side-effects you observe due to pharmacological management and how do you manage it?
13. What are the adjuvant analgesics in cancer pain management?
14. What are the pharmacological strategies for breakthrough pain and other acute pain crises?
15. What are the roles of anti-cancer therapy in the management of cancer pain?
16. Do you manage patients using Interventional Techniques? If yes, which interventional techniques and in what percentage of patients?
17. What are the relative efficacy and safety of current invasive treatments for the treatment of cancer-related pain?
18. Do you think current treatment guidelines for cancer pain management are sufficient? If no, what changes do you suggest?
19. According to you, what steps need to be taken to spread the awareness regarding cancer pain management?