Interventional Techniques for Cancer Pain Management

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Disclosure

- No financial or industry relationships to disclose.
- Off-label use of drugs will be discussed.
Objectives

- Evaluation of pain in cancer patients
- Review the indications of interventional pain techniques in cancer patients
- Discuss different modalities of interventional pain management
Incidence of Cancer Pain

Up to 70% of patients with advanced cancer report pain:

- Tumor related (67%) - Direct invasion of the tumor into nerves, bones, soft tissue, ligaments, and fascia

- Treatment related (23%)
  - Surgery related
  - Radiation related bone necrosis, myelopathy and plexopathies
  - Chemotherapy related mucositis, peripheral neuropathies, and aseptic bone necrosis

- Unrelated to cancer (10%)
Types of Pain

**Neuropathic pain**
- Described as burning, shooting, “electric-like”
- Results from damage or altered function of a nerve
- Caused by tumor invasion to any areas of the nerves
  - Brachial plexus invasion due to breast cancer
  - Tumor compression of nerves/spinal cord

**Nociceptive / Visceral pain**
- Described as a dull ache, throbbing or sharp pain
- Transmitted by “nociceptors” responsive to high-intensity mechanical, thermal, and chemical stimuli
- Tumor expansion inside viscera, soft tissue or bone
- Frequently occurs with metastasis to the bone – common progression of breast, prostate and lung cancers
Cancer Pain

- Prevalent and multifactorial
- Severe and chronic in 67% of patients with advanced disease
- 46% of dying patients are inadequately treated for their pain, as reported by family members.
- Close to 80% of cancer patients in pain are well managed by the 3-Step Ladder Model
- 15-20% of patients with inadequate pain control

The diagram illustrates a stepped approach to pain management:

1. **NON-OPIOIDS**
   
   +/- Adjuvant Medications

2. **MODERATE OPIOIDS**
   
   +/- non opioids

3. **STRONG OPIOIDS**
   
   +/- non opioids

4. **INTERVENTIONS**

The pain increases along the steps as the pain management becomes more intensive.
4th Step- Beyond WHO Ladder

- Neuroaxial Techniques
  - Epidural / Intrathecal Infusion Therapy
- Neuromodulation Techniques
  - Chemical
  - Cryoablation
  - Radiofrequency
- Neuromodulation Techniques
  - Spinal Cord and Peripheral Nerve Stimulation
- Vertebroplasty / Kyphoplasty

Indications (I)

- Intractable pain despite high doses of opioids with adjuvants
  - Persistent VAS>5
  - Neuropathic nature
  - Refractory after opioid rotation (minimum 2 different opioids)
  - Opioid induced hyperalgesia

- Pain amenable to interventional therapy
  Anatomical and clinical correlation
Indications(II)

- Uncontrolled side effects due to high dose systemic opioid therapy
  - Fatigue
    - More prevalent than pain in patients with metastatic cancer
  - Depressed level of consciousness/ Sedation
    - Dose-limiting problems
  - Constipation
  - Nausea
  - Delirium/ Confusion
  - Respiratory depression
Contraindications

- Coagulopathy – INR >1.3
- Thrombocytopenia < 100K (?)
- Sepsis
- Infection at injection/procedure site
- Tumor invasion at injection/procedure site
- Skin breakdown at injection/procedure site
- Patient refusal
- Poor access to treatment
Neuroaxial Techniques

- **Advantages:**
  - Targeted therapy- NMDA & opioid receptors, Ca\(^{+2}\) channels
  - Decreased systemic medication
  - Decreased toxicity

- **Disadvantages:**
  - Invasive
  - Risk for complications
  - Specialized treatments

Neuroaxial Techniques

Reduced Dose: Pain control with reduced side effects

- 300 mg oral morphine: 10 mg epidural morphine
- 300 mg oral morphine: 1 mg intrathecal morphine
Epidural Infusion Therapy

- **Anatomy**

- **Pros**
  - Reduced risk of respiratory depression and motor block

- **Cons**
  - 80-90% of drug is systemically absorbed
  - Possible dural fibrosis can occlude catheter
  - Greater dose requirement
  - Increased risk of infection with long-term use

- Mostly used as a trial method prior to implantation
- Consider if life expectancy < 3 months
Intrathecal Infusion Therapy

- **Anatomy**

- **Pros**
  - Lower drug dose
  - Faster onset of analgesia
  - Lower incidence of side effects
  - Longer interval between refills

- **Cons**
  - Potential CSF leakage leading to spinal headache
  - Increased risk of meningeal infection or neural injury
  - Intrathecal granulomas

Intrathecal Drugs

Morphine

- Action site: Substantia gelatinosa – Dorsal Horn
- Dose dependent analgesia- mu receptor
- The **ONLY** opioid approved by the FDA for IT use
- Effective in nociceptive pain
- Adverse effects
  - Somnolence, weight gain, nightmares, vomiting, itching, constipation, respiratory depression, decreased libido
- Granuloma formation- 1.5 – 12 mg/day
Intrathecal Drugs

Hydromorphone

- Semisynthetic hydrogenated ketone of morphine
- More potent and faster-acting due to greater lipophilic properties
- Mu receptor (primary), delta and k-opioid receptors
- Smaller spinal distribution than Morphine - Less SE
- Granuloma formation (?) – 1 case report
- Equianalgesic dose: 20% of IT Morphine dose
- Effective in nociceptive pain

Intrathecal Drugs

Bupivacaine

- Improvement in quality of pain relief
- Synergism to opioids
- Effective at the site of the catheter tip
- Nociceptive and neuropathic pain
- Stable with Morphine+Clonidine or Hydromorphone+Clonidine for 90 days at 37°C
Intrathecal Drugs

Clonidine

- Selective alpha-2-adrenergic agonist
- Lipophilic
- Approved by the FDA for epidural use
- Dose-dependent anti-hypersensitivity to mechanical stimuli in a rat model of neuropathic pain
- Stable with Hydromorphone
- SE: Reduced MAP & HR
Intrathecal Drugs

Ziconotide (SNX-111)
- A nonopioid analgesic and a voltage sensitive, N-type Calcium channel blocker
- Potent synthetic neuroactive peptide isolated from the venom of a marine snail
- SE: Elevated creatine kinase levels, sedation, somnolence, nausea, headache, neuropsychiatric symptoms, ataxia, gait disturbance, double vision
- Neuropathic agent

Intrathecal Drugs

- **Line 1**
  - Morphine/ Hydromorphone/ Ziconotide/ Fentanyl

- **Line 2**
  - Morphine/ Hydromorphone/ Fentanyl + Bupivacaine
  - Morphine/Hydromorphone/ Fentanyl + Ziconotide

- **Line 3**
  - Opioid + Clonidine

Implantable Drug Delivery Systems (IDDS)

- Hockey-puck sized
- Attached to a catheter
- Programmable
- Reservoir – 20 or 40 ml
- Internalized
- Low maintenance
- Costly, yet cost effective
Efficacy of IDDS

- Cancer Pain Trial 2002 by Smith TJ et al
  Clinical trial of efficacy of Intrathecal Drug Delivery System (IDDS) plus comprehensive medical management (CMM) vs. CMM alone for patients with refractory cancer pain
- Randomized
- Prospective
- International (5 countries)
- Multi-center (21 centers)

Efficacy of IDDS

At the end of 4 weeks:

- CMM+IDDS group reported:
  - Significant decrease in fatigue
  - Elevated level of consciousness
- Pain reduction (VAS)
  - ↓ 39.1% for CMM, ↓ 51.5% for IDDS
- Toxicity
  - ↓ 17.1% for CMM, ↓ 50.3% for IDDS (p=0.004)

At 6 months: (incidental finding)

- 54% of IDDS patients alive versus 37% of CMM patients
Outcomes

- Improved clinical success
- Reduced pain scores
- Relieved most toxicity of pain control drugs
- Increased survival for duration of 6 month trial

**Pain control = Increased survival**
Neurolysis

- Intentional injury to a nerve or group of nerves
  - Chemical (alcohol or phenol)
  - Thermal (heat- radiofrequency)
  - Surgical
  - Cryogenic (freezing)

- Predominantly neuronal axonal damage; cell body is preserved
Chemical Neurolysis

Pros:

- Targeted relief
- Usually single shot

Cons:

- Effective for 3-6 months at most
- Risk of neuritis, neurologic deficit, damage to non-neural tissue or nontargeted neural structures
- Incomplete pain relief
Cryoablation
Neurolytic Blockade and Corresponding Anatomic Structures

- Stellate Ganglion
  - Head and neck
- Gasserian Ganglion
  - Face/mouth, trigeminal distribution
- Thoracic sympathetic chain
  - Upper extremities, thorax, esophagus, lungs
- Celiac plexus
  - Pancreas, stomach, transverse colon
- Lumbar sympathetic chain
  - Lower extremities, ureters, kidneys, testes
- Hypogastric plexus
  - Uterus, ovaries, bladder, prostate, descending and sigmoid colon
- Ganglion impar
  - Perineum, rectum, anus, vagina, urethra, vulva
Celiac Plexus Block and Neurolysis

- First described by Kappis in 1919
- One of the most useful and effective neurolytic blocks
- Pancreatic, primary intraabdominal and hepatic metastatic tumors
- Network of neuronal ganglia under the diaphragmatic crus in the retroperitoneal space, anterolateral to the aorta
- Greater, lesser and least splanchnic nerves (sympathetic rami from T5-T12) and superior mesenteric ganglion
Celiac Plexus Block and Neurolysis

- **Anatomy**
  Sympathetic fibers from the splanchnic nerves, vagal parasympathetic fibers and visceral afferent fibers

- **Function**
  Nociceptive transmission innervating the pancreas, liver, gallbladder, stomach, spleen, kidneys, intestines and adrenals
Celiac Plexus Block and Neurolysis

Percutaneous Techniques (need fluoroscopic or CT guidance)

- Transcrrural Approach  Two needle
- Retrocrural Approach  Two needle splanchnic
- Transaortic Approach  Single needle through the aorta
- Anterior Approach  Single needle w/ CT or US guidance

Endoscopic US Guided Technique
Celiac Plexus Block and Neurolysis

Complications:
- Hypotension - transient
- Diarrhea - transient
- Hematuria from renal injury
- Pain at the site of injection
- Pneumothorax
- Impotence
- Paraplegia (1%) - Ischemia of anterior spinal cord due to vasospasm or mechanical injury to the Artery of Adamkiewicz
Celiac Plexus Block and Neurolysis

Efficacy:

- RCT of 24 patients show decreased use of analgesics in the group that received NCPB
- A meta-analysis of NCPB for pancreatic and other intra-abdominal cancer pain demonstrates 90% of the patients reported partial to complete relief at 3 months, while 70-90% patients had partial to complete relief at the time of death

Splanchnic Nerve RFL

Bilateral Thoracic Splanchnic Nerve Radiofrequency Thermocoagulation for the Management of End-Stage Pancreatic Abdominal Cancer Pain


- Retrospective study of 35 patients at the end of life followed for 6 months
- Sustained pain relief from 8.9/10 to 3-4/10
- Improved QOL and decreased opioid consumption
Superior Hypogastric Block and Neurolysis

Anatomy

- The sympathetic trunk from T10-L2 and the parasympathetic fibers from S2-S4 create neuronal network at the anterior projection of the sacral promontorium at L5-S1 level
- Located retroperitoneally in the subserous fascia of the common iliac bifurcation

Function

- Sensory information from the bladder, rectum, prostate, testes, vagina, uterus, ovaries and descending and sigmoid colon
Superior Hypogastric Block and Neurolysis

Percutaneous techniques:

Initially described by Plancarte in 1990 for the treatment of pelvic cancer pain

Requires fluoroscopic or CT guidance

- Posterior Approach: Two needle technique
- Transdiscal Approach: Through L5-S1 disc space
- Anterior Approach: Single needle technique
Superior Hypogastric Block and Neurolysis

Complications:

- Hypotension
- Pain at injection tract
- Bladder puncture
- Retroperitoneal hematoma
- L5- S1 nerve root injury
- Discitis (1-4%)
Superior Hypogastric Block and Neurolysis

Efficacy:

- A trial of 227 patients
- 72% reported effective pain relief with reduction of opioid consumption
- At 6 months, 69% had continued pain relief


- Only one RCT comparing opioid therapy with neurolytic SHP found decreased pain intensity, opioid consumption and increased quality of life

Ganglion Impar Block and Neurolysis

- First described by Plancarte in 1990 for the treatment of intractable perineal pain
- Primary indications are perineal pain due to anal or rectal cancer

Anatomy:
- Located anterior to the lower portion of the first coccygeal body
- Termination of the paravertebral sympathetic chains
Ganglion Impar Block and Neurolysis

Function:
- Contains visceral afferent fibers that innervate the perineum, distal part of the rectum, anus, distal urethra, distal third of the vagina and vulva

Techniques:
- Anococcygeal Approach
- Trans-Sacroccocygeal Approach
- Intercoccygeal Approach
- Coccygeal Transverse Approach
Ganglion Impar Block and Neurolysis

Complications:
- Rectal perforation
- Sacral nerve root injury
- Epidural injection
- Bowel or bladder dysfunction

Efficacy:
- Two prospective studies with good efficacy
- One study using RF lesioning with 50% decrease in pain scores
Conclusion

- The need and responsibility to treat pain
- Communication between disciplines to establish treatment goals
- Risk / Benefit ratio
- Patient preference
- Vigilance
- Multimodal therapy

“To cure sometimes, to relieve often, to comfort always”

Anonymous