THE PERILS OF PALLIATIVE CARE

When Palliative interventions can result in symptom burden

Hemant S. Murthy M.D
Fellow- Hospice and Palliative Medicine
Virginia Commonwealth University Health Systems
Richmond, Virginia

OBJECTIVES

✓ To discuss epidural analgesia: its benefits and potential complications when used in a palliative care setting
✓ To discuss Dexmedetomidine’s benefits as well as notable side effects when used as a palliative intervention
✓ To illustrate through a case report, how awareness of potential side effects of interventions can help discern iatrogenic causes from disease progression

Epidural Analgesia

◆ Epidural infusions, continuous or intermittent used for managing difficult pain, including cancer pain
◆ Administered epidurally, medications can reach the spinal cord by diffusion through the meninges
◆ Can provide pain relief by insertion in thoracic, lumbar and sacral regions
◆ Tunneled catheters used for longer duration of epidural medication

D. Papadopoulos, e-algos.com

Benefits

◆ Pain relief potentially achieved without interruption of motor or autonomic function.
◆ Reduced amount of epidural opiate required for systemic analgesia.
◆ Fewer opiate related side effects
◆ Severe complications from catheter management are rare
◆ Useful in predicting benefit of implantable analgesic pump


Case Presentation

◆ 54 year old woman admitted to Palliative Care Unit with severe, lumbosacral pain as well as bilateral leg pain.
◆ History of Breast Cancer, with prior known metastatic disease to pelvis and liver
◆ Tearful, severe 10/10 pain on minimal movement, but otherwise unremarkable examination and labs
◆ CT Pelvis and MRI Spine show worsening bony disease, new sacral fractures, and spinal metastases causing spinal stenosis

DISCLOSURE INFORMATION

DR. HEMANT MURTHY HAS DISCLOSED NO RELEVANT FINANCIAL RELATIONSHIPS.
Past Medical History:

- Invasive Ductal Carcinoma - Right Breast
  - Diagnosed in 1999- (T1 N0 M0, ER +, PR -, Her2 -), resected.
  - Recurrence in 2006, resulting in bilateral mastectomies, and hormonal adjuvants
  - Distant Metastasis (bone and liver) detected in 2008, progressed through multiple chemotherapy regimens.

History continued...

- Home Meds:
  - Trazadone, Lortab
- Social History
  - Non-smoker, no history of illicit drug use nor alcohol abuse
  - Married, no children, works as an investment banker
- Allergies
  - Dexamethasone (profound depression), Percocet (rash), Tape (rash)
- Family History
  - No known cancer history

Hospital course: day 1-5

- Intravenous Morphine and Hydromorphone administered via PCA
- Started on baclofen for back spasms
- Pain uncontrolled with escalating opiate doses but develops new onset anxiety, delirium, and agitation.
- Switched to intravenous fentanyl, baclofen discontinued. Required 1600 mcg over 24 hrs for mild improvement in mentation and pain.

Hospital course: day 6-13

- Epidural catheter placed on day 6, started on bupivacaine 4 mcg/hr, Foley catheter placed for precaution.
- Radiation treatment to spine also started, 30 Gy over 10 fractions
- Delirium resolved - now at baseline mental status
- Pain now 4/10, tolerable. Able to participate in Physical therapy
- Epidural titrated during therapy with bupivacaine, and later morphine added to epidural. Fentanyl lozenges used for breakthrough pain
- Comfortable on regimen, plan to discharge patient home.

Hospital course: day 14

- Epidural catheter migration noted on exam
  - Not dislodged, no dramatic change in pain response appreciated
- On exam, site is clean, dry and without erythema.
- Remains afebrile, no new physical findings, no change from baseline labs.
- Catheter replaced, placement and pain response confirmed with epidural test dose
- Discharge plan still intact.

Hospital course: day 15-22

- Pain increasing in back and legs, Patient crying and becoming increasingly delirious
- Epidural bupivacaine and morphine (1.5% dose increases daily) and fentanyl (12,000 mcg/day) ineffective
- IV methadone ineffective and prolonged QTc
- Stable vital signs. No change in labs from admission, urinalysis and chest x-ray unremarkable. No motor or sensory deficits on exam.
- IV infusion of Dexmedetomidine started and titrated to comfort.
- Pain improved, but delirium persists. Now with lethargy and somnolence
Day 23-24

- Erythema and small swelling at epidural site. Catheter removed.
- Labs reviewed, elevation in CRP, ESR only abnormalities.
- Urgent MRI w/sedation: large heterogeneous epidural fluid collection from T12 downward, causing severe compression of the cauda equina
- Emergent Laminectomy and fluid drainage - growing coagulase neg. staphylococcus. IV antibiotics started.
- Immediate improvement in pain, but delirium and confusion persist.

Day 25-present

- Pain continued to improve daily.
  - As Dexmedetomidine infusion decreases, delirium begins to resolve.
  - Dexmedetomidine stopped on day 31, delirium completely resolves on day 32.
  - With pain controlled on transdermal fentanyl and oral lozenges, patient is discharged home on day 37, receiving rehab and antibiotics as outpatient.

Three Months Later: Patient walked into her clinic, without assistance.

Epidural abscess

- Can occur either from bloodstream infection, or direct spread (osteomyelitis, catheter infection, pressure ulcer).

Symptoms/Signs at time of diagnosis (% of patients with findings):
- Back pain-most common finding 73%
- Epidural tenderness 58%
- Motor weakness 40%
- Radicular pain 38%
- Sensory abnormalities 34%
- Fever 32%
- Other less common symptoms:
  - Bladder/anal dysfunction, Confusion, headache, Nausea/vomiting, Paralysis
  - Leukocytosis 60%, Elevated ESR/CRP in 90% of patients at time of abscess discovery.

ALL SYMPTOMS, FINDINGS NON SPECIFIC

Imaging/Management:
- MRI with gadolinium (Gd-MRI) has a specificity and sensitivity above 90%.
- Definitive treatment of choice: surgical decompression w/ antibiotic therapy, or antibiotics alone if patient unable to survive surgical decompression.

Infection risk with epidural catheters

- Risk of infection in those receiving epidural therapy for more than 70 days approaches 12%.
- Incidence of infection extending to the epidural space is about 1%

Risk of infection in those receiving epidural therapy for more than 70 days approaches 12%
- Incidence of infection extending to the epidural space is about 1%

ANALGESIC SIDE EFFECTS

- Dural puncture (headache from spinal fluid leak)- treat symptomatically or with blood patch
- Epidural hematoma (rare but devastating, can compress cord leading to paraplegia)

Epidural complications

- Inadvertent high block-can cause paraesthesia or pain in thoracic/cervical roots
- Hypotension (usually preceded by nausea)
- Dural puncture (headache from spinal fluid leak)- treat symptomatically or with blood patch
- Epidural hematoma (rare but devastating, can compress cord leading to paraplegia)
- Neurologic injury (pain radiating to legs)
- Infection (meningitis, epidural abscess)
- Fibrosis from long term catheter placement
Reduction in prevalence in delirium compared to midazolam

Dexmedetomidine studied at various blood levels

- Double blind design study (dexmedetomidine vs. alfentanil vs. placebo)
- Cognition, reaction time and sedative properties more evident as blood levels of dexmedetomidine increased
- Broad analgesic effects- Tested with heat and electrical stimuli, and patient responses
- No relationship between analgesia and dexmedetomidine levels
- Improved pain tolerance, but not pain threshold

Common palliative medications

(.....and what to look out for)

- Opioids: Constipation, nausea, vomiting, pruritus, confusion, respiratory depression (usually in opioid naive patients), myclonous (at high doses)
- Morphine: hydromorphone: caution with renal impairment
- Oxycodon: caution in hepatic impairment
- Percocet: liver failure (at high doses due to acetaminophen toxicity)
- Methadone: cardiac arrhythmias (check QT interval), hallucinations, chronic fatigue
- Percocet: serotonin syndrome, confusion, sweating, fatigue, agitation, hallucinations, anorexia, depression, dysphoria. Avoid exposing transdermal patch to heat
- Lorazepam: psychomotor agitation (worse in elderly), hypotension, amnesia
- Methadone: cardiac arrhythmias (check QT interval), hallucinations, chronic fatigue
- Fentanyl: nausea, vomiting, pruritus, confusion, respiratory depression
- Morphine, Hydromorphone: caution with renal impairment
- Oxycodon: caution in hepatic impairment
- Percocet: liver failure (at high doses due to acetaminophen toxicity)
- Methadone: cardiac arrhythmias (check QT interval), hallucinations, chronic fatigue
- Percocet: serotonin syndrome, confusion, sweating, fatigue, agitation, hallucinations, anorexia, depression, dysphoria. Avoid exposing transdermal patch to heat
- Lorazepam: psychomotor agitation (worse in elderly), hypotension, amnesia
- Methadone: cardiac arrhythmias (check QT interval), hallucinations, chronic fatigue
- Fentanyl: nausea, vomiting, pruritus, confusion, respiratory depression

Concerns and cautions with dexmedetomidine

- Dose dependent bradycardia and hypotension most common adverse event
- FDA safety information (updated 2010): Use of dexmedetomidine beyond 24 hours has been associated with tolerance and tachyphylaxis
- Withdrawal symptoms with abrupt discontinuation of dexmedetomidine
  - Review of 4 studies*
  - Most common symptoms: nausea, vomiting, agitation (5%)
  - Less than 5% experienced hypertension or tachycardia requiring intervention
  - No cardiovascular events reported

* Kunisawa, T. Dexmedetomidine Hydrochloride as a Long-Term Sedative. Therapeutics and Clinical Risk Management 4th, 2011

Special Thanks to....

- Everyone here today for attending
- Dr. Laurel Lyckholm, P. Coyne RN and Bart Bobb RN
- Dr. Alice Beal
- The VCU Department of Hematology, Oncology and Palliative Care
- Ellie Coyne and the Massey Cancer Center/ Thomas Palliative Unit Volunteers
- Our Patients and their Families, who inspire us everyday


ASJ Task Force on Infectious Complications Associated with Neuraxial Techniques. Anesthesiology 2010; 112:530-545

Kunisawa S. Dexmedetomidine Hydrochloride as a Long-Term Sedative. Therapeutics and Clinical Risk Management 2011; 7:395-400


REFERENCES

REFERENCES