Pain Management Panel – back pain, CRPS, and cancer pain – what can "we" do ?

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The Tony Bennett Approach

Objectives

- Outline a rational pain management plan for a patient with non-surgical, chronic back pain
- Discuss the contemporary management of patients with Complex Regional Pain Syndrome (CRPS)
- Highlight the use of medications and interventional techniques in a terminal patient with cancer-related pain

WHAT MAKES CHRONIC PAIN SO HARD?

- Chronic pain LINGERS, causing:
- Failed expectations for treatment leading to cure
- Frustration amongst MDs and patients
- Changes in attitudes about regaining health, changed behavior, altered lifestyle, and changes in the nervous system = neuro-plasticity
- Chronic opioid use AND neuropathic pain, independently, decrease the set point in the CNS response for "pain" – the *combination* you see daily in your practice!

Management of chronic pain

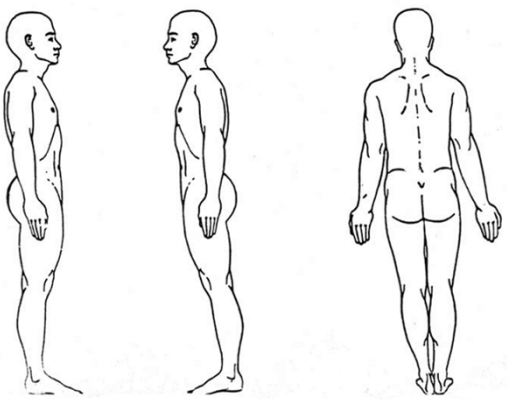
- We truly "manage" neuropathic pain, as we do diabetes & asthma
- **We need a patient who is active** in the evaluation, mgt planning and the Rx phases
- Ongoing education of the patient is your major challenge
- **Treat the cause >> symptoms, when possible

Goals of Chronic Pain Management

- Decrease the frequency and/or the intensity of the pain over time
- Increase the patient's ability to function
- Utilize contemporary medications
- Help the patient cope with residual pain & pain-related issues (entitlement, W. Comp)

Benefits of a Questionnaire

- Wealth of info in a familiar format
- Establishes a chronology for the pain
- Gives a favorable impression pre-visit
- Makes the doctor-patient time more efficient
- Provides a framework for follow-up evaluation, data collection, QI projects



Pain rating methods, reference

- A comparison of three self-report pain scales in adults with acute pain
- J Emerg Med 2015;48(1): 10-18
- Visual analog scale
- Color analog scale
- Numeric rating scale

The Physical Assessment

- It is hard to evaluate the patient in the face of severe pain, drug-seeking behavior, or an unstated agenda (that is counter to yours)
- Remember what's subjective vs objective
- The Hx and PE set up the treatment, so be thorough
- What can you dx with Hx & PE alone?
- Must have a PE before interventional Rx

Laboratory studies

- Don't prove the presence or absence of pain
- Don't correlate with the patient's stated intensity of pain or the alleged disability
- Are expensive
- Are subject to interpretation

A 42 yo male with neck pain

- Onset at work after slipping on a grease spot on the floor by heavy machinery.
- Conservative Rx with meds, PT, and injections to little benefit.
- Has had two surgical procedures
- What works the best for him is oxycodone, soma and rest.
- What are the physical, psychological and spiritual aspects of this case?
- What is the optimal pain management program?

How does one select "the" best patients for this therapy?

- Distill history & physical exam data
- Assess physical function, psychosocial fx, and quality of life
- Pain Med Questionnaire, SOAPP, ORT
- Risks assoc with: 1) pt or family h/o subst abuse or addiction, 2) psychiatric condition, 3) smoking, 4) young age, and 5) h/o pre-adolescent sexual abuse

Conclusions about opioid use

- The consequences of opioid use are based somewhat in their pharmacologic effects, which are systemic
- There are also *non*-pharmacologic results that are magnified by mis-use and abuse, which are both accidental and intentional
- There are hazards for both the acute and chronic users
- Understanding the pharmacology has not protected patients
- There is a huge effort on many fronts to provide corrective measures
- Treating a patient's pain based upon a numerical report of the intensity of the pain is not scientifically based

Lessons from recent research about the placebo effect – from art to science

- Brody H, Miller FG. JAMA 2011;306:2612-13
- Advances in research and ethics and physician comfort with the power of placebos
- Neurophysiology and neurochemistry understanding
- Psychological mechanisms – expectancy and conditioning

Post-operative analgesic effects of paracetamol, NSAIDs, glucocorticoids, gabapentinoids, and their combinations: a topical review

- Dahl JB, Nielsen RV, Wetterslev J, et al.
- **Acta Anaesthesiol Scand 2014; 58:1-17**
- "A diversity of combinations is currently employed in clinical practice, and no well-documented 'gold standards' exist."
- "The number of possible permutations of non-opioid analgesics and techniques is very large. The literature is characterized by trials of numerous combinations with different doses and dosing regimens, abundant small trials with low statistical power, and pronounced heterogeneity in terms of outcomes."
- "…recent studies have confirmed that many patients do not receive the prescribed intervention due to organizational problems with handling of these often rather complex prescriptions."

Adverse effects of perioperative paracetamol, NSAIDs, glucocorticoids, gabapentinoids and their combinations: a topical review

Mathiesen O, Wetterslev J, Kontinen VK, et al
Acta Anaesthesiol Scand 2014; 58: 1-17

"The main finding of the present review is that most data on adverse effects of the commonly used analgesics originate from trials with mainly small study populations, and studies where adverse effects were not primary outcome measures."

"Knowledge of benefit and harm related to multimodal pain treatment is deficient and needs clarification in large trials with prolonged observation."

The concern…

- "A diversity of combinations is currently employed in clinical practice, and no well-documented 'gold standards' exist."
- ***Postop analgesic effects of paracetamol, NSAIDS, glucocorticoids, gabapentinoids and their combinations: a topical review***
- ***Dahl JB, Nielsen RV, Wetterslev J, et al. Acta Anesthestiol Scand 2014;58:1=17***

Furthermore (the science issues)…

- "The number of possible permutations of non-opioid analgesics and techniques is very large. The literature is characterized by trials of numerous combinations with different doses and dosing regimens, abundant small trials with low statistical power, and pronounced heterogeneity in terms of outcomes."

Furthermore (the systems issues)…

- "…recent studies have confirmed that many patients do not receive the prescribed intervention due to organizational problems with handling of these often rather complex prescriptions."

Physical therapy

- As pain is dec., function should inc.
- ROM, strength, endurance
- Modalities (heat, cold, diathermy, TENS, massage, etc, etc)
- Patient must be active

Psychology/psychiatry

- Evaluation to ID psychiatric disease v attitude/behavior alterations
- Patient needs help coping
- Multiple therapeutic options
- Patient is free to make decisions about yea/nay for Rx, BUT he/she can't make that decision your problem

Complementary therapy, rehabilitation arenas

- Alternative/complementary therapy – LOTS
- Social rehab
- Vocational rehab

Coordinated program of Rx with approp f/u
Just taking the pain away doesn't solve all the pain-related problems

A primer on HRQOL in chronic pain medicine

- Vetter TR. Anesth Analg 2007;104:703-18
- "pain is a complex and individual experience that is often difficult for patients to fully describe using a conventional pain intensity scale."

Vetter, Anesth Analg 2007

- "Health-related quality of life encompasses those aspects of health and well-being valued by patients, specifically, their physical, emotional, and cognitive function, and their ability to participate in meaningful activities within their family, workplace, and community."

A case of Complex Regional Pain Syndrome

- A 24 yo male is involved in a MVA in which his wife was killed. He suffered bilateral acetabulum fxs which were fixed with ORIF acutely.
- One month postop his father returns to the hospital because he can't control the patient's pain with the medications provided.
- His LLE is hyper-sensitive, swollen, somewhat discolored, and cold.
- What is his management plan?

IV ketamine infusions for neuropathic pain management: A promising Rx in need of optimization

- Maher DP, Chen L, Mao J. A&A 2017;124:1-14
- "…certain characteristics of ketamine infusions may be associated with better clinical outcomes."
- "However, there are few studies designed to optimize ketamine infusion protocols by defining what an effective infusion protocol entails with regards to a respective neuropathic condition."

Preparing the Patient for Ketamine

- Prepare patient & family for potential effects of ketamine
  - The dose of ketamine we are using are for analgesia and reversal of opioid tolerance
  - Sometimes a patient may experience "dissociative effects"
    - State of catalepsy – eyes remain open with a slow nystagmic gaze (rotary)
    - Patients may have a reduced perception of external stimuli and reduced interaction with you and the family
    - Patients may report feeling "disconnected" from their body; an out-of-body experience or some other type of dream or illusion
    - Much of these experiences can be pleasant for the patient, especially if you suggest they think of a pleasant place they would like to be right now (i.e. beach, restaurant, etc.)

Preparing the Patient for Ketamine (continued)

- If a patient experiences an unpleasant dream/hallucination an extra dose of lorazepam should help relieve this effect
- The ketamine will not:
  - Depress respiration
  - Cause hypotension
- The ketamine may:
  - Cause hypertension and tachycardia
  - Increased secretions (salivation & lacrimation)
  - Muscle rigidity in the arms and legs (resemble myoclonus)
  - Mydriasis and nystagmus/diplopia

Ketamine Administration by the continuous infusion protocol

- Prior to initiation of infusion
  - Baseline EKG, BMP & LFTs
  - This must be reviewed with the LIP prior to proceeding
  - Baseline set of vital signs
- Understand the contraindications for use
  - Severe coronary artery disease
  - Severe glaucoma
  - Severe depression with suicidal ideation
  - Known or suspected schizophrenia
  - Significant liver dysfunction –
    - Bilirubin > 3mg/dl and Albumin < 2.8mg/dl and INR > 2.3

Initiating Ketamine Continuous Infusion Protocol

- Pre-medicate patient with lorazepam 1mg IV push
  - Prevents emergent reaction from ketamine
- Initial bolus dose 0.1-0.3mg/kg slow IV push over 1 minute (calculated within the EMR)
  - Avoid faster administration to prevent apneic episode
  - Effects will last 15-20 minutes so have infusion present and ready to start after bolus
  - Bolus used to attain steady state level more quickly
  - This is an analgesic dose, sub-anesthetic
  - Warn patient of potential dissociative effect before bolus
- Pre-medication and bolus will not be given to ERAS patients (ketamine will have already been started intra-operatively.

Ketamine Continuous Infusion Protocol (continued)

- All dosing is based on Ideal Body Weight
- After the continuous infusion is begun at 0.1mg/kg/hr it should not be increased for the first hour.
- Thereafter the infusion may be increased by 0.1mg/kg/hr increments every 60 minutes as needed to a maximum dose of 0.5mg/kg/hr
- **You will not be independently titrating this infusion -** These adjustments must be by an approved LIP order

Treating potential side effects of Ketamine

- Glycopyrrolate 0.2-0.4mg IV every 4 hours as needed for excessive salivation/lacrimation
  - Atropine eye drops, 3 drops sublingually every fours as needed may be used as a substitute if there is a glycopyrrolate shortage
- Lorazepam 1mg IV every 2 hours as needed for signs of frightening hallucination or delirium
- Clonidine 0.1mg orally twice a day to treat potential hypertension from ketamine
  - Hold for systolic BP < 100mmHG

Monitoring of Patient while on Ketamine Infusion

- Continuous pulse oximetry
- Vital signs and pulse oximetry readings;
  - Initiation of infusion – every 15 minutes for 1 hour then
  - ICU and IMU patients: Obtained according to ICU and IMU standards
  - Acute care patients: Palliative care and ERAS vital signs will follow EPIC order sets.
    - VS every 2 hours times 2, then every four hours thereafter
  - This schedule of vital signs will need to be repeated for any re-bolus or increase in continuous infusion rate
  - If patient able to self-report pain utilize the UVa Pain Rating Scale every four hours while on ketamine
  - If patient unable to self-report pain utilize the Critical-Care Pain Observation Tool (CPOT) every four hours while on ketamine

Monitoring of Patient while on Ketamine Infusion

- If patient is not intubated, respirations should be monitored for a full minute during vital signs – the rate, rhythm/pattern, depth and any pauses and presence of snoring or gurgling should be documented
  - Any deviation from normal – report to primary/consulting teams
- Oversedation
  - Richmond Agitation Sedation Scale (RASS) in the ICU setting every four hours and documented
  - Pasero Opioid-induced Sedation Scale (POSS) on acute care areas every four hours and documented

Monitoring of Patient while on Ketamine Infusion

- Place infusion on hold and notify prescriber if:
  - ICU or IMU:
    - For sustained systolic blood pressure change >20mmHg for 5 minutes or more
    - For sustained heart rate change < or >20 beats/minute for 5 minutes or more
  - Acute Care
    - Systolic blood pressure >180 or <90
    - Diastolic blood pressure >100 or <60
    - Rising level of sedation
    - Heart rate >120 or <60

Monitoring of Patient while on Ketamine Infusion

- Other symptoms that require the infusion to be placed on hold and notify prescriber if (reduce dose)
  - POSS assessment of Unacceptable-Frequently drowsy
  - Increasing RASS sedation score beyond goal
  - Depressed respiratory status
  - Respiratory rate < 12 breath/minute or persistent episodes of shallow breathing or apnea
  - Oxygen saturation < 90%
  - Increased secretions not responsive to glycopyrrolate or atropine
  - Unpleasant hallucinations, agitation or dysphoric reactions not relieved by lorazepam

A 76 yo female has recurrent colon cancer with metastatic spread to her liver and thoracolumbar spine

- She had originally been "OK" with 6 oxycodone a day and then methadone 5 mg TID.
- Back and abdominal pain have surpassed these medications but more such Rx makes her sleepy and constipated.
- A Palliative Care consults recommends chemo-Rx and XRT
- What options do 'we' have to offer?

Cancer Pain//End-of life issues

- Some states require End-of-life training for renewal of one's medical license
- There are many causes of persistent pain towards the end of life….AND…….
- Many symptoms that must be successfully managed: **pain**, *dyspnea*, fatigue, loss of mobility, *depression*, anxiety, feelings of uselessness, delirium, sleep disturbance, etc
- (Wang XS. Cleeland CS. Symptoms that cluster around cancer pain: a research agenda. Pain Clinical Updates, Endo Pharm, December 2006)

Ann Intern Med 2008;148(2)

- Qaseem A, Snow V, Shekelle P, et al.
- Evidence-based interventions to improve palliative care of pain, dyspnea, and depression at the end of life: A clinical practice guideline from the American College of Physicians. (Pages 141-146)
- Lorenz KA, Lynn J, Dy SM, et al.
- Evidence for improving palliative care at the end of life: A systematic review. (Pages 147-159)

Cancer pain, co-analgesics

- Think steroids (mood, appetite boost)
- Amphetamines (to overcome opioid sedation)
- Treating N/V, including the use of marinol
- Laxatives (bulk, osmotic, hyperosmolar)
- Prokinetics (to promote GI tract fx)
- Opioid antagonists, tramadol
- WHO ladder approach = graduating potency of meds titrated to the severity of the pain, up to SCS or IT Rx

How does one select "the" best patients for this therapy?

- Distill history & physical exam data
- Assess physical function, psychosocial fx, and quality of life
- Pain Med Questionnaire, SOAPP, ORT
- Risks assoc with: 1) pt or family h/o subst abuse or addiction, 2) psychiatric condition, 3) smoking, 4) young age, and 5) h/o pre-adolescent sexual abuse

Addiction does not = tolerance

- Tolerance = systematic adaptation to an agent in which the effectiveness of the agent decreases over time ***when there is no increase in the pain source***
- Don't develop tolerance to miosis or constipation
- There are different varieties: behavioral, physiologic, pharmacodynamic, long-term
- NMDA receptors, cholecystokinin and dynorphin may be involved

Apparent tolerance may relate to…

- Progression of the primary disease
- Sensitization of the CNS response
- Induction of nociceptive pathways not modulated by opioids, ie., A-beta fibers
- Production of active metabolites that have an anti-analgesic effect, ie., Morphine-3-glucur
- Pharmacokinetic interaction such as enzyme induction, ie., increased p450

Addiction does not = physical dependence

- Physical dependence is revealed when:
  - the agent is abruptly discontinued
  - the dose is rapidly decreased
  - an antagonist is given
- Symptoms = nausea, vomiting, abdominal cramping, insomnia, diarrhea, diaphoresis, hot flashes and autonomic dysfunction

Addiction does not = pseudo-addiction

- The patient *appears to be seeking drug* therapy but the goal is to gain more effective analgesia because the pain is being under-treated
- The anxious behaviors worry MDs but the pt wants pain relief not the drugs for non-analgesic effects
- The behavior goes away with adequate Rx

Neurotoxicity with chronic opioid use

- This can happen with ***any*** opioid but is esp. noticed in pts on high doses of opioids
- Sx = myoclonus, agitation, delirium, and hyperalgesia
- Rx = opioid rotation, reduction in dose?, use of adjuvant drugs like amphetamines, TCAs, AEDs, steroids, dexmedetomidine or other sedatives
- Equivalence tables aren't relevant to high doses so substitute drug dose is started at 30-50-75% of the calculated equivalent and upwardly titrated