

Non-opioid and adjuvant pain management

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Disclosures

▶ I have no financial disclosures*

My Background



- ▶ MD with Distinction in Research
- ▶ Internal Medicine & Psychiatry board certified
- ▶ Hospice & Palliative Medicine board certified
- ▶ Certificate in Medical Education

Objectives

- ▶ Review principles of pain management
- ▶ Review adjuvant analgesics
 - ▶ Inflammatory pain
 - ▶ Neuropathic pain
 - ▶ Bone pain
 - ▶ Bowel Obstruction

Patient Case: Mr. P

- ▶ 60 yo man with history of anxiety, chronic pain
- ▶ New diagnosis of malignancy of unknown primary
- ▶ "Stage II" sacral decubitus ulcer
- ▶ Failed ketamine trial at hospital
- ▶ Methadone 50mg q6h scheduled
- ▶ Valium 10mg TID
- ▶ Started on Fentanyl 50mcg q15 min PCA by weekend physician
- ▶ Hurting "everywhere"
- ▶ Goal is to die at home

General approach to pain management

- ▶ Detailed pain history
- ▶ Physical exam
- ▶ Associated factors

Adjuvant Analgesics

- ▶ Primary indication other than pain
- ▶ Can be used alone or in combination with analgesics
- ▶ Often used with opioids to enhance pain relief, treat pain that is refractory to opioids, or as an "opioid-sparing" agent
- ▶ Commonly used for pain syndromes

Inflammatory Pain Analgesics



Inflammatory Pain Analgesics

- ▶ NSAIDS
 - ▶ Inhibit COX-1 and COX-2
 - ▶ Inhibit prostaglandin synthesis
 - ▶ Administered orally, rectally, topically, intravenously, and intramuscularly
- ▶ Aspirin
 - ▶ Irreversibly inhibits COX-1 and COX-2
- ▶ COX-1 inhibition can affect gastrointestinal tract, kidneys, central nervous system, platelet function

Inflammatory Pain Analgesics

- ▶ NSAIDs are considered first line treatment for non-cancer pain
 - ▶ Inflammatory joint disease
 - ▶ Myalgias
 - ▶ Back pain
 - ▶ Headaches
 - ▶ Surgical pain

Inflammatory Pain Analgesics

- ▶ NSAIDs are helpful in cancer related pain
 - ▶ Bone pain – due to distention of the periosteum by metastases
 - ▶ Soft tissue pain – due to compression or distention of tissues
 - ▶ Visceral pain – due to irritation of the pleura or peritoneum

Adjuvant Analgesics - Corticosteroids

- ▶ Dexamethasone commonly used
- ▶ Works by inhibiting arachidonic acid cascade to reduce inflammation
- ▶ Improves appetite, nausea, malaise, and quality of life
- ▶ Multiple indications
- ▶ Multiple side effects

Adjuvant Analgesics - Paracetamol

- ▶ Also known as acetaminophen
- ▶ Mechanism of action is poorly understood
- ▶ Administered orally, rectally, and intravenously
- ▶ Used alone or with opioids
- ▶ Toxicity can occur with doses greater than 4g/day

Adjuvant Analgesics for Neuropathic Pain



"Of course you feel great. These things are loaded with antidepressants."

Adjuvant Analgesics for Neuropathic Pain

- ▶ Tricyclic antidepressants (amitriptyline, nortriptyline, doxepin, etc.)
- ▶ Used for fibromyalgia, spinal cord injury pain, cancer-related pain, depression, post-herpetic neuralgia
- ▶ Side effects include cardiotoxicity, orthostatic hypotension, somnolence, and anticholinergic effects
- ▶ Use lower dose if combining with a selective serotonin reuptake inhibitor

Adjuvant Analgesics for Neuropathic Pain

- ▶ Noradrenaline and serotonin reuptake inhibitors (venlafaxine, duloxetine, etc.)
 - ▶ Used for atypical facial pain, fibromyalgia, and chronic post-mastectomy pain
 - ▶ Side effects include nausea, headache, hypertension, sedation, insomnia, weight gain, and sexual dysfunction
 - ▶ Use lower dose of venlafaxine in patients with hepatic and renal impairment

Putting it all Together

Class	Drug (brand)	Indication	Dosing Range	Sedation	ACH	Insomnia	Orthostasis	GI	Weight gain
TCA	Amitriptyline (Elavil)	Fibromyalgia, Spinal cord injury pain.	150-300mg	++++	++++	0	+++	+	+
	Nortriptyline (Aventyl, Pamelor)	Cancer-related pain, Post-herpetic neuralgia	75-125mg	++	++	0	++		
	Doxepin (Sinequan, Adoprin)		10-80mg	++++	++	0	++		
SNRI	Duloxetine (Cymbalta)	Atypical facial pain, Fibromyalgia.	20-60mg	0	0	+	0	++	+
	Venlafaxine (Effexor)	Chronic post-mastectomy pain	37.5-225mg	0	+	+	0	++	+

Adjuvant Analgesics for Neuropathic Pain

- ▶ Carbamazepine
 - ▶ Trigeminal neuralgia, post-herpetic neuralgia, and diabetic neuropathy
 - ▶ Use limited by side effects: leukocytosis, thrombocytopenia, dizziness, drowsiness, ataxia, nausea, vomiting, blurred vision, **agranulocytosis**, aplastic anemia, and Stevens-Johnson syndrome
 - ▶ Obtain laboratory tests before and during treatment

Adjuvant Analgesics for Neuropathic Pain

- ▶ Gabapentin and pregabalin
 - ▶ Considered first line agents for treatment of non-malignant neuropathic pain
 - ▶ Side effects: Drowsiness, edema, weight gain, and dizziness
 - ▶ Maximum dose of gabapentin: 3600mg/day
 - ▶ Adjust for renal dysfunction

Adjuvant Analgesics for Neuropathic Pain

- ▶ Lamotrigine
 - ▶ Trigeminal neuralgia, HIV neuropathy, and central post-stroke pain
 - ▶ Most common side effect is an exfoliative rash
 - ▶ Usual effective dose is between 200-500mg/day

Putting it all Together Again

Drug (Brand)	Indication	Dosing Range	Sedation	ACH	Insomnia	Orthostasis	GI	Weight gain
Carbamazepine (Tegretol)	Trigeminal neuralgia, Post-herpetic neuralgia, Diabetic neuropathy	200-400mg	****	****	0	0	***	0
Gabapentin (Neurontin)	Diabetic neuropathy, Post-herpetic neuralgia, Spinal cord injury pain, Fibromyalgia	300-1200mg	***	+	0	0	***	+
Pregabalin (Lyrica)		75-300mg	***	+	0	0	**	+
Lamotrigine (Lamictal)	Trigeminal neuralgia, HIV neuropathy, Central post-stroke pain	200-500mg	***	**	+	0	***	0

Adjuvant Analgesics for Neuropathic Pain

- ▶ Lidocaine
 - ▶ Works by blocking sodium channels
 - ▶ IV route not shown to be effective in clinical trials
 - ▶ Clinical experience may justify IV use for refractory neuropathic pain
 - ▶ Contraindicated for patient with cardiac conduction disorders and seizure disorders
 - ▶ Topical route well tolerated

Adjuvant Analgesics for Neuropathic Pain

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ICUs Using Ketamine More Regularly as Alternative to Opioids

Drug Update column in AACN Advanced Critical Care journal reviews most common uses of ketamine in critical care

Article ID: 699558
 Released: 26-Aug-2018 7:05 PM EDT
 Source: Newsroom: American Association of Critical-Care Nurses (AACN)

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Adjuvant Analgesics for Neuropathic Pain

- ▶ Ketamine
 - ▶ Analgesic doses lower than anesthetic doses
 - ▶ Antagonist at the N-methyl-D-aspartate receptor
 - ▶ Also acts at many other receptors: such μ -opioid, muscarinic, monoaminergic, gammaaminobutyric receptors, etc.
 - ▶ Intravenous, oral, rectal, subcutaneous, and topical routes
 - ▶ Toxicities
 - ▶ Neuropsychiatric: dysphoria, hallucinations, nightmares
 - ▶ Cardiovascular: tachycardia, hypertension

Adjuvant Analgesics for Neuropathic Pain

- ▶ Alpha-2 adrenergic agonists (clonidine, tizanidine)
 - ▶ Chronic headache, non-malignant neuropathic pain, and some neuropathic cancer-related pain
 - ▶ Oral or transdermal route
 - ▶ Mechanism of analgesia is unknown
 - ▶ Side effects include somnolence, hypotension, and dry mouth

Adjuvant Analgesics for Bone Pain



"Let's not call it a 'career-ending' injury. Let's call it a 'character-building' injury."

Adjuvant Analgesics for Bone Pain

- ▶ Calcitonin and bisphosphonates
 - ▶ Bone metastases and vertebral compression fractures
 - ▶ Inhibit osteoclast activity
 - ▶ Subcutaneous or intranasal route
 - ▶ Side effects include renal toxicity, gastrointestinal toxicity, and osteonecrosis of the jaw
 - ▶ Use with caution in patients with renal and hepatic impairment

Adjuvant Analgesics for Bone Pain

- ▶ Radiopharmaceuticals
 - ▶ Absorbed at areas of high bone turnover
 - ▶ Strontium-89, Samarium-153
 - ▶ Given as monotherapy or with radiation therapy
 - ▶ Main side effect – myelosuppression
- ▶ Radiation therapy alone

Adjuvant Analgesics for Bowel Obstruction

- ▶ Octreotide
 - ▶ Inhibits the secretion of gastric, pancreatic and intestinal secretions
 - ▶ Reduces gastrointestinal motility
- ▶ Corticosteroids

Back to Mr. P

- ▶ Final regimen:
 - ▶ Methadone 60mg oral concentrate po q6h scheduled
 - ▶ Fentanyl 500mcg/hr continuous infusion
 - ▶ Fentanyl 500mcg q10min PCA
 - ▶ Toradol 30mg IV q6h scheduled
 - ▶ Dexamethasone 10mg IV daily
 - ▶ Ativan 2mg IV q8h scheduled
- ▶ Trapeze bar for bed
- ▶ Taught wife how to administer IV medications and wound care
- ▶ Patient returned home

Summary

- ▶ Start with history and physical exam to select appropriate adjuvant therapy
- ▶ Start low, go slow
- ▶ Monitor for side effects
- ▶ Can be used alone or with opioid therapy for patients with complex pain syndromes

Questions?
