The “Not-so serious” Burdens of Serious Illness

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Objectives

- Recognize a few selected non-pain symptoms that may appear benign but are either distressing to patients with serious illness or a harbinger of underlying illness

- Appreciate impact these symptoms have on quality of life

- Understand management strategies for these non-pain symptoms
Older Adults with Serious Illness

- Serious Illness: COPD, heart failure, strokes, renal insufficiency and failure, advance dementia, debility, peripheral vascular disease, cancer...

- Symptom Burdens: Pain vs. Non Pain Symptoms

- In the spotlight: Pain, Depression, Shortness of Breath
So many to choose from...

Akathesia Anhedonia Anorexia Anxiety Colic Confusion Constipation Cough Crying Death rattle/secretions Diarrhea Dizziness Drooling Dry skin Dysarthria Dysgeusia Dyspepsia Dysphagia Dysphoria Dyspnea Dysuria Failure to thrive Fatigue Fear Fecal incontinence Fever Flatulence Halitosis Hallucinations Hearing loss Hiccups Impotence Intestinal obstruction Irritability Memory loss Mucositis Muscle spasms Nausea Odor Panic attacks Peripheral edema Photosensitivity Polydipsia Polyuria Pruritus Restlessness Sexual dysfunction Sleep disorders Stomatitis Taste alterations Urinary frequency Urinary incontinence Visual problems Vomiting Xerostomia

Index, Oxford Textbook of Palliative Medicine, 1998
Today’s picks

- Hiccups
- Pruritus
- Fatigue
- Symptoms associated with Bowel Obstruction
Management Guidelines

• Perform history and physical exam
• Conceptualize likely causes
• Determine whether underlying cause is reversible (ie: curable)
• Discuss aim of treatment
  – to eliminate underlying cause, or to alleviate symptom only, or both
• Discuss treatment options and benefits and burdens
• Set *realistic* goals that can be achieved within an acceptable time frame
• Reassess FREQUENTLY
  – Monitor effectiveness and side effects
Case

- Mrs. Emma Jones is a 75 year old woman who comes in for a check up after not being seen for over a year and complains of hiccups for weeks that just won’t go away. She has tried gargling water, biting a lemon, holding her breath, and even had the neighbor’s kids try to startle her. Nothing seemed to work for long and she expresses desperation to get the hiccups to stop.
- She blames the hiccups for making her lose her appetite because they interfere with eating.
- Her exam was only remarkable for a moderately distended abdomen.
Hiccups

*(Singultus)*

- Very distressing to patients and family and can even be debilitating (wt loss, fatigue, insomnia...)
- Complex reflex pattern involving sudden contraction of the diaphragm with simultaneous closing of the glottis and producing the characteristic sound.
- Mediated by CNS via phrenic and vagus nerves
- Persistent > 48hrs, Intractable > 1 month
Hiccups

- Etiology
  - Psychological-Stress, excitement
  - Irritation of diaphragm (phrenic nerve)
    - gastric distension, liver disease, cancer, MI
  - Irritation of branches of Vagus Nerve
  - CNS lesions
  - Meds: IV steroids
  - Uremia
  - Idiopathic
    - more common in YOUNGER people
Hiccups

- First consideration is to work it up
- Pursue treatment while determining reversibility of cause
Hiccups

• Non-pharmacologic treatments
  – Interruption of the respiratory cycle
    • Coughing, breath-holding, hyperventilation, sneezing
  – Vagal Stimulation
    • Valsalva maneuver, carotid massage, NGT placement and removal
  – Time-honored home remedies
    • Gargling with water, biting a lemon, sipping sugar, startle response
  – Other interventions
    • Acupuncture, hypnosis, surgical ablation of the reflex arc then diaphragmatic pacing electrodes,
Hiccups

- Pharmacologic Treatments
  - Chlorpromazine (Thorazine)
    - The only FDA-approved agent for hiccups (intractable)
    - 25-50mg po TID or QID
    - Can also be given as a continuous IV infusion over several hours for intractable and debilitating hiccups
    - SEDATING, watch for EPS
    - Avoid if possible in the elderly

- Or...
Hiccups

- **Pharmacologic Treatments:**
  - Baclofen
    - The only drug studied in a RCT
    - 5mg po q8h did not eliminate hiccups, but provided symptomatic relief in some patients
    - Can dose escalate to achieve response
    - Watch for sedation and avoid in renal failure
  
  - Or...
Pharmacologic Treatments:
- Haldol 2-5mg IM / po loading dose followed by 1-4mg po q8h
- Phenytoin 200mg slow IV push followed by 300mg po daily. Effective in hiccups of CNS etiology
- Metoclopramide 10mg po q6h. Useful if etiology is stomach distension

** case studies only
- Duration of pharmacologic treatments: few days – weeks, stop treatment after symptoms stop
Case

- Mrs. Jones was prescribed baclofen 5mg po TID and potential side effects were explained, but she gave it a try because she could not endure the hiccups any longer.
- She was instructed to get some imaging done in the upcoming weeks.
- Two weeks later she returned for an urgent visit. She reported that she no longer had constant hiccups, but now complained of severe itching.
- Exam found her anxious and squirming in her seat with signs of skin excoriations and even blood all across her arms, thighs, chest and anywhere else within her fingernails’ reach.
Pruritus

- Very distressing and diminishes quality of life

- Triggered by either direct stimulation of skin itch receptors or centrally by drugs.

- Both histamine sensitive and non-histamine sensitive nerve fibers are involved
Pruritus – common causes

• Dermatologic
  – Dryness or wetness
  – Irritation
  – Eczema, psoriasis

• Metabolic
  – Liver or renal failure
  – Hypothyroidism

• Drugs
  – Opioids
  – Aspirin
  – Drug reactions

• Psychogenic

• Heme/Onc
  – Iron deficiency
  – Polycythemia
  – Thrombocytosis
  – Leukemia, lymphoma

• Infection
  – Scabies
  – Lice
  – Candida

• Allergy
  – Urticaria
  – Contact dermatitis
Pruritus

• Treatments: Topical
  – moisturizers and emollients effective for xerosis (dry skin). Urea containing products also helpful.
    • Most OTC preparations are mostly water based
  – Oatmeal Baths
  – Cooling Agents
    • Calamine or menthol in aqueous cream (0.5%-2.0%)
  – Anesthetic agents
    • EMLA creams (mixture of lidocaine and prilocaine)
  – Topical Steroids (hydrocortisone → clobetasol)
    • Very helpful for time limited use if eczema or other dermatitis identified
    • Ointment better, less chance of allergic reaction
    • Educate caregivers on safe handling
Pruritus

- **Treatments: Antihistamines**
  - Helpful if itch assoc. w/ histamine release
  - Can combine H1 and H2 receptor blockers
    - e.g. diphenhydramine or hydroxyzine and ranitidine
      - May have central and peripheral antihistaminic effects
  - Doxepin – tricyclic antidepressant
    - Potent antihistamine
    - For refractory cases use 10-30 mg po qhs
    - Topical doxepin in study
    - Agent of last resort
Pruritus

- Opioid Induced
  - non-immune mediated histamine release from mast cells vs direct opioid receptor activation
  - Antihistamines may be helpful
  - Mu opioid receptor antagonist (diluted naloxone) still in trial phases, Paroxetine and mirtazapine is anecdotal
  - Consider opioid rotation
Pruritus

- **Uremic Pruritus**
  - 60% of dialysis patients complain of uncontrollable itching
  - Sweat gland atrophy, anemia, calcium phosphate deposition
  - Histamine somewhat responsible, irritation of mu opioid receptors somehow involved
- **Treatments:**
  - Renal Transplant - definitive treatment
  - Improving anemia
  - Topical emolient+ capsaicin, UVB light therapy, gabapentin, mu opioid antagonists (naltrexone--> still in study)
Pruritus

- Cholestatic pruritus
  - Theories: Bile acid deposition vs opioid receptor irritation
  - Possible Treatments:
    - Cholestyramine
    - Rifampin 150mg bid
    - Opioid antagonists (naloxone)
    - Colchicine
    - Ursodiol (Ursodeoxycholic acid)
    - UVB light therapy
    - SSRI (Sertraline, paroxetine) and NSRI
Case

- After lotions and topical steroid creams failed to give her any relief from the itching, Mrs. Jones was prescribed hydroxyzine 25mg qhs and q8hrs prn with clear warnings about sedation, constipation, and instructions to discontinue use if she felt overly sedated.
Case

- She also complained of progressive fatigue. She was no longer as energetic as she once was and felt that she had to discontinue some of her daily activities since she was too tired.
Fatigue

- Very common and associated with most acute and chronic illnesses (as well as regular life)
- A state of sustained exhaustion, not relieved by rest
- Lack of physical and mental energy, inability to concentrate, poor memory
- Important to differentiate between sleep deprivation and fatigue associated with another illness
- Fatigability as sign of aging vs. sign of underlying illness and side effect of treatments
Fatigue

• Multiple causes – direct chemo effects, cumulative effect of radiation, systemic inflammatory response, hypermetabolic state of tumors, anemia, nutrition, hypothalamic-pituitary-adrenal effects, pain, stress...

• Cancer Related Fatigue
  • Prevalence data 15-90% of cancer patients report fatigue (75% of patients with advance or metastatic cancer report it)
  • Only 50% actually discuss it with health care providers
Fatigue

- Treatment- Is the cause reversible? Symptomatic relief?
  
- Non-pharmacologic approach
  - Exercise- to reduce muscle atrophy
  - Patient education, normal sleep requirements
  - Diet and nutrition
  - Treatment of anemia

- Psychosocial support
Fatigue

- Pharmacologic – all off label
- no FDA approved meds, no double-blinded trials
  - Stimulants (methylphenidate 5mg daily - bid)
  - Wake promoting agents (modafinil 100mg daily)
- Steroids
- Antidepressants – only if depression present as well
- Attempt a time limited TRIAL
Case

• Mrs. Jones’s imaging revealed stage IV metastatic ovarian cancer with liver metastasis and presumed malignant ascites.

• The news was devastating to Mrs. Jones and she wanted to explore treatment options in the hopes to achieve remission.
Case

- Over the next few months, Mrs. Jones underwent several debulking surgeries and was found to have carcinomatosis. She underwent neoadjuvant chemotherapy with cisplatin and her course was further complicated by development of a DVT for which she received anticoagulation.

- She had suffered with intermittent nausea and vomiting shortly after her chemotherapy, but was readmitted for nausea and vomiting associated with severe colicky abdominal pain.
Case

- Repeat CT of the abdomen/pelvis revealed a high grade bowel obstruction.
Bowel Obstruction

- Common in ovarian and colon cancer
- Also complication of bowel strictures from adhesions, volvulus, or fecal impaction
- Symptoms
  - Abdominal pain (colicky and/or continuous)
  - Nausea and vomiting
- Goals of treatment
  - Relief of symptoms (pain, nausea/vomiting)
  - Allow oral intake as tolerated
  - Permit pt to return to chosen care setting
  - Support of patient and family
Bowel Obstruction

- Why Bowel Obstructions hurt:
  - Abdominal distention from gas as well as pooling of intestinal secretions
  - Intestinal edema leading to poor absorption and thus more abdominal distension
  - Direct tumor invasion and inflammation
Bowel Obstruction

- Pain management should always be maintained
  - Opioid is mainstay
  - Can use sublingual (morphine), subcutaneous, or intravenous
  - Titrate to comfort
    - Avoid transdermal route given slow onset of action and difficult to titrate in setting of acute symptoms
  - Can use continuous infusion via pump or PCA
Bowel Obstruction

- Surgical management
  - Ideal in pts with good performance status
  - Poor prognostic indicators:
    - Ascites, carcinomatosis, palpable intra-abdominal masses, multiple bowel obstructions, prior obstructions

- Endoscopic approaches
  - Stenting
    - May include laser or balloon dilatation prior to stent
    - 64-100% relief of symptoms in colorectal obstructions
    - >70% relief of symptoms in upper GI obstructions (esophageal, gastric outlet, duodenal, jejunal)
  - PEG tube placement
    - “Venting” procedure to alleviate intractable N/V for upper GI obstructions
    - Offers possibility of intermittent oral intake for pleasure
    - Contraindication - ascites
Bowel Obstruction

**Medical Management**
- May require NG tube initially
  - When output < 100 cc/day, clamp NG tube for 12 hours and then remove if no complaints of worsening nausea or vomiting

**IV hydration**
- Restrict to 50 cc/hr during med titration phase
- D/C once symptoms controlled
- Continue only if:
  - Pt remains dehydrated despite oral intake **AND**
  - Use of hydration to extend life is consistent with goals of care
Bowel Obstruction

- Take advantage of other routes of administration when oral route no longer available
  - Alternatives:
    - Subcutaneous
    - Sublingual
    - Topical
    - Intravenous
    - Rectal
Bowel Obstruction

- Reduce Secretions:
  - Antimuscarinic/Anticholinergic drugs:
    - Reduce colicky pain due to smooth muscle spasm and bowel wall distension
    - Reduce saliva and secretions (up to 2 liters/day)
    - Scopolamine
      - 10 mg/hr sc/iv continuous infusion
      - 1 patch (1.5 mg) transdermal q72h
    - Glycopyrrolate
      - 0.2-0.4 mg sc/iv q2-4h
Bowel Obstruction

• Somatostatin analogs
  • Inhibit secretion of gastric & pancreatic enzymes
  • Decrease peristalsis and splanchnic blood flow
  • Octreotide (Sandostatin)
    • 50-100 mcg sc/iv q8h
    • 10-20 mcg/hr sc/iv continuous infusion
    • Titrate every 24 hrs until N/V and abd pain are controlled
• Fewer side effects than anticholinergic agents
Bowel Obstruction

- Corticosteroids
  - Consider in most patients
  - Reduction of edema around site of obstruction
  - May relieve nausea
  - Dexamethasone
    - Dosages studied vary greatly: 2mg - 80 mg IV daily to q8hrs
    - If ineffective, can discontinue
Pathophysiology of Nausea and Vomiting

Chemoreceptor Trigger Zone (CTZ)

Vomiting center

Cortex

Vestibular apparatus

GI tract

Neurotransmitters
- Serotonin
- Dopamine
- Acetylcholine
- Histamine
- Substance P
Anti-emetics

- Dopaminergic Antagonist
- Antihistamines
- Anticholinergics
- Serotonin antagonist
- Prokinetic agents
- Antacids
- Cytoprotective agents
- others
Dopaminergic Antagonist

- Dopamine mediated nausea: most common

- Prochlorperazine (Compazine)
  - 10-25mg PO q6h or 25mg PR q12h or 5-10mg IV q6h

- Metoclopramide (Reglan)
  - In addition is a prokinetic agent and at higher doses is serotonin antagonist
  - 10-20mg PO q6h (decrease dose in renal failure: max 5mg Q6h)

- Haloperidol
  - Acts on CTZ
  - 0.5-2mg PO IV/SQ q6h

- Promethazine (Phenergan) – also antihistamine
  - 12.5-25 mg IV or 25mg PO/PR q4-6h

- Trimethobenzamine (Tigan) – no longer used
  - 250mg PO q6-8h, 200mg PR q6-8h
Histamine Antagonist

- All those used for nausea can cause sedation
- Acts on the H1 receptors in the vomiting center and vestibular afferens
- Also have anticholinergic effects
- Diphenhydramine (Benadryl)
  - 25-50mg PO q6h
- Meclizine (Antivert)
  - 25-50mg PO q6h
- Hydroxyzine (Atarax, Vistaril)
  - 25-50mg PO q6h
Acetylcholine Antagonists (Anticholinergics)

- Opioid and anesthetics can trigger acetylcholine meditated nausea in the vestibular apparatus
- Helpful also if there is partial or complete bowel obstruction by decreasing peristalsis and secretions
- Scopolamine
  - 0.1-0.4mg SC/IV q4h
  - Transdermal patches q72h
  - 10-80 mcg/h by continuous IV/SC infusion
- Glycopyrrolate
  - 0.2mg SC/IV q4-6h
Serotonin antagonists

- Very effective for chemotherapy induced nausea
- Acts on CTZ, vagal nerves and enterochromaffin cells in the gut wall
- Can be used for refractory nausea of different types
  *New concern -- arrythmias
- Ondansetron (Zofran)
  - 8mg PO TID
- Granisetron (Kytril)
  - 1mg PO QD or BID
- Dolansetron
  - 100mg PO/IV q24h (1.8mg/kg)
Others

- Prokinetics:
  - Metoclopramide or erythromycin in cases of peristasis issues
- Antacids, H2 blockers, PPI can be used if there is associated hyperacidity
- Cytoprotective agents:
  - misoprostol/PPI for nausea caused by NSAID associated mucosal erosions
Others: unknown mechanisms

• Dexamethasone: intrinsic anti-emetic properties

• Tetrahydrocannabinol: ?
  • 2.5-5 mg PO TID

• Lorazepam: helpful in anticipatory nausea
Strategy for Management of Nausea and Vomiting

- Identify etiology
- Targeted therapy if possible to address the underlying cause
- Treat symptoms with antiemetic targeting certain neurotransmitter
- **Combination therapy** if needed
- REASSESS frequently
Bowel Obstruction

- **Antiemetics**
  - **Metoclopramide**
    - Prokinetic – contraindicated in total obstruction
    - May be helpful in partial obstruction
    - Time trial – stop if colic worsens
  - If not metoclopramide, try prochlorperazine +/- odansetron
  - **Haloperidol**
    - Dopamine antagonist
    - 0.5-1 mg iv/sc q6h
    - Less sedating
  - **Lorazepam**
    - 1-2 mg iv/sc q6h
    - Helpful if pt is anxious and sedation is welcome
Bowel Obstruction

- Satisfactory relief of symptoms is achieved in most patients
- Patients may still vomit several times/day, but usually preferable to NG tube
- No need to make pt NPO
- Pt will usually moderate their own oral intake to achieve balance between symptoms and pleasure
Take Home Points...

- If you can't eliminate the underlying problem, treat the symptoms.
- Very few treatments have been studied in robust clinical trials, so may have to try several different techniques and treatments.
- Reassess frequently and adjust as you go along.
References

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• Pruritus
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- Fatigue
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• Bowel obstruction