Symptom Management-
It takes a TEAM!

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Objective:

- Discuss a collaborative approach to providing supportive management of common side effects/symptoms with cancer treatments in the primary care setting.
The New World of Oncology:

Paradigm Shift:

“An important change that happens when the usual way of thinking about or doing something is replaced by a new and different way.”

Our patients with cancer now experience a very different journey.

What’s changing?
The Changing Picture of Cancer Treatments:

- Three big changes that are now adding to the challenge of symptom management and increase the need for a collaborative and multidisciplinary approach:
  1. Cancer is becoming a chronic disease with increasing complexity with multiple comorbidities.
  2. The Shift to new novel and different treatment modalities- targeted therapies and immunotherapy.
  3. Increasing availability of oral agents.
Paradigm Shift:
#1 Chronic Disease and Comorbidities

- Lung, Prostate, Breast, and Colorectal cancers account for more than 46% of cancer deaths in the U.S.
  - Significant decline in these top 4 deadliest cancers due to improved screening, treatment, and preventive interventions.


- Patients are living longer and treatment modalities now extended with maintenance regimens and palliative treatment options.
Chronic Disease and Comorbidities

- More than 60% of patients with cancer are diagnosed at age 65 or older and many have preexisting conditions that complicate clinical decisions.

- The presence of comorbidity in adult patients >65 yrs. Old could double or triple their probability of death. (NCI, 2016).

- National Cancer Institute (NCI) reported in 2016 that the top 4 cancers also have higher rates of comorbidity.
  - Lung: 52.9%
  - Colorectal: 40.7%
  - Breast: 32.2%
  - Prostate: 30.5%
Chronic Disease and Comorbidities

- Patients often have several other specialists in addition to the PCP’s managing their care: Cardiologist, Pulmonologist, Endocrinologist, Urologist, GYN, etc.

- Common Comorbidities:
  - Arthritis
  - COPD
  - Osteoporosis
  - Cardiac Ds.
  - Fibromyalgia
  - Osteopenia
  - Depression
  - Hypothyroidism
  - Osteopenia
  - Diabetes
  - Hypertension
  - Pulmonary Ds.
  - Dyslipidemia
  - Obesity

- Communication among all the providers and across disciplinary lines is vital and takes time and coordination.
Additional Support/Resources for a Collaborative Approach

- Supportive Care Clinic
- Cardio-Oncology program
- Oral Chemotherapy Clinical Team
- Lymphedema Clinic
- Palliative Care Support
- Alternative Therapies
  - Massage Therapy
  - Accupuncture
  - Aroma Therapy
  - Reflexology
  - Exercise Programs
Paradigm Shift
#2 Shifting Treatment Modalities

- With the development of more targeted therapies and immunotherapies, providers need to better understand the *mechanism of symptom development*.

- Differences in Symptom Management based on treatment approach:
  - Chemotherapy: Cytotoxic damage
    - Side effects/toxicities = “penias”; damage
  - Immunotherapy: Auto-immune reaction
    - Immune related adverse events (irAE) = “ititis”; inflammation
Paradigm Shift
#2 Shifting Treatment Modalities

- The Critical aspect for managing irAE’s is immediate and early identification and recognition.
  - Treatment involves minimizing and suppressing the immune reaction- steroids and withdrawal.
- irAE’s often can be reversed and controlled but create issues with comorbid conditions.
  - Diabetes, Hypertension, Renal disease, Cardiac disease.
- Changes in routine health maintenance and screenings.
  - Mammograms, Dexa Scan, Diabetes Health, Thyroid screening
Paradigm Shift:
#3 New Oral Agents

- Estimates put 25% of anticancer agents in the research pipeline are oral oncolytics.
- The FDA has been approving 1 new oral oncolytic every 2-4 months. Over 80 oral drugs are available currently.
- Convenient for patients to take orals at home, but this often means less direct contact time with the physician.
  - Relying on patient to report adverse reactions can delay appropriate intervention.
  - Safety- handling and administering medication at home.
  - Increases polypharmacy for the patient- increased risk of drug-drug interactions. Inhibitors and/or inducers.
    - Capecitabine (Xeloda)- should not be given with warfarin
    - Protein Pump Inhibitors- can decrease absorption and efficacy of oral agents
Symptom Management: It Takes a TEAM!

- Collaborative
- Multidisciplinary
- Continuity
- Informed

RESOURCES:
- NCCN guidelines
- ONS -PEP (Putting Evidence into Practice) Guidelines
- Pharmaceutical Companies-Supportive management
Anxiety and Depression:

- Distress Screening Tool- Scores for risk of Depression and Distress; identifies Key patient concerns.

- Community Cancer Network- counseling for patient’s and families; support groups.

- Alternative therapies- good option before adding another medication with increased risk of side effects or interactions.
  - Massage Therapy, Journaling, Meditation, Music Therapy, Yoga, Guided Imagery, Aromatherapy, Art Therapy
Anxiety and Depression:

- Medications: Keep on current medication if effective and not contraindicated.

- Recommended options:
  - SSIR’s: Fluoxetine, Sertraline, Paroxetine, Citalopram, Escitalopram
  - SNRI’s: Venlafaxine, Duloxetine
  - Tricyclic Antidepressants: Amitriptyline, Nortriptyline, Doxepin
  - Others: Mirtazapine, Bupropion, Trazodone

- Selection can depend on other side effects.
Anxiety and Depression:

- Methylphenidate - has been used for its mood elevating properties, to negate the effect of opioid-induced somnolence, and to improve cognitive functioning.
  - In review of 9 studies, Methylphenidate was found to be useful in treating depression, with 80% of the patients having a favorable response.

- Venlafaxine - effective treating hot flashes

- Duloxetine - better response in chemo induced peripheral neuropathy

- CAUTION: Tamoxifen - Avoid giving with Fluoxetine, Paroxetine, and Sertraline.
  - Better Options: Venlafaxine, Citalopram, Escitalopram
Anorexia/Loss of Appetite:

- Cancer Center- Nutritionist monitors and counsels patients struggling with these issues.

- Assess and treat other contributing factors: infections, thrush, nausea, depression.

- Encourage small frequent meals, emphasis on balance nutrition and adequate protein for healing.

- Oral hygiene/care is very important. Mouth rinses (salt water or baking soda and water) 3-4 times a day helps with dryness, altered taste, and mucositis.
Anorexia/Loss of Appetite:

- **Appetite Simulants:**
  - Mirtazapine- start low dose 7.5 mg at bedtime
  - Corticosteroids-low dose
  - Dronabinol
  - Megestrol acetate- available only in liquid form
    - Caution- coagulability risk
Anorexia/Loss of Appetite:

- Prokinetic agent for GI Motility can help with early satiety.
  - Metoclopramide
- Omega-3 Fatty Acids-triggers production of orexigenic neurotransmitters in food-intake regulatory nuclei in the hypothalamus.
Nausea/Vomiting:

- **Types:**
  - Acute, Delayed, Anticipatory, Breakthrough, Refactory

- Good history and assessment key to treatment approach.

- **NCCN guidelines** - goal is prevention.
  - Developed Emetogenicity Rankings for chemotherapy and provide recommendations for appropriate treatment.
  - Multiple drug regimens and combination regimens with Radiation treatment also increases risk of N/V.
Nausea/Vomiting:

- 1990’s the 5-HT3 receptor antagonists became a major advancement in controlling CINV (chemo induced N/V); used primarily as IV premeds.
  - Ondansetron (Zofran, Zofran ODT, Zuplenz)
  - Granisetron (Granisol, Sancuso, Sustol, Kytril)
  - Dolasetron (Anzmet)
  - Palonosetron (Aloxi)
  - Newer- NK-1 receptor Antagonist- Aprepitant (Emend)

- Often used in combination with Dexamethasone.
Nausea/Vomiting:

- For post treatment and Breakthrough or Delayed Nausea:
  - Often use 2 drug combos- can alternate for optimal prevention and control.
  - Ondansetron, Prochlorperazine Promethazine, Lorazepam, low dose dexamethasone.
  - Akynzeo: Oral capsule combination of 5-HT3 (Palonosetron) and NK-1 (Netupitant)
  - Granisetron -transdermal patch; apply and wear for 7 days.
  - Other alternatives: Metoclopramide, Olanzapine, Dronabinol
Constipation:

- Chemotherapy with increased incidence:
  - Vincristine  Vinblastine  Vinorelbine
  - Paclitaxel  Docetaxel  Oxaliplatin

- Also opioid analgesics, Antiemetics, Antidepressants, Calcium, Antacids.

- Good understanding of bowel pattern history.

- Prevention and early intervention.

- Stool softeners and stimulants- Colace, Senna

- Stronger laxative for acute episodes- Milk of Magnesia, Lactulose, Mag Citrate

- AVOID- enemas and suppositories in myelosuppressed patients
Constipation:

- **GI motility Stimulants:**
  - Polyethylene Glycol -
    - Educate patient stay hydrated; monitor electrolytes
    - Should NOT be administered to patients with compromised kidney function.
  - Metoclopramide

- **Opioid induced constipation:**
  - Methylnaltrexone (Relistor)-12 mg Sub Q; give QOD
  - Naloxegol (Movantik) 25 mg in am on EMPTY stomach; can reduce to 12.5 mg if not tolerated.
Diarrhea:

- Assess for other contributing factors: infection, medications, dietary irritants, other bowel disorders. Approach may differ dependent on treatment modality.

- Chemotherapy- diarrhea can be dose limiting toxicity; (5-FU, irinotecan).
  - Start with Loperamide, can add Lomotil and alternate.
  - Another option sometimes built into a treatment regimen is to use Sandostatin (Octreotide)
  - Tincture of Opium- liquid drops
  - Budesonide- Corticoid steroids- 6 mg capsule

- In Radiation therapy- Acute radiation enteritis can be seen in up to 70% of patients, depending on treatment and patient predisposing factors.
  - Psyllium Fiber- helps to absorb fluid and increase weight of stool
Diarrhea:

- Radiation therapy continued:
  - Probiotics- several studies in patients getting pelvic radiation showed some benefit.
  - Probiotics: Decrease gut pH, Improve immune function, Prevent colonization of pathogenic microorganisms, and Signal cells to stop production of virulence factors.

- In Immunotherapy-
  - The development of diarrhea with immunotherapy is different from that with chemotherapy or radiotherapy, and in severe cases patients can develop colitis and bowel perforation with potential need for colectomy.
  - Fatal cases of immune-mediated enterocolitis have occurred. The prevalence of colitis has been reported to be as high as 35% in patients treated with ipilimumab.
  - Hold treatment and treat with systemic corticosteroids or other immunosuppression agents.
  - Early detection and treatment most important.
Chemo Induced Peripheral Neuropathy (CIPN):

- Among patients treated with anticancer therapies known to increase the risk of peripheral neuropathy, 10%-100% will develop the condition.
  - Epothilones, Platinum analogs, Taxanes, and Vinca Alkaloids
- According to the research, peripheral neuropathy can cause pain and other sensory symptoms as well as patient safety concerns because of changes in dexterity, gait and balance problems, weakness, proprioception, and loss of some motor skills.
- Symptoms: numbness, tingling, increased cold sensation, decreased cutaneous sensation, stiffness, weakness.
Chemo Induced Peripheral Neuropathy (CIPN):

- **Meta Analysis:** No agents were recommended for the prevention of CIPN, but duloxetine is moderately recommended for the treatment of CIPN.

- Even though conclusive evidence is lacking to recommend tricyclic antidepressants (nortriptyline) or gabapentin, and a topical gel containing baclofen, amitriptyline, and ketamine for treatment of CIPN, the expert panel agreed that offering these agents based on treatment for neuropathic pain is reasonable.

- Best results noted with combination therapies that contained opioids as well.
Chemo Induced Peripheral Neuropathy (CIPN):

- Duloxetine 30 mg increased to 60 mg daily.
- Gabapentin 900 mg/day in divided doses increased to 1800 mg/day divided BID or TID.
- Pregabapentin (Lyrica)- 150 mg/day increased to 600 mg/day in divided doses
- Massage Therapy
- Topical compounds with lidocaine, steroid, gabapentin, baclofen, and/or menthol.
- Accupuncture
Fatigue:

- One of the most common side effects: 80% to 100% report experiencing fatigue during treatment and if often persists beyond the conclusion of treatment.

- Fatigue may be an isolated problem or occur as one element in a cluster of symptoms, such as pain, depression, dyspnea, anorexia, and sleep disturbance.

- Has adverse effects on functional status, mood, personal relationships, and well being.
Fatigue:

- Lots of research has been done on assessment of fatigue and interventions.
  - Exercise
  - Energy conservation and activity management
  - Measures to optimize sleep quality
  - Relaxation
  - Massage and healing touch therapy
  - Distraction- virtual reality immersion
  - Nutritional supplementation with Omega-3 fatty acids
Mucositis/Stomatitis:

- Estimated to occur in about 40% of patients secondary to chemotherapy and almost 100% of those receiving radiation for head and neck cancer.

- Approximately 80% of those undergoing hematopoietic stem cell transplantation will experience some level of oral mucositis.

- Oral mucositis is a dose-limiting side effect of cancer treatment, with more than one-third of patients discontinuing treatment because of the condition.

- Oral mucositis can be costly as well, necessitating hospitalization in 62% and tube feedings in 70% of patients with this symptom.

- Good oral hygiene and oral care protocol are key to prevention and faster recovery!
Mucositis/Stomatitis:

- Multiple options- Interventions focus on decreasing inflammation and pain; and increasing moisture/hydration.
  - Baking Soda and water; Salt water rinses
  - Honey
  - Diphenhydramine elixir mixed with Aluminum hydroxide and magnesium hydroxide 1:1 ratio
  - Variety of swish and spit mouth rinses using combinations of antifungal, antihistamines, and analgesics
  - Topical Triamcinolone
  - Viscous Lidocaine
  - Bensocaine Gel
  - Episil- mucosal protectant
  - SalivaMax-Calcium Phosphate Rinse
  - Betamethasone Solution/Dexamethasone
Long Term Complications to Consider:

- Survivorship programs have increased our awareness of the need to follow up on potential chronic and long term affects of cancer treatments.
  - Residual physical symptoms
  - Effects on Comorbidities
  - Osteopenia/Osteoporosis
  - Cognitive impairment (“Chemo Brain”)
  - Altered Sexuality/Relationships
References:

1. National Comprehensive Cancer Network-
   - Guidelines for Supportive Care Web site; https://NCCN.org


3. National Cancer Institute - 2016 Cancer Statistics

4. Oncology Nursing Society - Practice Resources-
   - Putting Evidence Into Practice (PEP); https://www.ons.org
Symptom Management Takes a TEAM!!!

Questions??????