



RECOGNITION AND MANAGEMENT OF TOXICITIES OF ORAL THERAPEUTICS IN HEMATOLOGIC MALIGNANCIES

Michelle Wright Mast, FNP-BC
Hematology Oncology of Indiana, PC



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Objectives

- Increase knowledge about oral medications used to treat hematologic malignancies
- Understand important aspects of nursing assessment and management of drug-related side effects and toxicities
- Increase knowledge about management of hematologic effects, cardiovascular effects, gastrointestinal effects, dermatologic and neurologic effects, as well as fatigue

Oral Chemotherapy Prevalence

According to Lisa Lohr, PharmD, and clinical oncology pharmacy specialist at the University of Minnesota, the use of oral chemotherapy drugs is becoming increasingly prevalent today. These therapies are being used for many different types and stages of cancer.

As recently as 2017, one in four drugs used for cancer treatment was available in oral form. As of July 5, 2018, 30% of cancer drugs being developed today are oral drugs. It is predicted that this trend will only continue to increase exponentially in the years ahead.

HOW does this change impact nursing practice?

- According to the journal of Hematology Oncology Pharmacy, Treatment-related toxicities due to oral anticancer drugs have been reported in up to 80% of patients, and 36% of those were severe.

Nurses can make positive impacts on patient outcomes

- Oncology Nurses have unique roles and training that allows them to often be the first care provider to interact with a patient in the clinic.
- They may recognize an adverse drug side effect or toxicity before the patient does.

Educating patients is vital

According to the 2016 American Society of Clinical Oncology/ONS Chemotherapy Administration Safety Standards, chemotherapy education should include these essential elements:

1. Treatment duration
2. Schedule of medications
3. Names of drugs and supportive medications
4. Drug-drug and drug-food interactions
5. Plan for missed doses
6. Side effects/when to report/how to manage
7. Safe storage/handling of drug & body secretions

Nursing roles in assessment for drug - related toxicities

- Provide education to patient
- Assure patients understands dosing/schedule of medications, rationale for tests to monitor treatment
- Provide resources and support group info
- Keep journal of side effects, and educate that most occur at home
- Encourage patient to call office with new symptoms
- Update medication list at each visit

Take detailed and thorough history

*** ASK ABOUT SIDE EFFECTS AT EACH VISIT**

- Describe symptoms: onset, timing, intensity, location, frequency, duration, radiation (pain), alleviating/aggravating factors
- Compare to past symptoms – worse, better, same
- Also ask caregiver's input – especially helpful if patient has memory issues

ORAL DRUGS USED FOR HEMATOLOGIC MALIGNANCY

Pomalidomide - for use in Multiple Myeloma, may be given together with Dexamethasone, typically given 21 of 28 days

Lenalidomide - for use in Multiple Myeloma, typically given 25 mg PO once daily on 21 of 28 day cycle, reduced dose for Cr Cl < 60 ml/min.

Bosutinib - for use in Ph+ CML, 400 to 500 mg daily

- **Acalabrutinib** - used for Mantle Cell Lymphoma if one prior therapy, 100 mg po BID +/- food, avoid PPIs
- **Enasidenib** - Relapsed or refractory AML, 100 mg PO daily +/- food
- **Midostaurin** - used for AML, Mastocytosis with hematologic neoplasm or mast cell leukemia for induction and consolidation
- **Venetoclax** - used for CML 20 mg daily increased to 400 mg daily, take with food
- **Ibrutinib** - used for CLL, mantle cell lymphoma, Waldenstrom's, 420 mg once daily (3) 140 mg caps with water

- **Idelalisib** - Relapsed CLL with rituximab, relapsed NHL, relapsed SLL, 150 mg po BID +/- food
- **Ponatinib** - CML resistant to prior therapies, 45 mg po once daily
- **Ixazomib** - used in Multiple Myeloma with Lenalidomide and Dexamethasone, often given 4 mg po days 1/8/15 on 28 d cycle
- **Duvelasib** - used for CLL, small lymphocytic lymphoma or follicular lymphoma (9/18)
- **Glasdegib** - AML in > 75 y.o. (11/18)
- **Ivosidenib** - treatment of AML in IDH1 mutation (7/18)
- **Gilteritinib** - AML with FLT3 mutation (11/18)

Toxicities and side effects

as listed in prescribing information

Hematologic:

Cytopenias: monitor CBC, notify MD or NP for counts that may indicate need for growth factor support, transfusions or holding/modifying chemotherapy, ask patient about bleeding, fevers, shortness of breath, palpitations.

DVT: Can occur 2/2 malignancy or 2/2 chemotherapy medications. Monitor for asymmetric swelling, new dyspnea, or tachycardia.

Cardiovascular effects:

CHF: Some chemotherapy medications can affect the heart's pumping ability, or affect heart rhythm (trastuzumab and bevacizumab). QTc prolongation, HTN also occur.

("Life with cancer - managing symptoms: cardiac toxicity" (2019 January 22)

Respiratory

Dyspnea: assess for when it occurs, whether or not associated with cough, ask about swelling, upper respiratory symptoms, concerns for pneumonitis depending on drug

Gastrointestinal

- **Nausea and vomiting:** Important to assess when it occurs (anticipatory vs. after chemo vs. refractory). Also ask about other meds that may impact
 1. Having pt. keep journal can help with management.
Encourage smaller more frequent meals.

Additional agents: Lorazepam, alprazolam

1. Ginger - 50/50 in terms of evidence of efficacy
2. Acupuncture/pressure- ASCO 2018 guidelines state it can be considered to help CINV

Schwartz, J. (2014), Hesketh, P. (2108), Aapro, M. (2104)

Diarrhea: Assess when this is occurring, number of stools, and whether or not is responding to anti-diarrheal medications. Patients often avoid taking anti-diarrheal out of fear of constipation.

- Loperamide and Diphenoxylate typically used first line unless concern for C. Difficile
- Patients with more than 4 stools per day need to be seen and likely need IVF (Fleishman, S. 2018)

Constipation:

Important to ask what NORMAL bowel pattern was prior to chemo (3 times/day to q 3 days normal)

- Polyethylene glycol- 17 grams in 4-8 oz. water/juice daily-can increase to twice daily if needed
- Can add senna 1-4 at HS if needed
- Instruct to strive for 2-3 qts. fluids daily as well
- being as physically active as able also helps

(Fleishman, S. 2018)

Mucositis/Stomatitis:

- According to the ONS, at least 40% of patients receiving chemotherapy experience this side effect
- frequent mouth care can help, every 4 hrs.
- use of baking soda rinses help prevent
- Dietary avoidance of foods/drinks that can worsen
- use of ice chips or popsicles can help
- compounded oral mouthwashes, Maltodextrin rinses

(Fleishman, S. 2018)

Dermatologic Toxicities

- Can be quite varied in appearance from rash to dry skin to open ulcers/sores, to pustular rash similar to acne, to life-threatening skin rashes like Steven Johnson's syndrome
- Rash can occur in up to 50% of patients treated with oral hematologic oncology medications
- Pruritis and rash can both adversely affect quality of life

Management of skin toxicities

- Have patients check hands and feet for blisters or open areas if on meds at risk for Hand-Foot syndrome
- Have patients keep a journal of skin symptoms and report any new rash, pruritus, erythema, swelling or open areas
- Educate patients on the importance of keeping skin moisturized with lotion
- Advise patients to protect skin exposed to sun, cold weather, or water
- Avoid tight-fitting clothing especially shoes (Povlovich, M., et al, 2014)

Neurologic Toxicities

- **Peripheral Neuropathy** - can be affected by other comorbid conditions (DM, arthritis, etc.)
 - can affect hands and/or feet
 - degree of damage often worsened depending on length of treatment
 - important to ask questions about ADLs like difficulty with fine motor skills, gait instability, falls

- Duloxetine 60 mg po daily - only evidence-based intervention that is recommended per Up to Date as of 7/30/18
- These meds are not recommended, but may be tried as long as patient understands they have limited data regarding efficacy:
 - *Gabapentin and Pregabalin both have limited data regarding their efficacy*
 - *Tricyclic antidepressants - have shown benefit for other neuropathic pain conditions*
 - *Topical compounded creams with Baclofen 10 mg/Amitriptyline 40 mg/Ketamine 20 mg - only one trial showed improvement in symptoms*

Cancer-related fatigue

- Defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and that significantly interferes with usual functioning.
- Tends to fluctuate over the course of treatment and may be present for months or years after cessation of treatment.
- Treat the underlying causes that we have measures for (anemia, comorbid conditions, emotional distress, nutritional deficiencies, sleep problems)(Fleishman, S. 2018; Mitchell, S., et al, 2007)

Conclusion

- Assess for side effects at every visit
- Always take a thorough history of symptoms
- Early intervention and continual patient education can prevent progression from mild side effects to toxicities

THANK YOU!

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Additional Resources for Nurses

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