Cancer Survivorship and the Role of Pharmacy

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Objectives

• Pharmacists:
  – Describe the definition of cancer survivorship and standards for survivorship care
  – Discuss screening, assessment and management of psychosocial and physical problems experienced by cancer survivors
  – Identify survivorship resources for health care professionals and patients, and the role of pharmacy in caring for cancer survivors

Objectives, continued

• Pharmacy Technicians:
  – Describe the definition of cancer survivorship
  – Discuss late effects and long-term psychosocial and physical problems experienced by cancer survivors
  – Identify the role of pharmacy in caring for cancer survivors

Disclosure

• I do not have any conflicts of interest to disclose in regards to the content of this presentation
Definition

- Survivorship
  - An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life
  - NOT limited to individuals who have no disease at the completion of treatment

Survival Statistics

- The number of people with a history of cancer in the United States has increased dramatically
  - 3 million in 1971 to more than 14 million today
- About 64% of cancer survivors were diagnosed with cancer five or more years ago
- More than half of cancer survivors are 65 years or older
Survival Statistics, continued

• Most common cancers among adult cancer survivors:
  – 22% breast
  – 20% prostate
  – 9% colorectal
  – 8% cervical, uterine or ovarian


Challenges faced by Survivors

• Cancer survivors often face physical, emotional, social and financial challenges as a result of their diagnosis and treatment

Survival Statistics, continued

• Incidence of childhood cancer has changed only slightly since 1970
  – However, the overall survival rate for childhood cancer has increased dramatically during this period
• Overall survival rate for childhood cancer is close to 80%
• Two-third of childhood cancer survivors have at least one chronic health condition


Standards for Survivorship Care

• Care of the cancer survivor should include:
  – Prevention of new and recurrent cancers and other late effects
  – Surveillance for cancer spread, recurrence, or second cancers
  – Assessment of late psychosocial and physical effects
  – Interventions for consequences of cancer and treatment (i.e. medical problems, symptoms, psychological distress, financial and social concerns)
  – Coordination of care between primary care providers and specialists to ensure that all of the survivors health needs are met

(National Comprehensive Cancer Network. Survivorship [Version 2.2015])
Secondary Cancers

- Genetic susceptibilities, shared causative factors (smoking, obesity and environmental exposure), and/or mutagenic effects of previous cancer therapy increase risk.
- Incidence differs based on cancer type.
  - 2% in lymphoma survivors to 30% in survivors of small cell lung cancer.
- Expected to increase as cancer survivors live longer.

Long-term Effects of Specific Agents

- Pulmonary fibrosis - Bleomycin
- Ototoxicity - Platinums
- Peripheral Neuropathies - Vinca Alkaloids, Platinums, Taxanes
- Cardiotoxicity - Anthracyclines

Psychosocial and Physical Effects

- Anthracycline-induced cardiac toxicity
- Anxiety and Depression
- Pain
- Fatigue
- Cognitive function
- Sexual function
- Sleep Disorders

Anthracycline-Induced Cardiac Toxicity

- Anthracyclines (eg. doxorubicin, epirubicin, daunorubicin) are used to treat many cancer types.
  - Breast cancer, lymphoma and sarcoma.
- Reactive oxygen species (ROS) cause oxidative injury, and the subsequent induction of apoptosis in cancer cells.
- Asymptomatic left ventricular ejection fraction (LVEF) decline reported between 10 – 50% in various studies.
Screening for Cardiac Toxicity

- All survivors should be assessed for heart failure within one year of anthracycline therapy
- Additional risk factors should be considered
  - Other cardiotoxic therapies, higher cumulative dose (eg, cumulative dose of 300 mg/m²), underlying cardiac issues

Assessment and Management of Cardiac Toxicity

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| A     | No structural disorder of the heart, but at risk for developing heart failure:  
  - H/o cardiotoxic chemotherapy  
  - H/o chest irradiation  
  - Hypertension, coronary artery disease  
  - Diabetes mellitus  
  - H/o alcohol abuse, rheumatic fever  
  - Family H/o cardiomyopathy  
|       | Address underlying risk factors: hypertension, lipids, tobacco use, obesity, metabolic syndrome, diabetes  
  - Recommend physical activity and healthy diet habits  
  - Consider referral to cardiologist |
| B     | Structural heart disease but no signs or symptoms of heart failure:  
  - Left ventricular hypertrophy  
  - Left ventricular dilation or hypocontractility  
  - Asymptomatic valvular disease  
  - Previous myocardial infarction  
|       | Measures under stage A  
  - Refer to cardiologist |
| C     | Signs and symptoms of heart failure  
|       | Refer to cardiologist |
| D     | Advanced structural heart disease and marked symptoms at rest despite maximal medical therapy  
|       | Refer to cardiologist |

Anxiety and Depression

- All patients with cancer should be evaluated for symptoms of depression and anxiety at their initial visit, at appropriate intervals and as clinically indicated
  - Post-treatment, recurrence, progression, transition to palliative and end-of-life care
- Screening should be done using a valid and reliable measure
  - Nine-item Personal Health Questionnaire (PHQ-9), Generalized Anxiety Disorder (GAD) 7-scale

Screening for Anxiety and Depression
Assessment and Management of Depression

<table>
<thead>
<tr>
<th>PHQ-9</th>
<th>None/mild (score 1-7)</th>
<th>Moderate (score 8-14)</th>
<th>Moderate to severe (score 15-21)</th>
</tr>
</thead>
<tbody>
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<td>Self-help; Group based therapy; Physical activity; Pharmacologic</td>
<td>Individual based therapy; Pharmacologic (combined)</td>
<td></td>
</tr>
</tbody>
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- Offer referral to supportive care services
- Self-help: Group based therapy; Physical activity; Pharmacologic
- Individual based therapy; Pharmacologic (combined)

PHQ-9

None/mild (score 1-7)

Moderate (score 8-14)

Moderate to severe (score 15-21)

Assessment and Management of Anxiety

<table>
<thead>
<tr>
<th>GAD-7</th>
<th>None/mild (score 0-4, 5-1)</th>
<th>Moderate (score 10-14)</th>
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GAD-7

None/mild (score 0-4, 5-1)

Moderate (score 10-14)

Moderate to severe (score 15-21)

Pharmacologic Interventions for Anxiety and Depression

- First-line treatment:
  - Selective serotonin reuptake inhibitors (SSRIs)
  - Selective-norepinephrine reuptake inhibitors (SNRIs)
  - Benzodiazepines

Pharmacologic Interventions for Anxiety and Depression, continued

**Concomitant Problems** | **Special Pharmacologic Consideration**
---|---
Substance Abuse | Minimize use of benzodiazepines
Pain syndromes (eg, neuropathy) | Serotonin-norepinephrine reuptake inhibitors (SNRI) Tricyclic antidepressants
Menopausal symptoms (eg, hot flashes) | Gabapentin (300-600 mg/day), Venlafaxine extended release (37.5-75 mg/day)
Fatigue | Bupropion
Insomnia | Mirtazapine, Benzodiazepines
Drug Interactions with Tamoxifen

Paroxetine, Fluoxetine and Bupropion

Tamoxifen → Endoxifen (active form) → CYP2D6

Paroxetine, Fluoxetine and Bupropion

Screening and Assessment of Pain

• All cancer survivors should be screened for pain at regular intervals
• Pain intensity should be quantified by the survivor
• Severe uncontrolled pain is a medical emergency

Pain

• More than one-third of cancer survivors experience chronic pain
  – Injury to somatic and visceral structures resulting in nociceptive pain
  – Neuropathic pain as a side-effect of chemotherapy or radiation therapy or by surgical injury to the nerves
• Pain in survivors is often ineffectively managed

Management of Pain

• Goals are to increase comfort, maximize function and improve quality of life
• Multidisciplinary approach is recommended
  – Pharmacologic, psychosocial interventions, physical therapy and interventional procedures
• Management of eight distinct pain syndromes addressed in the guidelines
  – Neuropathic pain, chronic pain syndromes, myalgias/arthralgias, skeletal pain, myofascial pain, GI/urinary/pelvic pain, lymphedema, post-radiation pain

Management of Neuropathic Pain

General measures
- Adjuvant analgesics
- Antidepressants
- Anticonvulsants
- Opioids
- Psychosocial interventions
- Consider hypnosis

Refractory pain
- Pharmacologic therapies
- Topical patches
- Creams
- Non-pharmacologic therapies
- Heat, ice, acupunture, etc.

Agent Dosing
- Tricyclic Antidepressants (Nortriptyline and desipramine)
  Start with a low dose and increase every 3-5 days; Starting dose 10-25 mg HS (increase to 50-150 mg HS)
- Duloxetine
  Starting dose 20-30 mg daily (increase to 60-10 mg daily)
- Venlafaxine
  Starting dose 37.5 mg daily (increase to 75-225 mg daily)
- Gabapentin
  Starting dose 100-300 mg HS (increase to 900-3600 mg daily in 2-3 divided doses)
- Pregabalin
  Starting dose 50 mg TID (increase to 100 mg TID)

Duloxetine for the Management of Neuropathic Pain
- ASCO guideline only recommends duloxetine for chemotherapy-induced peripheral neuropathies (CIPN)
- Smith et al studied the effect of duloxetine in a randomized, placebo-controlled trial of 231 patients with CIPN
  - Patients receiving duloxetine reported a significant decrease in pain compared with placebo (p = .003)

Fatigue
- Common complaint in individuals undergoing chemotherapy
  - May persist for months and years after cancer diagnosis
- Important to assess for possible comorbidities and/or medications
  - Cardiac dysfunction, endocrine abnormalities and/or anemia
  - Sleep aids, pain medications and/or antiemetics
Fatigue Management

- Patient/Family Education
- Physical Activity
- Psychosocial: Nutrition; Sleep Hygiene
- Pharmacologic

Pharmacologic Agents for the Management of Fatigue

- Evidence suggests that psycho-stimulants (e.g., methylphenidate) and other weakness agents (e.g., modafinil) can be effective in patients with active disease
- Small pilot studies have evaluated supplements, such as ginseng and vitamin D
  - No consistent evidence of their effectiveness

Cancer Survivorship Guidelines

- Available at www.NCCN.org


Cancer Survivorship Guidelines, continued

- Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline (Journal of Clinical Oncology ASCO Special Article)
- ASCO has developed guidelines on prevention and management of chemotherapy-induced peripheral neuropathy, fatigue, anxiety and depression, and fertility preservation

Available at http://www.instituteforquality.org/practice-guidelines
Breast Cancer Survivorship Guidelines

<table>
<thead>
<tr>
<th>Agent</th>
<th>Long-term Effect</th>
<th>Late Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamoxifen</td>
<td>Hot flashes</td>
<td>Increased risk of stroke</td>
</tr>
<tr>
<td></td>
<td>Changes in</td>
<td>Increased risk of endometrial cancer</td>
</tr>
<tr>
<td></td>
<td>menstruation</td>
<td>Increased risk of blood clots</td>
</tr>
<tr>
<td></td>
<td>Mood changes</td>
<td>Osteopenia in premenopausal women</td>
</tr>
<tr>
<td>Aromatase inhibitors</td>
<td>Vaginal dryness</td>
<td>Increased risk of osteoporosis</td>
</tr>
<tr>
<td></td>
<td>Decreased libido</td>
<td>Increased risk of fractures</td>
</tr>
<tr>
<td></td>
<td>Muscle/skeletal pain</td>
<td>Cholesterol elevation</td>
</tr>
<tr>
<td>Trastuzumab</td>
<td>Increased risk of cardiac dysfunction</td>
<td>Osteopenia in premenopausal women</td>
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</tbody>
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Adapted from Runowicz CD, Leach CR, Henry NL, et al. J Clin Oncol. Published online before print December 7, 2015.

Cancer Survivorship at Memorial Cancer Institute

Available at http://www.asco.org/practice-research/cancer-survivorship

Treatment Summary and Survivorship Care Plan

Chemotherapy Passport at Memorial Cancer Institute

Available at http://www.asco.org/practice-research/cancer-survivorship
Role of Pharmacy

• “From a medication standpoint, a lot of cancer therapies have lasting adverse effects—neuropathy, heart failure, and so on. All of those problems would be best managed by pharmacists who can assess treatment effectiveness and then work with patients to optimize their regimens.”
- Daniel Zlott, PharmD, National Cancer Institute

Role of Pharmacy, continued

• In the absence of a defined role for pharmacists in cancer survivorship teams, we should use this opportunity to create new possibilities for pharmacists and pharmacy technicians to optimize the care of cancer survivors
  – Assisting patients in creating cancer treatment and survivorship plans
  – Monitoring and management of effects of cancer diagnosis and treatment
  – Preventing drug-drug interactions
Assessment Question 1
Which of the following anti-cancer agents is associated with an increased risk of developing heart failure?
A. Doxorubicin
B. Trastuzumab
C. Epirubicin
D. All of the above

Assessment Question 2
A breast cancer survivor on tamoxifen has been complaining of hot flashes. She was recently diagnosed with depression. Which antidepressant would you recommend?
A. Paroxetine
B. Fluoxetine
C. Bupropion
D. Venlafaxine

Assessment Question 3
Which agent has the most evidence for the treatment of chemotherapy-induced peripheral neuropathy.
A. Duloxetine
B. Nortriptyline
C. Gabapentin
D. All of these agents have similar evidence

Summary
• The number of cancer survivors is increasing
• Cancer survivors face unique psychosocial and physical effects
• There are resources available on cancer survivorship for healthcare professionals
• We should create new possibilities for pharmacists and pharmacy technicians to optimize the care of cancer survivors
Questions

References