Medication’s Impact on Lymphedema
Emily Tesar MSN, RN, OCN
University of Missouri – Sinclair School of Nursing

Introduction
With cancer treatment improving, there are over 2.8 million breast cancer survivors in the U.S., with 15-28% suffering from breast cancer-related lymphedema (BCLR). As survivor population grows, so does their risk for developing other chronic diseases, such as cardiac disease, type 2 diabetes, COPD, cancer recurrence or new primary cancer.

Minimal literature exists regarding the effect that medications taken for chronic conditions have on breast cancer-related lymphedema. Why is this important? Research has found that BCLR is associated with:
1. Lower reported quality of life
2. Psychological distress
3. Fatigue, chronic pain, limitations in mobility
4. Increased rates of infection/cellulitis
5. Financial burden
6. Time constraints due to need to attend therapy

Objectives
1. Examine medications with a significant side effect profile for generalized edema: calcium channel blockers, NSAIDs, anti-cancer agents (cytotoxic and hormonal) anticonvulsants/antineurals, antidepressants, antidiabetics.
2. Examine new medications identified in objective #1 could mimic an exacerbation of lymphedema.
3. Establish the foundation for ongoing research in a Midwest cancer center and school of nursing.

Calcium Channel Blockers
1. Cardiac Diseases: hypertension, angina, certain dysrhythmias
   Ex: Diltiazem, Amlodipine, Fludipine, Verapamil
2. Peripheral Edema
   - incidence rate of 5-70%
   - edema is drug/dose dependent
   - edema results from disruption in capillary flow, resulting in fluid being forced from intravascular compartments into the interstitium
   - Movement of fluid in capillary circulation exceeds overall capacity of lymphatic system: especially with individuals who have a compromised lymphatic system secondary to damage/disease and slowly progressing, unilateral edema results.

NSAIDs
1. Non-steroidal anti-inflammatories effect sodium/water retention
   - increase tubular reabsorption of sodium: correlated to increased fluid retention/edema particularly in individuals with impaired lymphatic flow
2. Fluid retention seen in up to 25% of patients taking NSAIDs
3. NSAIDs have been found to make diuretic therapy less effective

Anti-Cancer Agents (cytotoxic and hormonal)
1. Cytotoxic Agents: Doxorubicin, a taxoid, drug, used in the setting of metastatic breast cancer
   - 44-65% of patients treated with this drug experience fluid retention
   - fluid retention often a dose-limiting side effect
   - two step process: (1) fluid congestion in interstitial space, and (2) inadequate lymphatic drainage
2. Hormonal Therapy: Anastrozole, an oral nonsteroidal aromatase inhibitor used to treat postmenopausal women with advanced breast cancer (lowers overall plasma estrogen levels)
   - peripheral edema is a common side effect
   - two phase III clinical trials: 9% (n=588) reported increasing limb size

Anticonvulsants/Antineurals
1. Pregabalin (Lyrica) and gabapentin (Neurontin)
   - used in the treatment of seizure disorders, neuropathic pain, sleep disorders and anxiety
   - pregabalin: 75% of patient’s taking pregabalin report edema

Antidepressants
1. Trazodone: tricyclic antidepressant: fewer anticholinergic and cardiac side effects than others in same class
   - report on 10 patients taking trazodone: 6/10 reported fluid retention with weight gain: 4.4-15 lbs
   - exact cause of fluid retention unclear, but authors note trazodone should be increased gradually in patients who have an underlying predisposition to edema or fluid retention

Antidiabetics (Thiazolidinedione)
1. Rosiglitazone (Avandia) and pioglitazone (Actos)
   - singular therapy: 5-10% edema incidence rate
   - combination therapy with insulin: 15-20% edema incidence rate

Ongoing Research
Possibility exists that certain medications exacerbate BCLR: discontinuing medication or altering dose might be only effective remedy. Therefore, researchers at a Midwest cancer center and school of nursing are examining the following:
1. Relationship between a known diagnosis of lymphedema and patterns or alterations in daily medication regimens with breast cancer survivors
2. The relationship between a new diagnosis of lymphedema and patterns or alterations in daily medication regimens in breast cancer survivors.

How? Cross-reference data (lymphedema and Breast Cancer Questionnaire/anthropometric limb measurements) taken over a period of 84 months on 159 women (BCLR) with medication usage (both OTC and prescribed).

This research could lead to the creation of a list of medications which should be used in caution with those suffering from BCLR. Understanding the impact these medications have on BCLR could potentially lead to improvements in healthcare management, QOL, psychological distress, infection and cellulitis rates, financial stressors, and time constraints.

References
Due to there being a high volume of reference, please contact Emily Tesar for the entire list. Thank you!

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Thank you!