

Medications That Cause Or Worsen Edema

By Paula J. Stewart, MD, CLT-LANA

Those treating lymphedema must be familiar with the hundreds of medications that can contribute to swelling. It has been known for a long time that narcotic medications and non-steroidal, anti-inflammatory drugs can contribute to edema in the extremities by separate mechanisms. It appears that narcotic medications in all likelihood will cause vasodilatation contributing to dependent edema and that non-steroidal, anti-inflammatories contribute to retention of sodium, which can in turn result in accumulation of free water in the soft tissues. There are, however, over 900 additional medications that can also contribute to edema. Being familiar with these medications may be useful in determining whether or not the effect of the medication is contributing to the swelling and could be the difference between successful management of lymphedema or not.

Unfortunately, the medications most likely to result in peripheral edema are, in fact, many of the chemotherapeutic agents used by cancer patients who then go on to develop lymphedema. There has been recent documentation that patients who remain on chemotherapy for prolonged periods of time may, in fact, be more susceptible to developing lymphedema, and this finding could be related to the fact that medications such as Docetaxel can cause peripheral edema in 33% to 47% of persons and **Cisplatin** can cause peripheral edema in 10% of patients who are prescribed this medication. **Trentinon** or Vesinoid (a Vitamin A derivative used for chemotherapy) can result in peripheral edema in 52% of those patients who are prescribed this medication.

Other medications with severe warnings for lymphedema include **Valproic acid** which can cause peripheral edema in 8% of all persons prescribed and the Glitazones used in the treatment of diabetes (Actos and Avandia) are especially prone to cause congestive heart failure and peripheral

edema in 5% to 15% in those utilizing this medication.

There are certain classes of medication that are especially prone to resulting in edema. Antihypertensives, such as ace inhibitors can result in peripheral edema in about 1% of those prescribed. Univasc results in approximately 10% and Aceon 4%.

The **adernergic agonists** such as Minipress **Vytorin**, **Cardura** or **Aldomet** can result in edema in 1% to 10% of persons prescribed these medications. Beta blockers such as Tenormin, Coreg, Labetalol, Toprol, Corgard, and Pindolol, which are used not only to control blood pressure, but rate also, can contribute to edema in 1% to 10% of persons taking these medications.

The calcium channel blockers are especially prone to causing edema and have a very significant dose relation to the incidence of edema,

depending on how much of the medication is prescribed.

Medications such as Nifedipine can cause up to 50% of those prescribed having peripheral edema. Verapamil has a 1.9% with medications such as Norvasc, Sular, Plendil, and Cardizem falling between 2% and 30%.

Other hypertensives such as nitrates which function by causing a vasodilatory effect have a very strong impact on formation of peripheral edema. Medications in this classification include Hydralazine, which is frequently associated edema and Minoxidil, which can result in an incidence of 7% edema. Anti-arrhythmics such as amiodorone, Norpace, or Flecainide (known also as Tambocor) often result in significant edema from 1% to 10%.

Many patients with lymphedema

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Highest Honors Bestowed On Jane Armer



Jane Armer, PhD, RN, FAAN, recently received one of the highest honors in the nursing profession from the American Academy of Nursing and a second prestigious award from the University of Missouri.

At the annual American Academy of Nursing convention held in Arizona on November 8, 2008, Dr. Armer was inducted as a Fellow of the American Academy of Nursing—the greatest honor bestowed in the nursing profession—for her outstanding contributions to nursing.

Dr. Armer, a professor of nursing at the University of Missouri, also received the Missouri University Faculty Alumni Award in October 2008, for her exceptional role in educating and mentoring students.

Dr. Armer is well known for her extensive research on anthropometric measurement of limb volume in post-BC LE; signs, symptoms and self-management of LE among women treated for breast cancer; and the psychological impact of LE. Her program of research focuses on the more than two million women in this country who are living with breast cancer and are, therefore, at a lifetime risk for lymphedema development.

Dr. Armer serves on the National Lymphedema Medical Advisory Board and chairs the NLN Research Committee. The NLN extends their heartfelt congratulations to Jane, a most deserving recipient. □

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suffer from peripheral vascular disease and phlebolympheidema. These patients are frequently on anticoagulants such as Cilostazol or Pletal and Clopidogrel or Plavix and Fondaparinux also known as Arixtra. These medications frequently result in edema in 4% to 10% of patients taking them.

Two of the most widely prescribed medications worldwide are Lipitor or Atorvastatin and Crestor or Rosuvastatin which are used to lower cholesterol and triglycerides. Unfortunately, these very widely prescribed medications can result in edema in between 1% and 10% of the population prescribed.

It is known that intermittent cyclic edema in young women is most likely linked to fluctuations in estrogens, so it is probably no surprise estrogens are associated with an increase in peripheral edema in 1% to 10% of patients. Evista is a SERM that can also increase edema from 3% to 14%. It may be surprising to some that androgens also contribute to edema in up to 10%.

Many of the anti-neoplastics can result in edema, including Casodex, Xeloda, Taxotere, Aromasin, Taxol, Tamoxifen, and Herceptin. Rates of edema associated with the use of these very commonly utilized chemotherapeutic agents range from 5% to 60%.

Antidepressants are also very widely utilized in patients worldwide, and very commonly in the lymphedema population. The antidepressants that most often are associated with edema are Serzone, Trazadone, also known as **Dyseril**, causing between 1% and 10% incidence of edema. Remeron is associated with a 2% incidence and Effexor, is associated with a 1% incidence.

As mentioned earlier in the discussion regarding cellulitis and secondary infections, Quinalones and Daptomycin are used as second line drugs for complicated bouts of cellulitis. Both of these drugs can contribute to edema. Daptomycin also known as Cubisin can result in a 7% incidence and the Quinalones a 1%

incidence. Gentamicin, which would be utilized for complicated infections only, can contribute to edema in 1% to 10%. Anti-epileptics in general will contribute to edema in 1% to 10%, Lyrica, which is used primarily for neuropathic pain management is especially edemagenic causing edema in 16%.

SELECTED OTHERS

- Anti-fungals such as Amphotericin resulting in 15% edema
- Anti-psychotics, both traditional and atypicals, cause edema in approximately 1%
- Bisphosphates used for osteoporosis result in 1% edema and those using Fosamax 8% edema.
- Actonel causes edema in 5% to 20%.

Zometa and other immuno-suppressants such as Cellcept or Rapamune can result in a staggering 27% to 64% in incidence of edema.

Parkinson agents in general result in edema in 1% to 10%.

CONCLUSION:

The typical lymphedema patient very often is medically complex and is prescribed multiple medications. It is important to understand the potential impact of those medications on lymphedema and peripheral edema and look for alternatives that may not contribute to the same degree. □

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