



Edema-causing medications

Take note of your medications and talk with your doctor

By Vaughan Keeley and Neil Piller

Introduction

Some medications may cause edema in people who do not normally have swelling. They can also exacerbate swelling in those who already have lymphedema and may be contributing factors in those who have chronic edema due to a number of causes, particularly the elderly. This means that the potential role of medications in the cause of edema needs to be considered in all people with chronic swelling.

Most medications which cause edema do so by increasing the amount of fluid filtered from the blood capillaries into the tissues but some may impair the lymph drainage.

Q Do many drugs cause edema?

A The list of medications which may cause edema is very long. For some, it may be a common side effect, but for others it is rarely seen. The most commonly used drugs which can cause edema are:

- calcium channel blockers e.g. amlodipine
- nonsteroidal anti-inflammatory drugs (NSAIDs) e.g. ibuprofen
- corticosteroids e.g. prednisolone
- hormones and related compounds e.g. tamoxifen

Calcium channel blockers (CCBs)

These are probably the medications most frequently implicated in causing edema, potentially affecting up to 50% of those who take them, depending upon the specific type and dose. They are used to treat high blood pressure. They cause edema by increasing capillary filtration of fluid and may also reduce lymphatic drainage.

The time to onset of edema after commencing CCBs may vary with different drugs, e.g. one month with amlodipine; two months with nifedipine.



Nonsteroidal anti-inflammatory drugs (NSAIDs)

These medications are commonly used in the treatment of a wide variety of conditions e.g. arthritis.

They cause edema by fluid retention. The likelihood of this depends upon the individual drug

e.g. up to 9% with naproxen.

Corticosteroids

Corticosteroids can cause sodium retention through a direct action on the kidney. This can result in fluid retention and hypertension. The effect is dependent upon the dose and duration of treatment. Corticosteroids are used to treat a variety of illnesses. These include some inflammatory conditions in which edema can be a feature e.g.

rheumatoid arthritis. In these situations long term corticosteroids can help reduce the inflammatory edema but may cause leg swelling. A decision about their continued use will depend on the balance of benefit v. side effects. In some conditions such as asthma, short courses of corticosteroids are used e.g. up to 2 weeks and during this time leg swelling is unlikely to occur. Corticosteroids are also used to treat peripheral edema in advanced cancer (they work by reducing the inflammatory edema around the cancer) but again decisions on duration and dose depend on weighing up the benefit v. side effects.

Sex hormones and related compounds

Whilst the combined oral contraceptive pill and hormone replacement therapy can cause edema in some women, hormone treatments such as those used in breast cancer e.g. tamoxifen, anastrozole and megestrol may lead to edema in 7 to 14% of women taking them.

Other drugs

Other drugs which may be responsible for edema include anticonvulsants used in pain management e.g. pregabalin (affects 5 to 12%), antidepressants e.g. trazodone (10%), anti-diabetics e.g. rosiglitazone (5%), antipsychotics e.g. risperidone (16%), bisphosphonates e.g. zoledronic acid (21%), chemotherapy agents e.g. docetaxel (47 to 64%) and immunosuppressants e.g. sirolimus (more than 10%).



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Q How can we tell if a medication is contributing to the edema?

A There may be a clear time relationship between starting the medication and the onset or worsening of swelling. For some medications, e.g. corticosteroids, the effect may take some weeks to develop.




Checking whether edema is a common side effect for a particular medication is important, but it is still necessary to consider the potential role of a medication, which only causes edema rarely. A medication may cause more widespread edema in someone with a pre-existing localized swelling, eg. it could cause swelling, eg. in both legs in someone who may have lymphedema previously affecting one leg only.

Q If a drug effect is suspected, how should this be managed?

A Ideally, e.g. with calcium channel blockers used to treat high blood pressure, the medication should be withdrawn or switched to another product. However in some circumstances where the blood pressure has been difficult to manage, continuing the medication but with a reduced dose may improve the edema. In some cases, however, the medication may be essential in treating a serious medical condition and therefore managing the side effect, eg. with compression garments or the use of diuretics in certain instances, may need to be considered.

Conclusions

For many people with chronic edema, the cause of the swelling is often multifactorial. Medications can play a significant part in this and it is important to consider what role they may have and whether changes should be made to improve the control of the edema. 

Some medications may cause edema in people who do not normally have swelling. They can also exacerbate swelling in those who already have lymphedema.

References

1. Keeley, V (2008) Drugs that may exacerbate and those used to treat lymphoedema. *Journal of Lymphoedema* 3(1).
2. Given the prevalence of use of Calcium Channel blockers the following older article may be of interest. It indicates their mechanisms of actions and provides a generic review of our thinking. Sica, D A Calcium Channel Blocker-Related Peripheral Oedema: Can It Be Resolved *Journal Clinical Hypertension* (Greenwich). 2003 5(4):291-4.

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