

LE Magazine July 2007

Ask the PHARMACIST

Integrating B Vitamins with Calcium Channel Blockers

By James S. Scozzari, RPh

Q: I take a blood pressure medication called nifedipine, a calcium channel blocker. I've heard that it can cause B-vitamin deficiency and swelling of the gums. Is this true?

A: I recommend that all patients who take calcium channel blockers like nifedipine also supplement with folic acid and vitamin B complex. There are many reasons to supplement with B vitamins while taking a calcium channel blocker.

Let's start with what nifedipine is and what it does. Nifedipine (Procardia®) is a calcium channel blocker, a specific class of drugs used to lower blood pressure. These drugs work by regulating the flow of calcium ions in the heart muscle and the smooth muscle cells lining the arteries.

Calcium is what is known as an *excitatory element*, because its entry into the muscle cells of the heart and blood vessel lining causes them to contract. By blocking calcium channels in the muscle of the heart and blood vessels, calcium channel blockers prevent calcium levels from building up in stimulated cells, leading to less contraction, increased blood vessel dilation, and decreased peripheral resistance. Because resistance and heart output drop, so does your blood pressure. With a decrease in blood pressure, your heart does not have to work as hard.

Calcium channel blockers also increase the supply of oxygen-rich blood to your heart, which is known as the "negative inotropic effect" (decreased force of heart contraction). One of the main advantages of calcium channel blockers over beta-blockers (another class of medication for high blood pressure) is that the heart remains responsive to stimulation by the sympathetic nervous system, which means your body's natural functions can control your blood pressure more effectively.

Many calcium channel blockers (nifedipine is one of them) also slow down the conduction of electrical activity within the heart. By blocking the calcium channel during the plateau phase of your heart muscle's action, these drugs can lower your heart rate. This is known as the "negative chronotropic effect" of calcium channel blockers. It is valuable in cases in which controlling the heart rate is an issue (for example, in people with atrial fibrillation), as well as in lowering the heart's workload.

There are four basic categories of calcium channel blockers:

- dihydropyridines
(such as nifedipine)

- phenylalkylamines
(such as verapamil)

- benzothiazepines
(such as diltiazem)

- tetralols
(such as bepridil, which is no longer sold in the US).

Because dihydropyridine calcium channel blockers such as nifedipine are the most potent vasodilators, they also have the strongest side effects. These may include headache, upset stomach, dizziness or lightheadedness, excessive tiredness, flushing (feeling of warmth), heartburn, fast heartbeat, muscle cramps, constipation, coughing, and nasal congestion.¹ Enlargement of the gum tissue around the teeth (gingival hyper-plasia) has also been noted in individuals using nifedipine, though only in rare cases.²

Some have suggested that the reason for this swelling of the gums, or gingival overgrowth, is a disruption in collagenase activation. Collagenase is an enzyme that breaks down the peptide bonds in collagen, the fibrous structural protein that supports tissues, including the gums. Activation of this collagenase is a normal function of the body and helps to reduce excessive tissue growth. It is thought that the changes in free-flowing calcium ions caused by calcium channel blockers may disrupt your body's intracellular collagen breakdown pathway, leading to increased tissue growth that results in a swelling of the gums.³

Additionally, this increase in tissue growth can result in an increased demand for folate. This overgrowth may actually alter folate reuptake in normal tissue, thus reducing the amount of folate available to the rest of the body. Deficiency of this essential B vitamin can also lead to elevated blood homocysteine levels, a significant biomarker of increased cardiovascular risk.⁴

Homocysteine is created when the body uses the amino acid methionine for essential methylation processes, particularly in the liver. Methylation is an important bodily process, but it leaves potentially dangerous homocysteine as a byproduct. Normally, the body converts this homocysteine back into methionine or uses it to create cysteine and other useful substances. However, if certain nutrients critical to the efficient conversion of homocysteine (such as folate and other B vitamins) are lacking, then homocysteine can accumulate. Increased homocysteine levels can increase your risk for a multitude of health problems, ranging from heart disease and stroke to depression and liver damage.

Clinical trials show higher mortality in patients taking calcium channel blockers for hypertension compared to patients using other types of drugs such as beta-blockers, diuretics, and angiotensin-converting enzyme (ACE) inhibitors.⁵ Because calcium channel blockers are associated with gingival overgrowth, and because other drugs known to cause gingival overgrowth (such as phenytoin) are associated with elevated levels of homocysteine,^{6,7} it follows that patients treated with calcium channel blockers might be at risk for increased homocysteine levels. Such an association might explain the excess mortality risk observed in patients treated with calcium channel blockers relative to those treated with other hypertension medications, since homocysteine may contribute to atherosclerotic heart disease. Strategies to achieve and maintain optimal blood levels of homocysteine—such as ensuring optimal intake of B vitamins—are thus important for individuals using calcium channel blockers such as nifedipine.

As mentioned previously, occurrences of gum tissue enlargement or B-vitamin deficiency as a result of taking nifedipine are extremely rare. However, I recommend that those taking a dihydropyridine-type calcium channel blocker like nifedipine use 800 mcg of folic acid and a good B-complex vitamin supplement each day as a precautionary measure. As always, if you are experiencing these or any of the other noted side effects associated with this type of medication, you should notify your health care professional immediately.

References

1. Available at: http://www.pdrhealth.com/drug_info/rxdrugprofiles/drugs/pro1352.shtml. Accessed April 26, 2007.
2. Available at: http://www.rxlist.com/cgi/generic/nifedip_ad.htm.
Accessed April 26, 2007.
3. Kataoka M, Kido J, Shinohara Y, Nagata T. Drug-induced gingival overgrowth--a review. *Biol Pharm Bull.* 2005 Oct;28(10):1817-21.
4. Selhub J. The many facets of hyperhomocysteinemia: studies from the Framingham cohorts. *J Nutr.* 2006 Jun;136(6 Suppl):1726S-30S.
5. Psaty BM, Heckbert SR, Koepsell TD, et al. The risk of myocardial infarction associated with antihypertensive drug therapies. *JAMA.* 1995 Aug 23;274(8):620-5.
6. Garzino-Demo P, Carbone M, Carrozzo M, Broccoletti R, Gandolfo S. An increase in gingival volume induced by drugs (phenytoin, cyclosporine and calcium antagonists). A review of the literature. *Minerva Stomatol.* 1998 Sep;47(9):387-98.
7. Apeland T, Mansoor MA, Strandjord RE. Antiepileptic drugs as independent predictors of plasma total homocysteine levels. *Epilepsy Res.* 2001 Nov; 47(1-2):27-35.

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.