LETTERS

Unresponsiveness to nifedipine treatment

TO THE EDITOR: Calcium-channel blocking agents are widely used for hypertension, ischemic heart disease, congestive heart failure, supraventricular tachyarrythmias, and in digital vasospasm (Raynaud's phenomenon).[1-3]

Well-known adverse effects of nifedipine are hypotension,[1] headache, flushing, and peripheral edema.[2] Other potential, although rare, adverse effects include diabetogenic effect,[3] liver damage,[4] eye pain and blurred vision,[5] and agranulocytosis in hemodialysis.[6]

We wish to report a case of increased blood pressure following nifedipine treatment.

A 41-year-old woman was admitted to the Department of Family Medicine with a two-day history of severe headache accompanied by dizziness and nausea. Her previous history was negative for hypertension, diabetes mellitus, and smoking. She experienced only occasional headache during the last few years.

On admission, her blood pressure was 150/120 mm Hg and her heart rate was 86 beats/min. Blood pressure was determined with a mercury sphygmomanometer on the right arm after a rest of ten minutes. The diastolic blood pressure was defined by the fifth Korotkoff phase. Recorded blood pressure was the mean of three determinations. The patient's physical and neurologic examination including fundus was unremarkable. Because of her blood pressure, which was associated with severe headache, treatment with nifedipine 10 mg sl was begun. Heart rate and blood pressure were measured every 5 minutes during the 30 minutes after treatment with nifedipine. The patient did not respond to treatment. Her blood pressure during 30 minutes gradually increased to 170/120 mm Hg with a heart rate of 88 beats/min. She received another dose of nifedipine 10 mg sl. During the subsequent 30 minutes her blood pressure and heart rate were measured continuously every five minutes. Within one hour of beginning nifedipine treatment, her blood pressure increased to 220/150 mm Hg and her heart rate was 90 beats/min. In the face of unresponsiveness to nifedipine she was treated with oral captopril 25 mg. Her blood pressure during the next 30 minutes gradually decreased to 220/120; 190/110; and then 130/80 mm Hg. She continued to receive captopril 25 mg tid.

On the following day the patient suddenly developed typical epileptic convulsions and was transferred to a medical center for further investigation. During hospitalization her physical and neurologic examination including fundus remained unremarkable. Blood pressure without antihypertensive treatment remained between 110/80 and 120/70 mm Hg. Laboratory examinations, including a complete blood cell count, a serologic test for syphilis, a urinalysis, and blood chemical analyses, revealed no abnormalities. Further examination of the patient, including computed tomography of the brain and magnetic resonance imaging revealed arterial-venous malformation versus hemorrhagic stroke in the left parietal lobe. The patient's epileptic fits were controlled with carbamazepine 100 mg tid.

During eight months of follow-up after discharge from the hospital the patient's blood pressure remained between 120/110 and 110/60 mm Hg without antihypertensive treatment. She continued to receive carbamazepine.

This report shows that unresponsiveness to nifedipine, although rare, may be observed. One of the potential disadvantages of nifedipine in hypertensive emergencies is hypotension or normotension,[1] hypotension with circulatory collapse,[7] cerebral edema, and hypertensive encephalopathy.[1] Paradoxic effects of nifedipine–aggravation of myocardial ischemia in or without angina[8,9] and any significant arterial blood pressure change during the period of treatment with nifedipine[8] have been reported as well.

Our patient was unresponsive to nifedipine with a continued rise in blood pressure and without significant change in heart rate.

Captopril is an orally active inhibitor of angiotensin-converting enzyme and has been widely used in the treatment of patients with mild to moderate essential hypertension; severe hypertension not responsive to conventional diuretic/beta-adrenoreceptor blockers; vasodilator regimen; and of patients with chronic congestive heart failure refractory to treatment with a diuretic and digitalis.[10] The fact that the patient responded well to captopril and not to nifedipine shows that, in this case, there was a disturbance of nifedipine-selective arteriolar vasodilatation[2] which leads to the blood pressure elevation. This phenomenon was perhaps associated with congenital brain anomaly (arterial-venous malformation) and with the hemorrhagic infarction.

Therefore, this report on our patient's curious reaction provides an interesting observation—blood pressure elevation after nifedipine treatment.

LIUBOV BEN-NOUN, M.D.

Family Physician Specialist
Department of Family Practice
Ben-Gurion University of the Negev
Mizpe-Ramon, Israel

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Relationship between tranylcypromine sulfate dose and monoamine oxidase inhibition

TO THE EDITOR: A relationship between platelet monoamine oxidase (MAO) activity and clinical antidepressant response has been demonstrated for patients receiving the nonspecific MAO inhibitor, phenelzine sulfate.[1-3] Patients responding to MAO inhibitor therapy have demonstrated significantly higher degrees of platelet MAO inhibition.[4,5] This inhibition as a measure of tranylcypromine's (TCP) clinical effectiveness is controversial. Previous studies have shown the effect of phenelzine is not superior to that of placebo until greater than 80 percent inhibition of platelet MAO is obtained.[6,7] We report a relationship between percent platelet MAO inhibition and TCP dose.

Five adult patients, aged 33–61 years, received TCP for management of their affective illness. Patients with renal, hepatic, or cardiovascular disease were excluded as were mentally retarded or court-committed patients. Each patient was given TCP 20 mg/d for at least one week. Blood concentrations of TCP were drawn at 0, 14, 20, and 24 hours following the last dose of the drug. Each patient, except for one nonresponding patient who was switched to electroconvulsive therapy, was then restarted at 30 or 40 mg/d for at least one week. Blood samples were drawn at times similar to those for the first set of samples. Platelet MAO activity was measured using tryptamine as the substrate according to the method of Murphy et al.[8] From these data we discovered a statistically significant correlation ($r^2 = 0.60$) between percent MAO inhibition and TCP dose, which is described by Equation 1 and presented in Figure 1:

$$\text{Percent MAO inhibition} = 118.8 \text{ (log TCP dose)} + 98.7 \qquad \text{Eq. 1}$$

Although no patient in this study achieved a percent MAO inhibition greater than 64.8, the resulting logarithmic relationship indicates that 80 percent MAO inhibition can be achieved with a tranylcypromine dose of 0.7 mg/kg/d ($p \leq 0.05$).

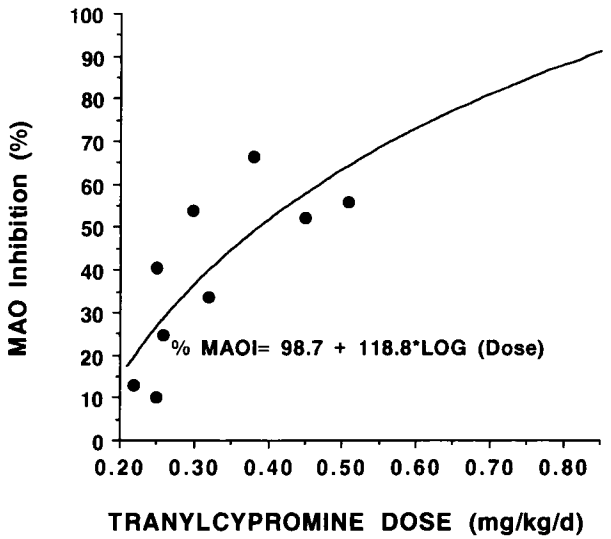

Figure 1. Logarithmic dose to percent MAO inhibition correlation for tranylcypromine.

A starting phenelzine dose of 1.0 mg/kg/d was recommended by Robinson et al. because it was likely to be associated with greater than 80 percent MAO inhibition, which is in turn associated with a positive antidepressant response. With a dose of phenelzine 60 mg/d for six weeks, 68 percent of patients with MAO inhibition of 80 percent or greater responded favorably and 79 percent of patients with MAO inhibition greater than 90 percent showed improvement. However, the response rate was only 44 percent in those achieving less than 80 percent inhibition, and the placebo improvement rate was only 32 percent. Because plasma tranylcypromine concentrations are poor predictors of response, this pilot study provides useful information indicating that an initial tranylcypromine dose of 0.7 mg/kg/d will achieve 80 percent MAO inhibition in platelets.

ROBERT A. GRASSO, B.S.Pharm.
Doctor of Pharmacy Student

PAUL J. PERRY, Ph.D.
Professor of Clinical Pharmacy
Adjunct Professor of Psychiatry

ARNOLD D. SHERMAN, Ph.D.
Research Scientist
Department of Psychiatry
University of Iowa
Iowa City, Iowa 52242

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Inadvertent administration of acetohexamide instead of acetazolamide

TO THE EDITOR: An 83-year-old man was hospitalized with a sudden onset of hypoglycemia. He had a past medical history of glaucoma, severe hypertension, degenerative joint disease, peptic ulcer disease, and chronic renal impairment. He did not, however, have any past history of diabetes. Upon admission he was taking acetazolamide, metoprolol, minoxidil, furosemide, and pentoxifylline orally and pilocarpine, timolol, and epinephryl borate eye drops. Our first suspicion for the cause of his unwarranted hypoglycemia was the beta-blocker medication he was on; however, after further investigation it was found to be due to something entirely different.

The patient was taking acetazolamide 250 mg tid to treat his glaucoma. His nursing home gave him two doses of a newly filled prescription of acetazolamide before he was admitted to our hospital. After retrieving the vial these tablets were dispensed in, we found that the medication it contained was not acetazolamide (Diamox) but rather acetohexamide (Dymelor). We believe this error happened due to one or more of the following reasons: (1) both the brand and generic names sound alike; (2) both tablets are white; and (3) both tablets come in a 250-mg strength.

Pharmacists should be aware of the potential for this mistake. Perhaps the manufacturers can help avoid this problem by imprinting the name of the drug directly on each tablet.

LISA A. OLSON
Pharmacy Student

DONALD R. MILLER, Pharm.D.
Associate Professor of Pharmacy
North Dakota State University
Fargo, North Dakota 58105

AMAR GOSWAMI, M.D.
Resident
Department of Medicine

A. CHERYL MCASKILL, M.D.
Staff Internist
Department of Medicine

WILLIAM P. NEWMAN, M.D.
Chief, Endocrinology and Metabolism
Department of Medicine
Veterans Affairs Medical Center
Fargo, North Dakota

Peripheral neuropathy in HIV patient after isoniazid therapy initiated

TO THE EDITOR: Isoniazid (INH) is an effective antituberculosis agent that has been used routinely since 1952. Soon after INH was released reports of peripheral neuropathy started appearing in the literature.[1-4] Peripheral neuropathy is the most common complication of INH therapy, occurring most often in "slow acetylators" and patients who are malnourished, uremic, alcoholic, or diabetic. Biehl and Vilter demonstrated that peripheral neuropathy was caused by a drug-induced deficiency of vitamin B_6.[5] The neuropathy is usually dose-related, occurring in 44 percent of patients receiving greater than 16 mg/kg/d.[5]

A 27-year-old HIV-positive man presented with increased temperature and was found to have moderate infiltration on chest X-ray. The patient had experienced a 9-kg weight loss over the past two months (ideal body weight 80 kg; actual body weight 68 kg).

Mycobacterium tuberculosis was cultured by bronchoscopy and INH 300 mg/d therapy was initiated. Ten days after INH was begun the patient started complaining of severe foot pain. Pyridoxine 50 mg/d and amitriptyline 75 mg qid were initiated. The pain resolved over 20–30 days. The INH dose was 4.9 mg/kg/d and other medications included rifampin 600 mg/d, pyrazinamide 1500 mg/d, and zidovudine 200 mg q4h.