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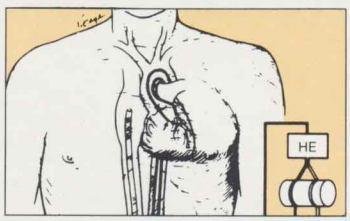

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LOW-CALORIE CHOLESTYRAMINE POWDER APPROVED

Containing fewer than two calories per dose, a new cholestyramine formulation offers a dietetic alternative to other preparations of this drug. Questran Light (Bristol Myers), like other cholestyramine products, is indicated as first-line drug therapy for management of hyperlipidemia.[1]

Cholestyramine, a bile acid sequestrant, is recommended by the National Heart, Lung and Blood Institute as the first drug of choice for management of hypercholesterolemia.[2] Patient compliance has been a limiting factor with cholestyramine powder because it reportedly has an unpleasant taste and can be messy to prepare.

However, Questran Light has advantages that should improve patient compliance, according to a company statement. Because NutraSweet (rather than sucrose) is used to make the new drug palatable, it contains only 1.6 calories compared with Questran, which has fourteen, and Cholybar (Warner Lambert), which contains 60. All three of these drugs contain four grams of cholestyramine per dose. Questran Light's flavor is reportedly improved, and it can be mixed in half the amount of liquid that Questran requires.

A company spokesman says that the "light" formulation will cost the same as Questran but less than Cholybar. (Costs to the pharmacist are about $0.81 for each packet of the Questran products and $0.90 for each Cholybar).

References

1. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. JAMA 251(3):351, 1984.
2. National Cholesterol Education Program. Report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Arch Intern Med 148:36, 1988.

BETA BLOCKER WITH MILD ISA

A new once-daily beta blocker for management of hypertension has recently become available. Long used in Europe, penbutolol (Levatol, Reed & Carnrick, Piscataway, NJ) was approved by the Food and Drug Administration in December of 1987 but has just been launched in this country.

In clinical trials, Levatol significantly reduced systolic, diastolic, and mean arterial blood pressure while causing few side effects.[1] Less than 2% of patients developed depression or insomnia, and only 0.5% of men became impotent. The most common side effect was headache (7.8% vs. 6.1% for placebo). The drug is noteworthy for its once-daily dosing schedule, which boosts patient compliance.[2]

Levatol also possesses mild intrinsic sympathomimetic activity,[3] which minimizes bradycardia at rest and permits modest increases in heart rate during exercise. For the same reason, peripheral vasoconstriction occurs only rarely with use of this drug, according to the manufacturer.

The usual starting dose of Levatol is 20 mg given once daily. Patients have tolerated doses of 40 and 80 mg in clinical trials, but these doses did not improve antihypertensive efficacy.[2]

The manufacturer also offers a patient premium, billed as a "Depressurizing Program." This adjunctive program offers big discounts on items ranging from relaxation tapes to blood pressure monitors. It is automatically sent to patients when they fill their prescription for Levatol.

References

1. Marone C et al. Antihypertensive efficacy and tolerance of penbutolol: Results of a cooperative study in 227 patients. Curr Med Res Opin 9(6):417, 1985.
2. From package insert. Reed & Carnrick, Piscataway, NJ, 1988. Data on file at Reed & Carnrick.
2. Nyberg G et al. Intrinsic sympathomimetic activity of penbutolol. Eur J Clin Pharmacol 16:381, 1979.

MEVACOR NOW AVAILABLE IN 40 MG TABS

Previously marketed as 20 mg tablets, lovastatin (Mevacor, MSD, West Point, PA) is now available in a 40-mg strength. The newer dosage is intended to foster greater patient convenience and compliance for those who must take larger doses, according to an MSD spokesman, and should offer "a modest price advantage."

The recommended dose range of lovastatin (indicated as an adjunct to diet for reduction of total and low-density lipoprotein cholesterol levels) ranges from 20-80 mg/day in single or divided doses.

PHASIC-RELEASE NTG PATCH FAILS TO PREVENT TOLERANCE

Despite recent reports that a convenient phased-release nitroglycerin patch could be used once daily without attenuation of

effect, a new study has cast doubt on this concept. At the doses used in this study, the investigational patch needed to be removed periodically like its continuous-release predecessor or it rapidly lost its effect.

For the time being, at least, "we're back to square one," according to cardiologist Sigmund Silber of the University of Alabama, Birmingham, who has headed studies of transdermal phased-release nitroglycerin in this country. Speaking at the March 1989 scientific sessions of the American College of Cardiology in Anaheim, CA, Dr. Silber said that even threefold fluctuations of plasma nitrate levels did not prevent tolerance development. His study's hypothesis had been that the known prevention of attenuation with isosorbide dinitrate using eccentric regimens (which produce variations in plasma levels) could be extrapolated to nitroglycerin (NTG), but this was not borne out.

In this placebo-controlled, double-blind study,[1] twelve patients with angina and abnormal exercise test results were randomized to a phased-release 20 mg NTG patch or to placebo. All patients underwent measurement of serum NTG levels and exercise testing at two, ten, and 24 hours following patch application. Despite wide fluctuations in serum NTG levels in patients in the treatment group, according to Silber, the "remarkable antiischemic effect after the first application (measured by ST depression on exercise testing) was less pronounced after ten hours. By the second day, there was considerable attenuation of exercise-induced antiischemic effect." Time to onset of angina likewise increased during the first day but was lost by the second, he said.

"Plasma level fluctuations may prevent tolerance development with low-dose patches, but will not work for mid-or high-dose patches," Silber noted. (Phasic patches that did not induce tolerance on testing delivered 7.5 mg of glycerol trinitrate over 24 hours).[2,3] The minimal nitrate-free interval for these patches has not been established, he added. "Perhaps removing this phased patch briefly—for 90 minutes per day—would be sufficient to prevent tolerance development."

References

1. Silber S et al. A newly developed nitroglycerin patch with phased release (abstr). J Am Coll Cardiol 13(2):231A, 1989.
2. Parker JO. Antianginal effects of phasic-release nitroglycerin system during acute and sustained therapy. Official Satellite Symposium, Tenth Congress of the European Society of Cardiologists. Vienna, August 31, 1988.
3. Krepp HP. Anti-ischemic effects of phasic release nitroglycerin system. Official Satellite Symposium, Tenth Congress of the European Society of Cardiologists, Vienna, August 31, 1989.

FISH OIL BENEFITS QUESTIONABLE

Although a diet high in fish is associated with reduced risk of coronary heart disease, the National Research Council says that these benefits cannot be extrapolated to fish oil. In its report,[1] which complements the 1988 Surgeon General's Report on Nutrition and Health, the Council stated that "there is insufficient evidence that fish oil supplements are beneficial, and the absence of long-term adverse effects has not been established."

Manufacturers of fish oil had previously sought FDA-approved labeling that these supplements helped to control serum lipids and to reduce the risk of heart disease. However, studies to date have not borne this out.

The recommendation against fish oil supplements was part of the most comprehensive scientific analysis to date of potential health risks and benefits stemming from diet. The Council's overall message was that Americans can substantially reduce their risks of heart disease, cancer, and other chronic diseases by changing their eating habits.

Reference

1. National Research Council. *Diet and Health: Implications for Reducing Chronic Disease Risk*. Washington, DC, March 1989.

LINK BETWEEN DIURETICS, RENAL CANCER TO BE STUDIED

The question of whether diuretic use is associated with renal cell cancer will be explored in a large-scale human study, according to the National Cancer Institute (NCI), Bethesda MD.

The issue was raised by the results of two pilot studies, which show a five-fold increase of renal cancer among diuretic users, particularly women. The relationship "seems biologically plausible, since diuretics act directly on the renal tubules where renal cell cancers originate," according to a statement issued by NCI. The study will also evaluate other risk factors, including obesity, smoking, diet, occupational exposures, and genetic susceptibility.

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