

Bone Densitometry Said to Belong in Primary Care

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SAN FRANCISCO — Measuring bone mineral density in older patients is as justifiable as measuring lipids, Dennis M. Black, Ph.D., said at a meeting on osteoporosis sponsored by the University of California, San Francisco.

Lipid testing and treatment for high cholesterol is accepted as an integral part of primary care, but bone densitometry and treat-

ment for low bone density aren't as readily accepted, said Dr. Black, professor of epidemiology and biostatistics at the university. That's partly because measurements and treatments for osteoporosis came along well after tests and treatments for heart disease and its risk factors, he explained.

By the numbers, the value of bone density testing stacks up nicely against the value of lipid testing. Studies have shown that people with cholesterol measurements in the highest quartile have four

times the risk for heart disease compared with people whose cholesterol measurements are in the lowest quartile, Dr. Black said. Stratifying hip bone density by quartile, the risk for hip fracture increases 10-fold in people whose bone density is the lowest quartile compared with those in the highest quartile.

Heart disease risk increases from about 0.5% in the lowest low-density lipoprotein (LDL) quartile to about 4% in the highest lipid quartile. Hip fracture risk in-

creases from about 0.5% in the highest quartile of hip bone density to about 10% in the quartile with the least hip bone density.

Cost-effectiveness compares well, too, he added. Screening lipid levels in a 52-year-old woman and treating her for an LDL level greater than 160 mg/dL costs about \$400,000 per quality-adjusted life-year. Screening bone density in a 65-year-old woman and treating her with bisphosphonates for a T-score of -2.5 (suggesting osteoporosis) costs about \$30,000 per quality-adjusted life-year, "which is considered cost-effective," Dr. Black said.

The National Osteoporosis Foundation recommends bone mineral density testing for all women aged 65 years and older, and for postmenopausal women with a risk factor for osteoporosis.

The definition of risk factors for osteoporosis is a bit murky. Dr. Black includes postmenopausal women who have a history of fracture after menopause, whose mothers have a history of fracture

(especially hip fracture), who take steroids, or who have very low body weight. Very low body weight commonly is considered being below 125 pounds, but that depends somewhat on height, he added.

Lipid testing is accepted as an integral part of primary care but bone densitometry and treatment for low bone density aren't as readily accepted.

The U.S. Preventive Services Task Force recommends bone mineral density measurements for all women above age 60. Medicare covers bone density tests for women over age 65.

Dr. Black recently analyzed 16 years of follow-up data on women in the Study of Osteoporotic Fractures and found that a single measurement of hip bone density is a good predictor of fracture risk. In these white women with a mean age of 71 years, 5% of those in the highest quartile of hip bone density developed a hip fracture over the 16-year period, compared with 32% of women in the lowest quartile of hip bone density.

The difference was "fairly dramatic" he said. Women with the lowest quartile of hip bone density on a single measurement at the start of the study had an immediate increase in risk for hip fracture that continued as far out as 16 years.

"If it's not possible to repeat bone density measurements in 2, 3, or 4 years, you know that the (one) value that you have is still going to be predictive long term," he said.

There is a growing recognition that T scores shouldn't be used for peripheral measurements. If a patient brings you a printout from a wrist bone density measurement that she got in a pharmacy, use that as an opportunity to talk about bone health and maybe get a more central bone density measurement, he suggested. ■

ZOVIRAX® (acyclovir) Ointment 5% Begins to Comfort on Contact to Heal Herpes Fast

Symptoms With Primary First Episode of Genital Herpes*

Duration vs Placebo*

Itching	4.4 days shorter (P<0.01)
Pain	1.8 days shorter (P<0.05)
Lesion duration	4.6 days shorter (P<0.05)
Viral shedding from lesions	3.3 days shorter (P<0.001)

*Duration of itching: ZOVIRAX® Ointment (3.6 days) vs placebo (8.0 days) at primary first episode of genital herpes.

Duration of pain: ZOVIRAX® Ointment (5.2 days) vs placebo (7.0 days) at primary first episode of genital herpes.

Duration of lesion: ZOVIRAX® Ointment (11.2 days) vs placebo (15.8 days) at primary first episode of genital herpes.

Duration of viral shedding: ZOVIRAX® Ointment (2.3 days) vs placebo (5.6 days) at primary first episode of genital herpes.

Reference: 1. Corey L, Benedetti JK, Critchlow CW, et al. Double-blind controlled trial of topical acyclovir in genital herpes simplex virus infections. *Am J Med.* 1982;73:326-334.

ZOVIRAX® (acyclovir) Ointment 5%

INDICATIONS AND USAGE

ZOVIRAX (acyclovir) Ointment 5% is indicated in the management of initial genital herpes and in limited non-life-threatening mucocutaneous Herpes simplex virus infections in immunocompromised patients.

CONTRAINDICATIONS

ZOVIRAX Ointment 5% is contraindicated in patients who develop hypersensitivity to the components of the formulation.

WARNINGS

ZOVIRAX Ointment 5% is intended for cutaneous use only and should not be used in the eye.

PRECAUTIONS

General: The recommended dosage, frequency of applications, and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION). There are no data to support the use of ZOVIRAX Ointment 5% to prevent transmission of infection to other persons or prevent recurrent infections when applied in the absence of signs and symptoms. ZOVIRAX Ointment 5% should not be used for the prevention of recurrent HSV infections. Although clinically significant viral resistance associated with the use of ZOVIRAX Ointment 5% has not been observed, this possibility exists.

Drug Interactions: Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with ZOVIRAX Ointment 5%.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Systemic exposure following topical administration of acyclovir is minimal. Dermal carcinogenicity studies were not conducted. Results from the studies of carcinogenesis, mutagenesis, and fertility are not included in the full prescribing information for ZOVIRAX Ointment 5% due to the minimal exposures of acyclovir that result from dermal application. Information on these studies is available in the full prescribing information for ZOVIRAX Capsules, Tablets, and Suspension and ZOVIRAX for Injection.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Acyclovir was not teratogenic in the mouse, rabbit, or rat at exposures greatly in excess of human exposure. There are no adequate and well-controlled studies of systemic acyclovir in pregnant women. A prospective epidemiologic registry of acyclovir use during pregnancy was established in 1984 and completed in April 1999. There

were 749 pregnancies followed in women exposed to systemic acyclovir during the first trimester of pregnancy resulting in 756 outcomes. The occurrence rate of birth defects approximates that found in the general population. However, the small size of the registry is insufficient to evaluate the risk for less common defects or to permit reliable or definitive conclusions regarding the safety of acyclovir in pregnant women and their developing fetuses. Systemic acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether topically applied acyclovir is excreted in breast milk. Systemic exposure following topical administration is minimal. After oral administration of ZOVIRAX, acyclovir concentrations have been documented in breast milk in 2 women and ranged from 0.6 to 4.1 times the corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg per day. Nursing mothers who have active herpetic lesions near or on the breast should avoid nursing.

Geriatric Use: Clinical studies of ZOVIRAX Ointment did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Systemic absorption of acyclovir after topical administration is minimal (see CLINICAL PHARMACOLOGY).

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

In the controlled clinical trials, mild pain (including transient burning and stinging) was reported by about 30% of patients in both the active and placebo arms; treatment was discontinued in 2 of these patients. Local pruritus occurred in 4% of these patients. In all studies, there was no significant difference between the drug and placebo group in the rate or type of reported adverse reactions nor were there any differences in abnormal clinical laboratory findings.

Observed During Clinical Practice: Based on clinical practice experience in patients treated with ZOVIRAX Ointment in the US, spontaneously reported adverse events are uncommon. Data are insufficient to support an estimate to their incidence or to establish causation. These events may also occur as part of the underlying disease process. Voluntary reports of adverse events that have been received since market introduction include:

General: Edema and/or pain at the application site.

Skin: Pruritus, rash.

OVERDOSAGE

Overdosage by topical application of ZOVIRAX Ointment 5% is unlikely because of limited transcutaneous absorption (see CLINICAL PHARMACOLOGY).

DOSAGE AND ADMINISTRATION

Apply sufficient quantity to adequately cover all lesions every 3 hours, 6 times per day for 7 days. The dose size per application will vary depending upon the total lesion area but should approximate a one-half inch ribbon of ointment per 4 square inches of surface area. A finger cot or rubber glove should be used when applying ZOVIRAX to prevent autoinoculation of other body sites and transmission of infection to other persons. **Therapy should be initiated as early as possible following onset of signs and symptoms.**

HOW SUPPLIED

Each gram of ZOVIRAX Ointment 5% contains 50 mg acyclovir in a polyethylene glycol base.

It is supplied as follows:

15-g tubes (NDC 64455-993-94)

3-g tubes (NDC 64455-993-41)

Store at 15° to 25°C (59° to 77°F) in a dry place.

Manufactured by
GlaxoSmithKline
Research Triangle Park, NC 27709
for

BIOVAIL
Pharmaceuticals, Inc.

Bridgewater, NJ 08807

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