New JAOA section to focus on federal activities

With this issue, JAOA begins publication of a monthly "Federal Update" column. It will feature significant news from the federal government. The initial emphasis will be on Food and Drug Administration (FDA) material.

See Federal Update on page 281

The FDA items will be brief and related to regulatory activities. Of primary interest will be marketing approvals and labeling changes on new drugs. But, the section will also focus on FDA actions on new medical instrumentation, products resulting from developments in the biotechnology field, and problems with the food supply. Obviously, the everyday practices of osteopathic physicians are significantly affected by such information.

Because medical practice surely will become more sophisticated as it heads toward the 21st century, so may FDA activities expand to reflect these changes. We expect that this section will serve as a continuing conduit of important news.

Although the "Federal Update" section will emphasize the FDA, other health-related arms of the government will be featured periodically: the Centers for Disease Control, the Health Resources and Services Administration, the National Institutes of Health, and the Health Care Financing Administration.

The section represents the beginning of important changes to make JAOA more relevant to each osteopathic physician. We welcome your comments about it and your suggestions about how we can serve you better.

THOMAS WESLEY ALLEN, DO

Spring brings a breath of smoke-free air on campus

The movement toward a smoke-free environment continues. On the first day of spring, March 20, 1989, the University of Medicine and Dentistry of New Jersey and its School of Osteopathic Medicine will join four other colleges of osteopathic medicine which ban smoking in all of their facilities. These include the New York College of Osteopathic Medicine of the New York Institute of Technology, the Southeastern University of Health Sciences Southeastern College of Osteopathic Medicine, the Texas College of Osteopathic Medicine, and the University of Osteopathic Medicine and Health Sciences College of Osteopathic Medicine and Surgery.

A recent JAOA survey revealed that all but one of the remaining 11 colleges of osteopathic medicine ban smoking in common areas. However, smoking is allowed in restricted areas, such as private offices and lounges.

Kudos to these institutions that have gone "smoke free." Too many health-related institutions have failed to follow this lead which would illustrate their sincere commitment to health.

Health promotion and disease prevention are not new concepts to osteopathic physicians. Our philosophical foundations are based on the ancient tenet of prevention. We must take the lead in demonstrating health practices that benefit our patients, employees, and visitors alike.

The case against smoking remains clear. Let us accept the challenge to make every health care institution—from physicians' offices to medical schools—completely smoke-free.

THOMAS WESLEY ALLEN, DO

IN THE EVOLUTION OF AN ANGINA ATTACK

↓ *SUPPLY*
↑ *DEMAND*

↓ *LV FUNCTION*

ECG CHANGES

ANGINA

PROCARDIA indications: Patients with proven or suspected vasospastic angina, and patients with classic effort angina who remain symptomatic despite adequate doses of beta blockers and/or nitrates or who cannot tolerate these agents.

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PROCARDIA[®] (NIFEDIPINE) PREVENTS THE PAIN... PROTECTS THE ANGINA PATIENT AT EVERY STAGE

SUPPLY/DEMAND ● PROCARDIA increases myocardial oxygen supply and reduces demand

LV FUNCTION ● PROCARDIA helps to maintain or enhance parameters of left ventricular function¹

ECG CHANGES ● PROCARDIA decreases the incidence of ischemic ECG changes²

ANGINA ● PROCARDIA reduces episodes of both painful and painless ischemia^{3,4}

PROCARDIA[®]
(NIFEDIPINE) Capsules 10 mg and 20 mg

PREVENTS THE PAIN...
PROTECTS THE ANGINA PATIENT

Please see PROCARDIA[®] (nifedipine) brief summary on following page.

In the evolution of an angina attack,

PROCARDIA®

(NIFEDIPINE) Capsules 10 mg and 20 mg

PREVENTS THE PAIN... PROTECTS THE ANGINA PATIENT

References:

1. Vetovec GW, Parker VE: Acute electrophysiologic, hemodynamic and left ventricular effects of nifedipine and beta-blocker interactions: Maintenance of global and regional left ventricular wall motion. *Am J Cardiol* 1985; 55:21E-26E.
2. Oakley GDG, Fox KM, Dargie HJ, et al: Objective assessment of treatment in severe angina. *Br Med J* 1979; 2:1540.
3. Stone PH, Muller JE, Turi ZG, et al: Efficacy of nifedipine therapy in patients with refractory angina pectoris: Significance of the presence of coronary vasospasm. *Am Heart J* 1983; 106:644-652.
4. Data on file. Medical Department, Pfizer Laboratories, Pfizer Inc., New York.

Brief Summary

PROCARDIA® (nifedipine) Capsules

INDICATIONS AND USAGE: I. **Vasospastic Angina:** PROCARDIA (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PROCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

II. **Chronic Stable Angina (Classical Effort-Associated Angina):** PROCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in these patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PROCARDIA and beta-blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See WARNINGS.)

CONTRAINDICATIONS: Known hypersensitivity reaction to PROCARDIA.

WARNINGS: Excessive Hypotension: Although in most patients, the hypotensive effect of PROCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PROCARDIA together with a beta blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PROCARDIA and a beta blocker, but the possibility that it may occur with PROCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out. In PROCARDIA treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for PROCARDIA to be washed out of the body prior to surgery.

Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those who have severe obstructive coronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting PROCARDIA or at the time of dosage increase. The mechanism of this effect is not established.

Beta Blocker Withdrawal: Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PROCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PROCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PROCARDIA.

Congestive Heart Failure: Rarely, patients, usually receiving a beta blocker, have developed heart failure after beginning PROCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event.

PRECAUTIONS: General: Hypotension: Because PROCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PROCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. (See WARNINGS.)

Peripheral edema: Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PROCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

Laboratory tests: Rare, usually transient, but occasionally significant elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT and SGPT have been noted. The relationship to PROCARDIA therapy is uncertain in most cases,

...With an Excellent Side-Effects Profile

PROCARDIA side effects are usually mild and include dizziness, peripheral edema, nausea, weakness, headache and flushing (each in about 10% of patients); transient hypotension (about 5%); exacerbation of angina occurs rarely.

but probable in some. These laboratory abnormalities have rarely been associated with clinical symptoms, however, cholestasis with or without jaundice has been reported. Rare instances of allergic hepatitis have been reported.

Limited clinical studies have demonstrated a moderate but statistically significant decrease in platelet aggregation and increase in bleeding time in some PROCARDIA (nifedipine) patients. No clinical significance for these findings has been demonstrated. Positive direct Coombs test with/without hemolytic anemia has been reported.

Although PROCARDIA has been used safely in patients with renal dysfunction and has been reported to exert a beneficial effect in certain cases, rare, reversible elevations in BUN and serum creatinine have been reported in patients with pre-existing chronic renal insufficiency. The relationship to PROCARDIA therapy is uncertain in most cases but probable in some.

Drug Interactions: Beta-adrenergic blocking agents: (See INDICATIONS and WARNINGS.) Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PROCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates: PROCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Digitalis: Administration of PROCARDIA with digoxin increased digoxin levels in nine of twelve normal volunteers. The average increase was 45%. Another investigator found no increase in digoxin levels in thirteen patients with coronary artery disease. In an uncontrolled study of over two hundred patients with congestive heart failure during which digoxin blood levels were not measured, digitalis toxicity was not observed. Since there have been isolated reports of patients with elevated digoxin levels, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing PROCARDIA to avoid possible over- or under-digitalization.

Coumarin anticoagulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom PROCARDIA was administered.

Cimetidine: A study in six healthy volunteers has shown a significant increase in peak nifedipine plasma levels (80%) and area-under-the-curve (74%) after a one week course of cimetidine at 1000 mg per day and nifedipine at 40 mg per day. Ranitidine produced smaller, non-significant increases. If nifedipine therapy is initiated in a patient currently receiving cimetidine, cautious titration is advised.

Carcinogenesis, mutagenesis, impairment of fertility: Nifedipine was administered orally to rats for two years and was not shown to be carcinogenic. When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose. *In vivo* mutagenicity studies were negative.

Pregnancy: Pregnancy Category C. Nifedipine has been shown to be teratogenic in rats and embryotoxic in rats, mice and rabbits. There are no adequate and well controlled studies in pregnant women. PROCARDIA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

ADVERSE REACTIONS: The most common adverse events include dizziness or lightheadedness, peripheral edema, nausea, weakness, headache and flushing, each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PROCARDIA or concomitant antihypertensive medication. Additionally, the following have been reported: muscle cramps, nervousness, dyspnea, nasal and chest congestion, shortness of breath, diarrhea, constipation, gastrointestinal cramps, flatulence, inflammation, joint stiffness, shakiness, jitteriness, sleep disturbances, blurred vision, difficulties in balance, dermatitis, pruritus, urticaria, fever, sweating, chills, sexual difficulties, thrombocytopenia, anemia, leukopenia, purpura, allergic hepatitis, gingival hyperplasia, depression, paranoid syndrome, transient blindness at the peak of plasma level, erythromelalgia, and arthritis with ANA (+). Very rarely, introduction of PROCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

HOW SUPPLIED: PROCARDIA soft gelatin capsules are supplied in:
Bottles of 100: 10 mg (NDC 0069-2600-66) orange #260, 20 mg (NDC 0069-2610-66) orange and light brown #261. Bottles of 300: 10 mg (NDC 0069-2600-72) orange #260, 20 mg (NDC 0069-2610-72) orange and light brown #261. Unit dose packages of 100: 10 mg (NDC 0069-2600-41) orange #260, 20 mg (NDC 0069-2610-41) orange and light brown #261.

The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

More detailed professional information available on request.

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