

Omega-3 Supplement Fails to Cut Post-MI Events

BY MITCHEL L. ZOLER

ORLANDO — Daily treatment of recent myocardial infarction patients with an omega-3 fatty acid supplement for 1 year failed to show a beneficial effect on the rate of sudden cardiac death or other adverse cardiovascular events in a controlled trial of about 3,800 patients.

One reason why the fish oil-derived supplement did not have benefit may be

that most patients were on optimal medical therapy, including aspirin, clopidogrel, a statin, a beta-blocker, and an ACE inhibitor, Dr. Jochen Seneges said at the annual meeting of the American College of Cardiology. “There is almost nothing you can do on top of this—the event rates were so unexpectedly low,” said Dr. Seneges, a professor at the Stiftung Institute for Cardiac Infarction Research in Ludwighafen, Germany.

Despite the lack of benefit from an omega-3 fatty acid supplement in this large study, some experts said it is premature to change existing American Heart Association guidelines that call for a high level of oily fish consumption in people without documented coronary heart disease, and a high level of either oily fish consumption or a daily omega-3 fatty acid supplement in patients with documented coronary heart disease (Circulation 2006;114:82-96).

“I don’t think we’d change the recommendations at this point” said William S. Harris, Ph.D., director of the cardiovascular health research center at the University of South Dakota in Sioux Falls, and a member of the AHA nutrition committee that made the 2006 fish oil recommendations.

He noted that the treatment studied by Dr. Seneges lasted for just 1 year. “Two other major studies [of an omega-3 fatty acid supplement], GISSI-HF [Lancet 2008;372:1223-30] and JELIS [Lancet 2007;369:1090-8] showed the benefits accrue after the first year. I’d be willing to reconsider [the AHA recommendations] if a 3- to 5-year study showed the same thing” as Dr. Seneges’ current study, Dr. Harris said in an interview.

“I was a little surprised at the results [from Dr. Seneges’ study], but it is certainly possible that there are no additional effects of omega-3 fatty acid supplements on cardiovascular risk in patients with cardiovascular disease who are optimally treated,” said Emily B. Levitan, Sc.D., a cardiovascular epidemiologist at Beth Israel Deaconess Medical Center in Boston. The results from his study “are important, and help dispel the idea that omega-3 fatty acids are a panacea.”

The Randomized Trial of Omega-3 Fatty Acids on Top of Modern Therapy After Acute Myocardial Infarction (OMEGA) trial enrolled patients within 3-14 days after a myocardial infarction at 104 centers in Germany during October 2003–June 2007. In addition to their usual post-MI treatment, patients were randomized to receive 1 g daily of omega-3 fatty acids or placebo. The patients’ average age was 64, and about three-quarters were men.

Patients received a prescription formulation of omega-3 fatty acids (Zodin) marketed by the Norwegian company Pronova. The same formulation is licensed for U.S. sale as Lovaza (previously called Omacor) by GlaxoSmithKline. The study was funded in part by Pronova, and Dr. Seneges reported receiving compensation as a speaker for Pronova.

After a year of treatment, the rate of sudden cardiac death, the study’s primary end point, was an identical 1.5% in the two treatment arms, each with about 1,900 patients. The results also showed no significant differences between the active-treatment and control groups for other clinical measures, including total mortality, repeat MI, and stroke. The patients receiving omega-3 fatty acid did show a significant reduction in their serum level of triglycerides, a known benefit of omega-3 supplementation.

The unexpectedly low incidence of sudden cardiac death in the study cut its power for detecting a between-group difference from the planned 80% to 50%. Despite this, Dr. Seneges was skeptical as to whether a larger or longer study with greater power would have eventually produced a difference between the omega-3 and control groups because the events curves “were almost superimposable,” he said.

moxatag[™] (amoxicillin extended-release tablets) 775 mg

The following is a brief summary only; see full Prescribing Information for complete product information.

RX ONLY

INDICATIONS AND USAGE

MOXATAG is a once-daily amoxicillin product indicated for the treatment of tonsillitis and/or pharyngitis secondary to *Streptococcus pyogenes* (*S. pyogenes*), more commonly referred to as ‘strep throat’, in adults and pediatric patients 12 years or older.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of MOXATAG and other antibacterial drugs, MOXATAG should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

DOSAGE AND ADMINISTRATION

The recommended dose of MOXATAG is 775 mg once daily taken within 1 hour of finishing a meal for 10 days. MOXATAG should be taken approximately the same time every day. The full 10-day course of therapy should be completed for effective treatment of tonsillitis and/or pharyngitis secondary to *S. pyogenes*.

Do not chew or crush tablet.

CONTRAINDICATIONS

MOXATAG is contraindicated in patients with known serious hypersensitivity to amoxicillin or to other drugs in the same class or patients who have demonstrated anaphylactic reactions to beta-lactams.

WARNINGS AND PRECAUTIONS

Anaphylaxis and Hypersensitivity Reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with MOXATAG, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens. If an allergic reaction occurs, MOXATAG should be discontinued and appropriate therapy instituted.

Clostridium difficile Associated Diarrhea (CDAD)

Clostridium difficile Associated Diarrhea (CDAD) has been reported with nearly all antibacterial agents, including amoxicillin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued.

Superinfections

The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur, amoxicillin should be discontinued and appropriate therapy instituted.

Mononucleosis Rash

A high percentage of patients with mononucleosis who receive ampicillin develop an erythematous skin rash. Thus, ampicillin-class antibiotics should not be administered to patients with mononucleosis.

Development of Drug-Resistant Bacteria

Prescribing amoxicillin in the absence of proven or strongly suspected bacterial infection or treating prophylactically is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

False-Positive Urinary Glucose Tests

High urine concentrations of ampicillin may result in false-positive reactions when testing for the presence of glucose in urine using Clinistix[®], Benedict’s Solution or Fehling’s Solution. Since this effect may also occur with amoxicillin, it is recommended that glucose tests based on enzymatic glucose oxidase reactions (such as Clinistix[®]) be used.

ADVERSE REACTIONS

In a controlled Phase 3 trial, 302 adult and pediatric patients (≥12 years) were treated with MOXATAG 775 mg once-daily for 10 days. The most frequently reported adverse reactions (>1%) which were suspected or probably drug-related are vaginal yeast infection (2.0%), diarrhea (1.7%), nausea (1.3%) and headache (1.0%).

DRUG INTERACTIONS

Probenecid

Probenecid decreases the renal tubular secretion of amoxicillin.

Concurrent use

of MOXATAG and probenecid may result in increased and prolonged blood levels of amoxicillin.

Other Antibiotics

Chloramphenicol, macrolides, sulfonamides, and tetracyclines may interfere with the bacterial effects of penicillin. This has been demonstrated *in vitro*; however, the clinical significance of this interaction is not well documented.

Oral Contraceptives

As with other antibiotics, amoxicillin may affect the gut flora, leading to lower estrogen reabsorption and potentially resulting in reduced efficacy of combined oral estrogen/progesterone contraceptives.

USE IN SPECIFIC POPULATIONS

Pregnancy: Teratogenic Effects. Pregnancy Category B.

Reproduction studies have been performed in mice and rats at doses up to 2000 mg/kg (12.5 and 25 times the human dose in mg/m²) and have revealed no evidence of impaired fertility or harm to the fetus due to amoxicillin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

It is not known whether use of amoxicillin in humans during labor or delivery has immediate or delayed adverse effects on the fetus, prolongs the duration of labor, or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.

Nursing Mothers

Penicillins have been shown to be excreted in human milk. Amoxicillin use by nursing mothers may lead to sensitization of infants. Caution should be exercised when amoxicillin is administered to a nursing woman.

Pediatric Use

The safety and effectiveness of MOXATAG in pediatric patients 12 years of age and older have been established based on results of a clinical trial that included adults and pediatric patients (12 years or older). The safety and effectiveness of MOXATAG in pediatric patients younger than 12 years has not been established.

Geriatric Use

This drug is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Renal Impairment

MOXATAG has not been studied in patients with renal impairment; however, a reduction of amoxicillin dose is generally recommended for patients with severe renal impairment. Therefore, MOXATAG is not recommended for use in patients with severe renal impairment (CrCl <30 mL/min) or patients on hemodialysis.

OVERDOSAGE

In case of overdose, discontinue medication, treat symptomatically, and institute supportive measures as required. If the overdose is very recent and there is no contraindication, an attempt at emesis or other means of removal of drug from the stomach may be performed.

Interstitial nephritis resulting in oliguric renal failure has been reported in a small number of patients after overdosage with amoxicillin.

Crystalluria, in some cases leading to renal failure, has also been reported after amoxicillin overdosage in adult and pediatric patients.

Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of amoxicillin.

For additional information about overdose treatment, call a poison control center (1-800-222-1222).

HOW SUPPLIED/STORAGE AND HANDLING

MOXATAG tablets for oral administration are provided as blue film-coated, oval-shaped tablets that contain 775 mg of amoxicillin. The tablets are printed with “MB-111” on one side in black edible ink. MOXATAG is packaged in bottles as follows:

Presentation	NDC Code
Bottles of 30	11042-142-03

Storage

Store at 25° C (77° F); excursions permitted to 15–30° C (59–86° F) [See USP Controlled Room Temperature.]

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Germantown, Maryland 20876 USA

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