

Hospital Type, Location Influence Quality of Care

BY ALICIA AULT
Contributing Writer

Academic hospitals in general and nonacademic hospitals located in the Northeast and Midwest appear to offer greater quality than nonteaching facilities or those in other geographic regions for certain conditions, according to a recent study by Ashish K. Jha, M.D., and colleagues at the Harvard School of Public Health.

VYTORIN® (ezetimibe/simvastatin)

VYTORIN: There are insufficient data for the safe and effective use of VYTORIN in pediatric patients. (See Ezetimibe and Simvastatin below.)

Ezetimibe: The pharmacokinetics of ezetimibe in adolescents (10 to 18 years) have been shown to be similar to that in adults. Treatment experience with ezetimibe in the pediatric population is limited to 4 patients (9 to 17 years) with homozygous sitosterolemia and 5 patients (11 to 17 years) with HoFH. Treatment with ezetimibe in children (<10 years) is not recommended.

Simvastatin: Safety and effectiveness of simvastatin in patients 10-17 years of age with heterozygous familial hypercholesterolemia have been evaluated in a controlled clinical trial in adolescent boys and in girls who were at least 1 year post-menarche. Patients treated with simvastatin had an adverse experience profile generally similar to that of patients treated with placebo. **Doses >40 mg have not been studied in this population.** In this limited controlled study, there was no detectable effect on growth or sexual maturation in the adolescent boys or girls, or any effect on menstrual cycle length in girls. Adolescent females should be counseled on appropriate contraceptive methods while on therapy with simvastatin (see CONTRAINDICATIONS and PRECAUTIONS, Pregnancy). Simvastatin has not been studied in patients younger than 10 years of age, nor in pre-menarchal girls.

Geriatric Use

Of the patients who received VYTORIN in clinical studies, 792 were 65 and older (this included 176 who were 75 and older). The safety of VYTORIN was similar between these patients and younger patients. Greater sensitivity of some older individuals cannot be ruled out. (See CLINICAL PHARMACOLOGY, Special Populations and ADVERSE REACTIONS.)

ADVERSE REACTIONS

VYTORIN has been evaluated for safety in more than 3800 patients in clinical trials. VYTORIN was generally well tolerated.

Table 1 summarizes the frequency of clinical adverse experiences reported in ≥2% of patients treated with VYTORIN (n=1236) and at an incidence greater than placebo regardless of causality assessment from 3 similarly designed, placebo-controlled trials.

Table 1*
Clinical Adverse Events Occurring in ≥2% of Patients Treated with VYTORIN and at an Incidence Greater than Placebo, Regardless of Causality

Body System/ Organ Class Adverse Event	Placebo (%)	Ezetimibe 10 mg (%)	Simvastatin** (%)	VYTORIN** (%)
	n=311	n=302	n=1234	n=1236
<i>Body as a whole – general disorders</i>				
Headache	6.4	6.0	5.9	6.8
<i>Infection and infestations</i>				
Influenza	1.0	1.0	1.9	2.6
Upper respiratory tract infection	2.6	5.0	5.0	3.9
<i>Musculoskeletal and connective tissue disorders</i>				
Myalgia	2.9	2.3	2.6	3.5
Pain in extremity	1.3	3.0	2.0	2.3

* Includes 2 placebo-controlled combination studies in which the active ingredients equivalent to VYTORIN were coadministered and 1 placebo-controlled study in which VYTORIN was administered.

** All doses.

Post-marketing Experience: The adverse reactions reported for VYTORIN are consistent with those previously reported with ezetimibe and/or simvastatin.

Ezetimibe: Other adverse experiences reported with ezetimibe in placebo-controlled studies, regardless of causality assessment: *Body as a whole – general disorders:* fatigue; *Gastrointestinal system disorders:* abdominal pain, diarrhea; *Infection and infestations:* infection viral, pharyngitis, sinusitis; *Musculoskeletal system disorders:* arthralgia, back pain; *Respiratory system disorders:* coughing.

Post-marketing Experience: The following adverse reactions have been reported in post-marketing experience, regardless of causality assessment: Hypersensitivity reactions, including angioedema and rash; elevated creatine phosphokinase; elevations in liver transaminases; hepatitis; thrombocytopenia; pancreatitis; nausea; cholelithiasis; cholecystitis; and, very rarely, myopathy/rhabdomyolysis (see WARNINGS, Myopathy/Rhabdomyolysis).

Simvastatin: Other adverse experiences reported with simvastatin in placebo-controlled clinical studies, regardless of causality assessment: *Body as a whole – general disorders:* asthenia; *Eye disorders:* cataract; *Gastrointestinal system disorders:* abdominal pain, constipation, diarrhea, dyspepsia, flatulence, nausea; *Skin and subcutaneous tissue disorders:* eczema, pruritus, rash.

The following effects have been reported with other HMG-CoA reductase inhibitors. Not all the effects listed below have necessarily been associated with simvastatin therapy. *Musculoskeletal system disorders:* muscle cramps, myalgia, myopathy, rhabdomyolysis, arthralgias.

Nervous system disorders: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, dizziness, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy, psychic disturbances.

Ear and labyrinth disorders: vertigo.

Psychiatric disorders: anxiety, insomnia, depression, loss of libido.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included 1 or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, dermatomyositis, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, eosinophilia, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal system disorders: pancreatitis, vomiting.

Hepatobiliary disorders: hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma.

Metabolism and nutrition disorders: anorexia.

Skin and subcutaneous tissue disorders: alopecia, pruritus. A variety of skin changes (eg, nodules, discoloration, dryness of skin/mucous membranes, changes to hair/nails) have been reported.

Reproductive system and breast disorders: gynecostasia, erectile dysfunction.

Eye disorders: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Abnormalities: elevated transaminases, alkaline phosphatase, γ -glutamyl transpeptidase, and bilirubin; thyroid function abnormalities.

Laboratory Tests

Marked persistent increases of serum transaminases have been noted (see WARNINGS, Liver Enzymes). About 5% of patients taking simvastatin had elevations of CK levels of 3 or more times the normal value on 1 or more occasions. This was attributable to the noncardiac fraction of CK. Muscle pain or dysfunction usually was not reported (see WARNINGS, Myopathy/Rhabdomyolysis).

Concomitant Lipid-Lowering Therapy

In controlled clinical studies in which simvastatin was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with simvastatin or cholestyramine.

Adolescent Patients (ages 10-17 years)

In a 48-week controlled study in adolescent boys and girls who were at least 1 year post-menarche, 10-17 years of age with heterozygous familial hypercholesterolemia (n=175), the safety and tolerability profile of the group treated with simvastatin (10-40 mg daily) was generally similar to that of the group treated with placebo, with the most common adverse experiences observed in both groups being upper respiratory infection, headache, abdominal pain, and nausea (see CLINICAL PHARMACOLOGY, Special Populations and PRECAUTIONS, Pediatric Use).

The authors found that academic hospitals performed slightly better than nonacademic facilities in treating heart attack and heart failure, but underperformed in the case of pneumonia. Not-for-profit hospitals significantly outscored for-profits in all measures in those conditions, they said.

However, the data do not support the idea that “‘good’ hospitals are easy to identify or are consistent in their performance across conditions,” the authors pointed out.

The study was the first to use national hospital data submitted as part of the Hospital Quality Alliance (N. Engl. J. Med. 2005;353:265-74).

The HQA is a joint effort of the Centers for Medicare and Medicaid Services, the Joint Commission on Accreditation of Healthcare Organizations, the American Hospital Association, and consumer groups, including the AARP. Under the Medicare Modernization Act, hospitals have financial incentives to report quarterly to CMS on a specific set of quality indicators. Initial data became publicly available in November 2004, which led Dr. Jha and colleagues to conduct their analysis.

In all, 3,558 hospitals reported on their performance in the first half of 2004, cit-

ing quality measures for acute myocardial infarction, heart failure, and pneumonia. To be included, each hospital had to report on at least 25 discharged patients. Of the participating hospitals, 16% were for-profit, 8% were members of the Council of Teaching Hospitals, and 62% were in urban settings.

The authors measured the mean performance for the 3,558 hospitals and variability of performance across the country.

They also sought to determine whether a high level of performance in treating one disease translated into equally good care in the other conditions. They investigated whether profit status, number of beds, geographic area, and academic involvement affected performance.

The heart attack measures included whether aspirin and β -blockers were given within 24 hours of admission and at discharge and if ACE inhibitors were given to patients with left ventricular systolic dysfunction. For heart failure, the measures included assessment of left ventricular function and whether an ACE inhibitor was given. For pneumonia, hospitals were measured on the timing of initial antibiotics, vaccination, and assessment of oxygenation.

The hospitals' scores reflected the pro-

portion of patients who satisfied the criterion for the performance measure.

Overall, hospitals did best at conducting an oxygenation assessment in pneumonia patients; the mean performance score was 98%, plus or minus 5%. Hospitals had their lowest scores in rates of vaccinations for pneumonia: 43%, plus or minus 27%.

There were huge variations among regions. For the pneumonia composite score, there was a 23% difference between top-ranked Oklahoma City and bottom-ranked San Bernardino, Calif. There was a 12% difference between high and low performers on heart attack, and a 21% difference between the top and bottom for heart failure.

The authors found that high performance scores for acute myocardial infarction predicted equally good performance in heart failure, but not for pneumonia. For instance, 73% of the hospitals that were in the top decile of scores for acute MI were in the top quartile for heart failure, and less than 1% were in the bottom quartile. But only 33% of the hospitals in that top decile for acute MI were in the top quartile for pneumonia.

Limitations of the study include the fact that the investigators limited their evaluation to only 10 measures of the quality of care for 3 clinical conditions, and the results focused on process measures rather than patient outcomes, the authors noted.

Most of the Joint Commission Performance Measures Show Improvement at 2-Year Mark

BY ALICIA AULT
Contributing Writer

A set of process measures established by the Joint Commission on Accreditation of Healthcare Organizations has helped hospitals to improve performance, according to a study of the first 2 years of implementation.

The study, by Scott C. Williams, Psy.D., and his colleagues at the commission, found that improvements were made in 15 of 18 standardized measures, with no deterioration of quality in any of those areas (N. Engl. J. Med. 2005;353:255-64).

In 2002, the commission began measuring performance in the 18 measures at 3,377 of 4,644 hospitals accredited by the organization. Nonparticipating hospitals either did not offer the services being measured or had an average daily census of fewer than 10 patients. The facilities could choose to submit data on at least two of these: acute myocardial infarction, heart failure, pneumonia, and pregnancy and related conditions.

They did not track the pregnancy measures, as two of the measures applied to rare events, and the third, vaginal birth after cesarean section, is controversial, Dr. Williams and his associates said.

The study covered hospitals that submitted data from the third quarter of 2002

to the second quarter of 2004, with 3,087 of the 3,377 hospitals initially identified as study participants. Of those, 1,473 submitted data on heart attack measures, 1,946 on heart failure, and 1,797 on pneumonia.

Of the 18 measures, 17 looked at death in the hospital after acute myocardial infarction; the other 17 assessed processes of care. There was no improvement in the death measure, but the authors said most of the improvements in the process measures being assessed would not have influenced mortality. There was no significant drop in the mean time to thrombolysis for patients with acute MI or in mean time to give antibiotics for pneumonia.

For acute MI, researchers looked at measures such as whether aspirin was given within 24 hours of admission and prescribed at discharge, whether an ACE inhibitor was prescribed at discharge for patients with left ventricular systolic dysfunction, and the mean time from arrival to thrombolysis or percutaneous coronary intervention.

For heart failure, hospitals were tracked on whether they had given patients smoking cessation counseling and discharge instructions on medication, diet, weight, and worsening of symptoms, and whether an ACE inhibitor was prescribed at discharge for patients with left ventricular systolic dysfunction.

For pneumonia, the commission monitored whether there was an oxygenation assessment within 24 hours of admission and whether pneumococcal screening, vaccination, or both had been given at discharge, or if blood specimens were cultured before starting an antibiotic.

By the end of the study period, more than 90% of MI patients at most hospitals received aspirin at admission. Although only 74% of patients received ACE inhibitors at discharge at the lowest performing hospitals, 83% received them at the highest performing facilities.

The biggest improvement was seen in offering smoking cessation counseling. Rates went from a range of 1%-7% at the lowest performing hospitals at baseline to a range of 57%-68% at the study's end. At high-performing facilities, however, rates dropped from an 80%-98% range at baseline to a range of 74%-85% at the end.

Even after improvement, pneumococcal vaccination rates were still low, ranging from 35% in the lowest performing hospitals to 66% at the high end.

The investigators noted that one potential drawback of the study—its reliance on self-reported data—could introduce bias.

And, they said, the picture could change as public reporting of hospital data becomes more prevalent and pay for performance spreads.

 MERCK/Schering-Plough Pharmaceuticals

Manufactured for: MERCK/Schering-Plough Pharmaceuticals
North Wales, PA 19454, USA
©Merck/Schering-Plough Pharmaceuticals, 2005.
All rights reserved.

20506478(11)603-VYT