

Initiative Improved Knowledge of COPD Care

BY SUSAN LONDON

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

VANCOUVER, B.C. – A live, interactive, case-based educational initiative improved primary care physicians' knowledge of chronic obstructive pulmonary disease, according to study results reported at the meeting.

In a cross-sectional study of 50 primary care physicians who participated in the initiative and 50 similar nonparticipants, the former were more likely to know that alveolar destruction is a pathophysiologic feature of COPD (94% vs. 74%) and that women have greater susceptibility to the harmful effects of smoking (90% vs. 54%), according to Dr. Nicola A. Hanania and his coinvestigators.

Additionally, when presented with case vignettes, the participants were more likely to recognize the presence of COPD in dyspnea patients (90% vs. 74%).

"Even though this was sort of a one-time ... cross-sectional survey, we believe that educational initiatives such as this one may at least improve the knowledge about COPD – both diagnosis and management," commented Dr. Hanania, an associate professor of medicine at Baylor College of Medicine, Houston.

Explaining the need for primary care-focused efforts, he noted that "the majority of COPD patients are [seen] in the primary care arena."

But statistics show that "COPD remains under-recognized and underdiagnosed in about 50% of the population out there, not only in the United States but in other countries as well. It also remains undertreated," even though the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines now stress that it is a treatable disease.

The initiative studied – called Improving COPD Patient Outcomes: Breaking Down the Barriers to Optimal Care – was designed to improve primary care providers' knowledge and competency in the guideline-based diagnosis, staging, and management of COPD, Dr. Hanania said.

It consisted of a series of live half-day meetings conducted over a 3-month period that included short lec-

tures, a video on correct use of inhaler devices, and small-group workshops that incorporated detailed case discussions and hands-on demonstrations and practice in the use of spirometry.

A total of 769 physicians attended the meetings. The investigators assessed the initiative's effectiveness with a case vignette-based survey, given to a randomly selected subset of 50 participants and 50 nonparticipants with similar demographics and practice characteristics.

The number of patients with COPD seen weekly was 11 for participants and 15 for nonparticipants. The mean number of years in practice was 28 and 24, respectively. And both groups were about equally divided between family physicians and internal medicine physicians. Participants were somewhat more likely to be in solo practice (45% vs. 38%) or work in a government facility (25% vs. 0%), and less likely to be in group practice (31% vs. 58%).

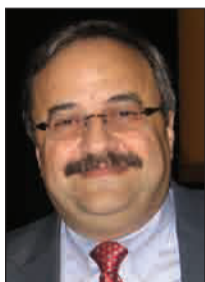
Survey results showed that in the area of diagnosis, the participants were more likely than the nonparticipants to recognize COPD in case vignettes of patients with dyspnea (90% vs. 74%, $P = .007$) and to be aware of the greater susceptibility of women compared with men to the harmful effects of smoking (90% vs. 54%, P less than .001).

Also, when asked which of several pathophysiologic features was one of COPD, participants were more likely to correctly answer alveolar destruction (94% vs. 74%, $P = .007$). (The other options were muscular deconditioning, synovial inflammation, and increased ventricular filling pressure.)

While the groups did not differ significantly in terms of how likely they were to use spirometry for diagnosis and staging of COPD, participants were more likely than nonparticipants to indicate that difficulty in obtaining spirometry results in the office setting was a very significant barrier to COPD management (27% vs. 12%). "Maybe they acknowledged that it is an important tool, but they cannot do it," he commented.

The groups were statistically indistinguishable with respect to their approaches to caring for patients with repeated exacerbations and improving adherence, and their selection of appropriate maintenance therapy.

The survey also asked about barriers to managing



Participants were 50% more likely than nonparticipants to provide evidence-based, guideline-driven COPD care.

DR. HANANIA

VITALS

Major Finding: Participants were more likely than nonparticipants to know that alveolar destruction is a pathophysiologic feature of COPD (94% vs. 74%), to know that women are more susceptible than men to the harmful effects of smoking (90% vs. 54%), and to correctly identify COPD in patients with dyspnea (90% vs. 74%).

Data Source: A cross-sectional survey of 50 primary care physicians who participated in a COPD educational initiative and 50 similar primary care physicians who did not.

Disclosures: The initiative meetings were supported by an educational grant from Novartis Pharmaceuticals. Dr. Hanania did not have any conflicts of interest related to the study.

COPD, according to Dr. Hanania.

In addition to difficulty with spirometry, the groups were similarly likely to rate as very significant a patient's nonadherence to a recommendation to stop smoking, the complexity of the medical regimen, and a lack of clarity about the staging of COPD severity.

A calculation of the initiative's quality of education index showed that participants were 50% more likely than nonparticipants to provide evidence-based, guideline-driven COPD care, Dr. Hanania reported. "We estimate that participation in this half-day program can potentially improve the care of many patients per week, but this needs to be further tested," he commented.

"We did not attempt to look at long-term [outcomes] – retention of knowledge or practice change – which are very important," Dr. Hanania acknowledged. But a similar, ongoing initiative, being conducted by the ACCP, is currently assessing impact on real-life practice.

That initiative is including not only physicians but also physician assistants and nurse practitioners, Dr. Hanania said. "In our primary care setting in the U.S., nonphysician extenders – PAs, nurse practitioners – play a major role in encountering COPD, and those are people we like to target." Furthermore, their role will likely increase if health care reform proceeds and primary care physicians are overwhelmed by demand.

The initiative meetings were supported by an educational grant from Novartis Pharmaceuticals. Dr. Hanania had no relevant conflicts of interest. ■

Healthy People 2020 Adds Sleep Health, COPD to Goals

BY SHARON WORCESTER

The Department of Health and Human Services launched its Healthy People 2020 goals on Dec. 2, and among the objectives set forth in its "ambitious, yet achievable" 10-year agenda for improving the nation's health are substantial improvements in sleep health, respiratory disease outcomes, and levels of tobacco use.

Sleep Health

Sleep health is a new topic in the Healthy People initiative. The main focus is on increasing public knowledge of how adequate sleep and treatment of sleep disorders lead to improvements in health, productivity, wellness, quality of life, and safety on the roads and in the workplace.

"Poor sleep health is a common problem, with 25% of U.S. adults reporting in-

sufficient sleep or rest at least 5 out of every 30 days," the report states.

The public health burden is substantial, and awareness of the problem is lacking; thus, Healthy People 2020 seeks to provide a "well-coordinated strategy to improve sleep-related health."

Objectives are to:

- ▶ Increase the proportion of persons with symptoms of obstructive sleep apnea who seek medical care (from 25.5% to 28%).
- ▶ Reduce the rate of vehicular crashes per 100 million miles traveled that are due to drowsy driving (from 2.7 to 2.1).
- ▶ Increase the proportion of students in grades 9-12 who get sufficient sleep, defined as 8 hours or more on an average school night (from 30.9% to 33.2%).
- ▶ Increase the proportion of adults who get sufficient sleep, defined as 8 or more

hours for those aged 18-21 years, and 7 or more hours for those aged 22 years and older (from 69.6% to 70.9%).

Respiratory Disease

The respiratory disease category focuses on asthma and chronic obstructive pulmonary disease, and the main goal is to "promote respiratory health through better prevention, detection, treatment, and education efforts," according to the report, which states that asthma affects 23 million people in the United States and COPD affects 13.6 million U.S. adults.

The cost to the health care system is high, and society pays through higher health insurance rates and lost productivity and tax dollars. Annual expenditures for asthma alone are estimated at nearly \$21 billion.

Healthy People 2020 seeks to reduce asthma-related deaths, hospitalizations, emergency department visits, activity limitations, and missed school or work days, and to increase the proportion of asthma sufferers who receive appropriate care. Improved surveillance at the state level is another goal.

For example, goals for 2020 in regard to asthma-related deaths include reductions from 11.0 to 6.0 deaths per 1 million people aged 35-64 years, and from 43.3 to 22.9 per 1 million people aged 65 and older. Goals regarding annual asthma-related hospitalization include a reduction from 41.4 to 18.1 per 10,000 children under age 5, from 11.1 to 8.6 per 10,000 people aged 5-64 years, and from 25.3 to 20.3 per 10,000 adults aged 65 years and older.

Goals regarding appropriate asthma care include specific improvements in the

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number of patients who receive written asthma management plans, instructions for inhaler use, education about appropriate response to an asthma episode, and follow-up visits each year.

COPD-related objectives include reducing associated activity limitations, deaths, hospitalizations, and emergency department visits, and improving diagnosis among adults with abnormal lung function.

Specific goals include a reduction from 23.2 to 18.7 in the percentage of adults

with COPD aged 45 years and older who experience activity limitations from COPD, and a reduction from 112.4 to 98.5 in the number of COPD-related deaths per 10,000 people aged 45 years and older.

Tobacco Use

Tobacco use is not a new topic in the Healthy People initiative, but ongoing efforts to reduce use are needed, according to the report, because tobacco use remains the single most preventable cause of death and disease in the United States. About 443,000 Americans die from to-

bacco-related illnesses each year, and for every 1 who dies, 20 more suffer with at least one serious tobacco-related illness.

Healthy People 2020 seeks to "provide a framework for action to reduce tobacco use to the point that it is no longer a public health problem for the nation."

Based on more than 4 decades of evidence, it is clear, according to the report, that the toll tobacco use takes on families and communities can be significantly reduced by fully funding tobacco control programs, increasing the prices of tobacco products, enacting smoke-free policies, controlling access to products,

reducing tobacco advertising and promotion, implementing antitobacco media campaigns, and encouraging and assisting users to quit.

Healthy People 2020 addresses tobacco use prevalence, health system changes, and social and environmental changes. Among the key goals for adults are:

- ▶ Reducing the percentage of adult cigarette smokers (from 20.6% to 12.0%).
- ▶ Reducing the percentage of adult users of smokeless tobacco (from 2.3% to 0.3%).
- ▶ Reducing the percentage of adult cigar smokers (from 2.2% to 0.2%).

In adolescents, goals include reducing the percentage of those who used tobacco in the past month from 26% to 21%, and reducing the percentages who said they used cigarettes, smokeless tobacco, and cigars in the past month from 19.5% to 16%, from 8.9% to 6.9%, and from 14% to 8%, respectively.

Initiation of tobacco use among children, adolescents, and young adults is also addressed, with a goal of reducing initiation of tobacco use in general among those aged 12-17 years from 7.7% to 5.7%, and among those aged 18-25 years from 10.8% to 8.8%.

Other goals regarding tobacco use include increasing smoking cessation attempts by adult and adolescent smokers, and increasing smoking cessation during pregnancy.

Numerous goals are also set in regard to health system changes, and social and environmental changes.

For example, the report calls for increases in comprehensive Medicaid insurance coverage for nicotine dependency treatment, increased tobacco screening and cessation counseling in health care settings, reductions in the proportion of nonsmokers exposed to secondhand smoke, increases in the proportion of persons covered by indoor worksite policies that prohibit smoking, and increases in tobacco-free environments in school facilities and at school events.

Additionally, efforts should be made to eliminate state laws that preempt stronger local tobacco control laws, to reduce illegal sales to minors, and to reduce exposure to tobacco advertising and promotion among 6th-12th graders.

Also, federal and state taxes on tobacco products should be increased, the report states.

Healthy People 2020 has been in development since 2007. A panel of health experts drew on input from public and private health officials, preventive medicine experts, representatives from 2,000 health organizations, and thousands of public comments.

The initiative expands upon topics from Healthy People 2010, includes a number of new topic areas, and will incorporate the Internet and other technology media in getting the message out about disease prevention and health promotion.

The ultimate goals, according to HHS officials, are to avoid preventable diseases in the first place and to promote improved quantity and quality of life for all Americans.

Hypertriglyceridemia: Patients with fasting serum TG levels above 500 mg/dL were excluded from the diabetes clinical trials. In the phase 3 diabetes trials, 637 (63%) patients had baseline fasting serum TG levels less than 200 mg/dL, 261 (25%) had baseline fasting serum TG levels between 200 and 300 mg/dL, 111 (11%) had baseline fasting serum TG levels between 300 and 500 mg/dL, and 9 (1%) had fasting serum TG levels greater than or equal to 500 mg/dL. The median baseline fasting TG concentration for the study population was 172 mg/dL; the median post-treatment fasting TG was 195 mg/dL in the WELCHOL group and 177 mg/dL in the placebo group. WELCHOL therapy resulted in a median placebo-corrected increase in serum TG of 5% (p=0.22), 22% (p<0.001), and 18% (p<0.001) when added to metformin, insulin and sulfonylureas, respectively [See Warnings and Precautions (5.2) and Clinical Studies (14.2) in the full prescribing information]. In comparison, WELCHOL resulted in a median increase in serum TG of 5% compared to placebo (p=0.42) in a 24-week monotherapy lipid-lowering trial [See Clinical Studies (14.1) in the full prescribing information].

Treatment-emergent fasting TG concentrations ≥500 mg/dL occurred in 4.1% of WELCHOL-treated patients compared to 2.0% of placebo-treated patients. Among these patients, the TG concentrations with WELCHOL (median 604 mg/dL; interquartile range 538-712 mg/dL) were similar to that observed with placebo (median 644 mg/dL; interquartile range 574-724 mg/dL). Two (0.4%) patients on WELCHOL and 2 (0.4%) patients on placebo developed TG elevations ≥1000 mg/dL. In all WELCHOL clinical trials, including studies in patients with type 2 diabetes and patients with primary hyperlipidemia, there were no reported cases of acute pancreatitis associated with hypertriglyceridemia. It is unknown whether patients with more uncontrolled, baseline hypertriglyceridemia would have greater increases in serum TG levels with WELCHOL [See Contraindications (4) and Warnings and Precautions (5.2)].

Cardiovascular adverse events: During the diabetes clinical trials, the incidence of patients with treatment-emergent serious adverse events involving the cardiovascular system was 3% (17/566) in the WELCHOL group and 2% (10/562) in the placebo group. These overall rates included disparate events (e.g., myocardial infarction, aortic stenosis, and bradycardia); therefore, the significance of this imbalance is unknown.

Hypoglycemia: Adverse events of hypoglycemia were reported based on the clinical judgment of the blinded investigators and did not require confirmation with fingerstick glucose testing. The overall reported incidence of hypoglycemia was 3.0% in patients treated with WELCHOL and 2.3% in patients treated with placebo. No WELCHOL treated patients developed severe hypoglycemia.

6.2 Post-marketing Experience

The following additional adverse reactions have been identified during post-approval use of WELCHOL. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Drug Interactions with concomitant WELCHOL administration include:

- Increased seizure activity or decreased phenytoin levels in patients receiving phenytoin. Phenytoin should be administered 4 hours prior to WELCHOL.
- Reduced International Normalized Ratio (INR) in patients receiving warfarin therapy. In warfarin-treated patients, INR should be monitored frequently during WELCHOL initiation then periodically thereafter.
- Elevated thyroid-stimulating hormone (TSH) in patients receiving thyroid hormone replacement therapy. Thyroid hormone replacement should be administered 4 hours prior to WELCHOL [See Drug Interactions (7)].

Gastrointestinal Adverse Reactions

Bowel obstruction (in patients with a history of bowel obstruction or resection), dysphagia or esophageal obstruction (occasionally requiring medical intervention), fecal impaction, pancreatitis, abdominal distension, exacerbation of hemorrhoids, and increased transaminases.

Laboratory Abnormalities

Hypertriglyceridemia

7 DRUG INTERACTIONS

Table 4 lists the drugs that have been tested in *in vitro* binding or *in vivo* drug interaction studies with colessevelam and/or drugs with postmarketing reports consistent with potential drug-drug interactions. Orally administered drugs that have not been tested for interaction with colessevelam, especially those with a narrow therapeutic index, should also be administered at least 4 hours prior to WELCHOL. Alternatively, the physician should monitor drug levels of the co-administered drug.

**Table 4
Drugs Tested in *In Vitro* Binding or *In Vivo* Drug Interaction Testing or With Post-Marketing Reports**

Drugs with a known interaction with colessevelam ^a	cyclosporine ^c , glyburide ^a , levothyroxine ^a , and oral contraceptives containing ethinyl estradiol and norethindrone
Drugs with postmarketing reports consistent with potential drug-drug interactions when coadministered with WELCHOL	phenytoin ^a , warfarin ^b
Drugs that do not interact with colessevelam based on <i>in vitro</i> or <i>in vivo</i> testing	cephalexin, ciprofloxacin, digoxin, warfarin ^b , fenofibrate, lovastatin, metformin, metoprolol, pioglitazone, quimidine, repaglinide, valproic acid, verapamil

^a Should be administered at least 4 hours prior to WELCHOL

^b No significant alteration of warfarin drug levels with warfarin and WELCHOL coadministration in an *in vivo* study which did not evaluate warfarin pharmacodynamics (INR). [See Post-marketing Experience (6.2)]

^c Cyclosporine levels should be monitored and, based on theoretical grounds, cyclosporine should be administered at least 4 hours prior to WELCHOL.

In an *in vivo* drug interaction study, WELCHOL and warfarin coadministration had no effect on warfarin drug levels. This study did not assess the effect of WELCHOL and warfarin coadministration on INR. In postmarketing reports, concomitant use of WELCHOL and warfarin has been associated with reduced INR. Therefore, in patients on warfarin therapy, the INR should be monitored before initiating WELCHOL and frequently enough during early WELCHOL therapy to ensure that no significant alteration in INR occurs. Once the INR is stable, continue to monitor the INR at intervals usually recommended for patients on warfarin. [See Post-marketing Experience (6.2)]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B. There are no adequate and well-controlled studies of colessevelam use in pregnant women. Animal reproduction studies in rats and rabbits revealed no evidence of fetal harm. Requirements for vitamins and other nutrients are increased in pregnancy. However, the effect of colessevelam on the absorption of fat-soluble vitamins has not been studied in pregnant women. This drug should be used during pregnancy only if clearly needed.

In animal reproduction studies, colessevelam revealed no evidence of fetal harm when administered to rats and rabbits at doses 50 and 17 times the maximum human dose, respectively. Because animal reproduction studies are not always predictive of human response, this drug should be used in pregnancy only if clearly needed.

8.3 Nursing Mothers

Colessevelam hydrochloride is not expected to be excreted in human milk because colessevelam hydrochloride is not absorbed systemically from the gastrointestinal tract.

8.4 Pediatric Use

The safety and effectiveness of WELCHOL as monotherapy or in combination with a statin were evaluated in children, 10 to 17 years of age with heFH [See Clinical Studies (14.1) in the full prescribing information]. The adverse reaction profile was similar to that of patients treated with placebo. In this limited controlled study, there were no significant effects on growth, sexual maturation, fat-soluble vitamin levels or clotting factors in the adolescent boys or girls relative to placebo [See Adverse Reactions (6.1)].

Due to tablet size, WELCHOL for Oral Suspension is recommended for use in the pediatric population. Dose adjustments are not required when WELCHOL is administered to children 10 to 17 years of age. WELCHOL has not been studied in children younger than 10 years of age or in pre-menarchal girls.

8.5 Geriatric Use

Primary Hyperlipidemia: Of the 1350 patients enrolled in the hyperlipidemia clinical studies, 349 (26%) were ≥65 years old, and 58 (4%) were ≥75 years old. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Type 2 Diabetes Mellitus: Of the 1128 patients enrolled in the four diabetes studies, 249 (22%) were ≥65 years old, and 12 (1%) were ≥75 years old. In these trials, WELCHOL 3.8 g/day or placebo was added onto background anti-diabetic therapy. No overall differences in safety or effectiveness were observed between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Hepatic Impairment

No special considerations or dosage adjustments are recommended when WELCHOL is administered to patients with hepatic impairment.

8.7 Renal Impairment

Type 2 Diabetes Mellitus: Of the 1128 patients enrolled in the four diabetes studies, 696 (62%) had mild renal insufficiency (creatinine clearance [CrCl] 50-80 mL/min), 53 (5%) had moderate renal insufficiency (CrCl 30-50 mL/min), and none had severe renal insufficiency (CrCl <30 mL/min), as estimated from baseline serum creatinine using the Modification of Diet in Renal Disease (MDRD) equation. No overall differences in safety or effectiveness were observed between patients with CrCl <50 mL/min (n=53) and those with a CrCl ≥50 mL/min (n=1075).

10 OVERDOSAGE

Doses of WELCHOL in excess of 4.5 g/day have not been tested. Because WELCHOL is not absorbed, the risk of systemic toxicity is low. However, excessive doses of WELCHOL may cause more severe local gastrointestinal effects (e.g., constipation) than recommended doses.



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