

Obesity Doesn't Worsen Child's Asthma Outcomes

BY DIANA MAHONEY
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BOSTON — Obesity has little impact on the disease-related outcomes of asthma in children, despite the fact that being overweight is an established risk factor for the respiratory condition, reported Umit B. Emre, M.D.

Unlike adults, in whom obesity is associated with higher asthma morbidity, obese or overweight children with asthma

have symptoms and morbidity that are "more or less comparable" with those of normal-weight children, Dr. Emre said in a presentation at the annual meeting of the American College of Allergy, Asthma, and Immunology.

Dr. Emre and colleagues at Beth Israel Medical Center in New York analyzed data from 85 children and adolescents who were evaluated for asthma at a community-based pediatric pulmonary practice from 1999 to 2003. Asthma was the primary diagnosis for all of the children included in the analysis, and there were no other diseases present. Baseline characteristics, including age, gender, and race, were similar across the group.

The investigators classified the children by asthma severity and by weight using standard body mass index measures. With respect to asthma severity, 32 of the patients were classified as having intermittent asthma, 42 had persistent mild asthma, and 11 had persistent moderate-severe asthma. In terms of weight status, 31 were classified as normal weight, 21 were overweight, and 33 were obese.

The disease severity proportions did not

differ between normal, overweight, and obese children, said Dr. Emre. Drug use, emergency treatments, and lung-function test performance were also similar across the board.

Asthma severity, while not predicted by obesity, was itself a predictor of controller therapy use and emergency department visit and/or hospitalization. "As could be expected, rates of drug use and emergency care were highest for children classified as having persistent moderate to severe asthma," Dr. Emre commented. "Weight classification was not a determinant for either of these outcomes."

Weight also was not independently correlated with lung function in these patients. The mean forced expiratory volume in 1 second for both the overweight/obese and normal weight groups was approximately 83% of predicted flow, and the mean peak expiratory flow in midlung volume for

both was approximately 77% of predicted volume, independent of body mass index.

The study may be limited by selection bias in that the patients were not randomly selected, and all those included had more serious asthma than that which might be seen in the normal pediatric practice, making it more difficult to detect differences that might be related to weight. "Or it may just be that the link becomes more significant over time, as other problems associated with obesity become more problematic, possibly exacerbating asthma symptoms," he said.

To better understand the full impact of obesity on asthma in young patients, Dr. Emre and colleagues have undertaken a prospective study to address the inherent limitations to a retrospective analysis. "We're looking at different asthma-related disease outcomes, including quality of life, and are trying to detect any weight-based differences," he noted.

Obese or overweight children with asthma have symptoms and morbidity that are 'more or less comparable' with those of normal-weight children.

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.

Genetic Use: Of the patients who received VYTORIN™ (ezetimibe/simvastatin) 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 (%) n=311	Ezetimibe 10 mg (%) n=302	Simvastatin** (%) n=1234	VYTORIN** (%) n=1236
Body as a whole – general disorders				
Headache	6.4	6.0	5.9	6.8
Infection and infestations				
Influenza	1.0	1.0	1.9	2.6
Upper respiratory tract infection	2.6	5.0	5.0	3.9
Musculoskeletal and connective tissue disorders				
Myalgia	2.9	2.5	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.

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; increased CPK; elevations in liver transaminases; hepatitis; thrombocytopenia; pancreatitis; nausea; cholelithiasis; cholecystitis; and, very rarely in patients taking an HMG-CoA reductase inhibitor with ezetimibe, 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, arthralgia.

Nervous system disorders: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresthesia), 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: gynecomastia, 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).

Asthma Challenges Teens' Ability to Fit In

BY DIANA MAHONEY
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BOSTON — Having asthma can make adolescent patients feel different from their peers, "and there is nothing worse to an adolescent than feeling different," according to Alysa Brimer, a medical student at the University of Missouri, Kansas City.

In addition to the negative social consequences of asthma—including lack of participation in school-based clubs, athletics, and social events—this negative self-perception may decrease patients' compliance with their medication regimens.

Creating social clubs and group athletic activities exclusively for asthmatic youths may go a long way toward mitigating patients' damaged self-esteem and increasing the likelihood of treatment compliance, Ms. Brimer said in a presen-

tation at the annual meeting of the American College of Allergy, Asthma, and Immunology.

Ms. Brimer and colleagues at Children's Mercy Hospital in Kansas City, Missouri, investigated the factors that make asthmatic youths feel different from their healthy friends, and hypothesized that groups made up of asthmatic peers might improve their self-perception.

The investigators reviewed data from an ongoing survey of children with asthma who were 8-18 years old.

The anonymous questionnaire, which was offered to patients seen in the primary care and adolescent clinics at the hospital, included multiple-choice and open-ended questions designed to explore the youths' feelings about their disease and its effect on their lives.

One-third of the respondents had negative feelings about their asthma, and nearly 40% reported that their diagnosis made

them feel different from their healthy peers.

"Outward reminders of their asthma made the kids particularly self-conscious," Ms. Brimer stated. "Many of them—more than one third—said they felt uncomfortable using an inhaler in front of their friends."

Although nearly 94% of the youth said they enjoyed participating in group activities, especially recreational sports, 45% said they felt restricted or excluded from school activities because of their asthma. "This tells us that maybe we should be looking for ways to incorporate the social preference for team or group activities into an intervention, such as an asthma club," said Ms. Brimer. "The desire to belong to a group is a powerful motivator, especially among adolescents. There may be ways to use that desire to help asthmatic youth adjust to the disease and its treatment regimen."

Vaccination Opportunities Often Missed for Asthmatic Children

WASHINGTON — Missed opportunities for immunizing children with asthma happen to occur frequently during the influenza season, Kevin J. Dombkowski, Dr.P.H., and his colleagues reported in a poster presentation at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

In the study funded by the Michigan Department of Community Health, administrative claims and immunization registry records were analyzed for 5,993 children aged 5-18 years with persistent asthma who were continuously enrolled in the Michigan Medicaid program during 2001-2003.

In each year studied, 79% of the children had at least one office visit during the influenza season.

Yet, influenza vaccination had been documented for only 14% during the 2001-2002 season and 18% during the 2002-2003 season, with just 7% vaccinated in both seasons, said Dr. Dombkowski, senior research associate in the division of general pediatrics, University of Michigan, Ann Arbor.

Among children with no evidence of influenza vaccination, 77% had at least one missed opportunity in the 2001-2002 flu season; 75% had a missed opportunity in the 2002-2003 season.

During both seasons, nearly all children (95%) with a missed opportunity had made at least one "sick" visit to an outpatient provider, and 22% had at least one preventive medicine visit, Dr. Dombkowski said in an interview with FAMILY PRACTICE NEWS.

A majority of the missed opportunities (55%) occurred during October-November, considered the optimal period for influenza vaccination, while 77% occurred prior to February, the historical peak of flu season.

"There's a lot of opportunity for improvement out there," he said.

—Miriam E. Tucker

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