Statins, Vitamin D, and COPD

Luca Mascitelli, Francesca Pezzetta and Mark R. Goldstein

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asthma showed up in higher proportions. In our study, for every patient, and it is no surprise that GERD and cough-variant illnesses. So in any persistent lower respiratory tract illness, we performed the same thorough, nonselective investigation on every patient, and it is no surprise that GERD and cough-variant asthma showed up in higher proportions. In our study, for reliability, several of the investigations/treatments required patient cooperation, so our patient group was somewhat older.

Quality of Workup: Chang’s group performed a selective workup, introducing a selection bias and making the results of prevalence less thorough. Gastroesophageal reflux disease (GERD) itself is linked to higher prevalence of lower respiratory tract infections and illnesses. So in any persistent lower respiratory tract illness, it becomes important to exclude GERD. Unlike Chang’s workup, we performed the same thorough, nonselective investigation on every patient, and it is no surprise that GERD and cough-variant asthma showed up in higher proportions. In our study, for reliability, several of the investigations/treatments required patient cooperation, so our patient group was somewhat older.

Wet Cough May Represent Bacterial Causes: In our setting, such patients would be filtered by the pediatricians and not reach us, the subspecialists. Additionally, a fine study by Mello et al. has shown that neither the character nor the timing of cough is a good predictor of the cause.

The Comment on Dry Cough Is Provocative: A number of our patients had dry cough of >16-weeks duration, even 30-weeks duration, despite interventions. How much longer would one be expected to wait for spontaneous resolution of dry cough? The natural history of short-duration dry cough will obviously be different from an already long-duration dry cough. Our patients had already crossed the 12-weeks mark without resolution of symptoms. Obviously, none of our children had cough scores of zero after 12 weeks.

The Visual Analog Scale: The visual analog scale is a validated tool used to quantify cough very effectively in our setting as well as several other settings. The patient is his or her own control. It is, at worst, a semiojective measure. This tool works well in our setting but may not be appropriate in other settings, where cough diaries may work better.

Briefly, our data were obtained in a very thorough manner in a typical urban/suburban population in the United States with high-quality pediatric care. Thus, the population referred for subspecialty care may be different from a rural population in another country. Finally, the learning objective of this dialogue for the readership should be to most certainly understand the population characteristics in any study before alloting merit and relevance of the data to their own practice. We thank Chang and colleagues for prompting this discussion.

Vikram Khosho, MD, PhD
Dean Edell, MD, MPH, FCCP
New Orleans, LA

Affiliations: From the West Jefferson Medical Center.
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Correspondence to: Vikram Khosho, MD, PhD, Pediatric Specialty Center, West Jefferson Medical Center, 1111 Medical Center Blvd, South 650, Marrero, LA 70072; e-mail: vkhosho@ sbeglobal.net

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To the Editor:

Janda and colleagues, in their review recently published in CHEST (September 2009), highlighted that statin drugs can have a beneficial role in patients with COPD through their pleiotropic antiinflammatory and immune modulatory effects. We suggest that the same immunomodulatory action might be reached in a safer and cheaper way by adequate vitamin D levels.

Vitamin D status is usually divided into three categories, based on serum 25-hydroxyvitamin D [25(OH)D] levels: “deficient” (≤ 20 ng/mL), “insufficient” (20.1-29.9 ng/mL), and “sufficient” (≥ 30 ng/mL). Serum 25(OH)D levels have been decreasing significantly for more than a decade, resulting in a majority of the US population being vitamin D-insufficient. Indeed, according to the current definition, it is estimated that more than 1 billion people worldwide have impaired serum levels of vitamin D. Patients with COPD should be considered at high risk of vitamin D insufficiency because of reduction of outdoor activity, increased glucocorticoids-induced catabolism, impaired activation as a consequence of renal dysfunction, and a lower storage capacity in muscle and fat due to wasting. Indeed, it has recently been found that patients with COPD, without chronic use of systemic glucocorticoids, have increased risk for osteoporosis and low levels of vitamin D, which is correlated with the severity of disease. Furthermore, the peak in winter and early spring, when 25(OH)D levels are lowest, of exacerbations of autoimmune diseases as well as exacerbations of COPD are in line with the hypothesis that vitamin D, COPD, and adaptive immunity are linked.

On the other hand, in clinical practice, muscle complaints are a frequent side effect of statin therapy: statins may exacerbate muscle performance and increase falling risk in elderly subjects. In fact, an important systemic consequence of COPD is muscle weakness, and this is associated with an increased risk of mortality. Vitamin D plays a role in influencing skeletal muscle function, with deficiency resulting in muscle weakness reversed with vitamin D supplementation. Furthermore, vitamin D supplementation has also been shown to reduce the risk of falls among elderly individuals, and it has been suggested that vitamin D deficiency might explain much of the observed muscle performance decline and
increase in falls among elderly statin-treated patients. Therefore, because of the cost and side effects of statins drugs, their questionable benefit in the elderly (particularly in the primary prevention of cardiovascular disease), and the increased risk of osteopenia and osteoporosis in COPD, patients with COPD should have adequate levels of vitamin D before considering statin therapy.

Luca Mascitelli, MD
Udine, Italy
Francesca Pezzetta, MD
Tolmezzo, Italy
Mark R. Goldstein, MD
Bonita Springs, FL

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Response
To the Editor:

We thank Mascitelli and colleagues for their response to our article (September 2009). They suggested that because of the side effects of statin drugs, their questionable benefit in the elderly population, and the increased risk of osteopenia and osteoporosis in COPD, patients with COPD should have adequate levels of vitamin D before considering statin therapy.

Vitamin D therapy in COPD is an intriguing consideration. Given that vitamin D is inexpensive and safe, it would be a desirable treatment option if proven to be effective. We agree that there is an increased risk of osteopenia and osteoporosis in patients with COPD and that patients with vitamin D deficiency should be supplemented for prevention of this. However, the benefit of vitamin D on outcomes in COPD remains to be proven, and currently the effectiveness of this therapy is inferential and based on population analyses. We do not know at the present time that vitamin D has the same effect on COPD outcomes such as exacerbation rates, pulmonary function, exercise capacity, COPD mortality, and all-cause mortality as statins may have, as illustrated in our systematic review. Furthermore, there is no evidence that vitamin D therapy would obviate the reported benefits of statin therapy.

Vitamin D has been shown to decrease falls and improve muscle strength in the general population, and we acknowledge that statins do have side effects, including myopathy and rhabdomyolysis that may worsen respiratory muscle function in patients with COPD. However, these side effects of statin therapy are very rare. The incidence of statin-induced myopathy, defined as any muscle symptom (pain, tenderness, or weakness) and accompanied by a creatine kinase concentration >10 times normal, is one in 10,000 patients, whereas that of rhabdomyolysis is three in 100,000 patients. Specifically in patients with COPD, the only randomized controlled trial identified in our review (Lee et al) reported that no patients in their study had a statin-induced adverse event.

Mascitelli and colleagues raise an interesting point and highlight the need to consider innovative and multifaceted approaches to the treatment of patients with COPD. We would suggest that vitamin D therapy, as with statin therapy, in COPD requires further investigation but as complementary lines of thought rather than parallel or exclusionary ones.

Surinder Janda, MD
Kirily Park, MD
Mark FitzGerald, MB, MD
Mahyar Etminan, PharmD, MSc, (Epid)
John Swiston, MD, FCCP
Vancouver, BC, Canada

Affiliation: From the Department of Medicine, University of British Columbia.

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Correspondence to: John Swiston, MD, FCCP, Division of Respiratory, University of British Columbia, Vancouver General Hospital, 2775 Laurel St, Seventh Floor, Vancouver, BC V5Z 1M9 Canada; e-mail: swiston@interchange.ubc.ca

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