Effective Health Care

Sleep Apnea in the Symptomatic Gout Population

Results of Topic Selection Process

The topic, *Sleep Apnea in the Symptomatic Gout Population*, focuses on the relationship between gout and sleep apnea. The nominator theorizes that sleep apnea may cause acute gout flares, and is interested in whether the resolution of sleep apnea mitigate the incidence of gout flares.

The relationship between sleep apnea and gout is not well understood. Two studies have examined the association between sleep apnea and gout. A cross-sectional study[1] found that after controlling for confounding variables (i.e., diabetes, hypertension, ischemic heart disease, diuretic drug use) there was a significant association between gout and sleep disorders *other than sleep apnea*. However, more recently, a large population-based cohort study[2] found that individuals with sleep apnea had a 50% increased risk of gout. The authors conclude that "findings call for the investigation of the potential benefits of correcting sleep apnea–induced hypoxia on the risk of hyperuricemia and gout flares."

This area of research is currently undeveloped, and primary research is needed to investigate the benefits of interventions for sleep apnea on the incidence of gout flares; thus, it cannot be addressed by a systematic review. No further activity will be undertaken on this topic.

References:

1. Roddy, E., Muller, S., Hayward, R., Mallen, C. (2013). The association of gout with sleep disorders: a cross sectional study in primary care. *BMC Musculoskeletal Disorders*, 14: 119-124.
2. Zhang, Y., Peloquin, C., Dubreuil, M., Roddy, E., Lu, N., Neogi, T., Choi, H. (2015). Sleep Apnea and the Risk of Incident Gout: A Population-Based, Body Mass Index–Matched Cohort Study. *Arthritis and Rheumatology*, 67; 12: 3298-3302.

Nomination

Topic Number: 0667 **Received On:** 04/18/2016

Topic Name: Sleep Apnea in the Symptomatic Gout Population

Nominator: Individual

Nomination Summary: The nominator is interested in a clinical study of the association between gout and sleep apnea, in order to improve treatments for both conditions. The nominator has specific interest in the prevalence of sleep apnea in the symptomatic gout population relative to the general population. The nominator theorizes that sleep apnea may trigger gout attacks; thus the treatment and resolution of sleep apnea may mitigate gout attacks. The nominator also theorizes that gout could be a risk factor for sleep apnea, and could potentially used to identify those with sleep apnea. The main outcome of interest would be the

development of a useful biomarker for sleep apnea, allowing for wide-spread screening before effects become irreversible. The nominator is also interested in “the demonstration of a new nonpharmaceutical therapy for treatment of gout.” The nominator asserts that this topic is important because the link between gout and sleep apnea is often overlooked and under-researched. The nominator hopes that an AHRQ systematic review will identify knowledge gaps and inform research priorities in the gout population.

Key Questions from Nomination:

Key Question 1: In adult patients with gout, what is the prevalence of sleep apnea in the symptomatic gout population relative to its prevalence of gout flares?

Key Question 2: In adult patients with gout and comorbid sleep apnea, does the resolution of sleep apnea mitigate the incidence of gout flares?

Key Question 3: In adult patients with gout, how can the presence of symptomatic gout (defined as the formation of monosodium urate crystals in body tissues and fluids) or asymptomatic gout best be used to screen for sleep apnea?

Original Nomination

Topic Suggestion Description

Date submitted: 11/21/2012

Briefly describe a specific question, or set of related questions, about a health care test or treatment that this program should consider.

Topic summary: a clinical study of the association of gout with sleep apnea, leading to improved treatment of both diseases.

For adult patients with gout: what is the prevalence of sleep apnea in the symptomatic gout population relative to its prevalence in the general population; to what degree does resolution of sleep apnea mitigate the incidence of gout flares; and how can the presence of gout (defined as the formation of monosodium urate crystals in body tissues and fluids), whether symptomatic or not, best be used to screen for sleep apnea.

Relevant groups: a randomly selected cohort of gout patients for the study.

The anticipated benefits would accrue to gout patients as well as the large majority of individuals with sleep apnea who remain undiagnosed.

Anticipated health-related benefits:
(1) Of primary importance would be the development of a straightforward useful biomarker for sleep apnea, allowing wide-spread screening for this disease before its life-threatening, often irreversible, consequences develop.
(2) Of secondary importance would be the demonstration of a new nonpharmaceutical therapy for treatment of gout.

Importance

Describe why this topic is important.

One aspect of gout which is too often overlooked in guidelines and in practice is that most gout flares are initiated during sleep. The sleep connection has been known at least since Dr. Thomas Sydenham wrote about it in 1683. A recent study by Dr. Hyon Choi et al [1] confirms Dr. Sydenham's observation. It is a very important clue to the pathogenesis of gout whether symptomatic or not.

Many gout flares are probably a direct result of sleep apnea, and overcoming the sleep apnea can cure the gout. Although Kelley's Textbook of Rheumatology lists respiratory insufficiency as a cause of acidosis leading to hyperuricemia, the hypoxemia of sleep apnea actually has three effects which can lead to an overnight gout flare in short order. Effect #1 is cellular catabolism in which ATP degradation is accelerated, culminating irreversibly in the transient cellular generation of excess uric acid fed into the blood, faster than any food would cause [2,3]. Effect #2 is transient hypercapnia and acidosis, so that the blood can hold less uric acid in solution [2,3]. Effect #3 is a long term deterioration of the kidneys' glomerular filtration rate so that removal of uric acid from the blood is slowed[4]. Thus, with sleep apnea there is an abrupt increase in the influx of uric acid in the blood, slowed efflux, and abruptly reduced storage capacity -- perfect storm conditions for monosodium urate precipitation. Furthermore, after awakening and normal

breathing is restored, the first two effects dissipate so that a blood test taken during waking hours misses their peaks. And if monosodium urate has precipitated recently, then the measurement of serum uric acid is greatly undervalued.

Gout have missed this connection for so long, especially since gout has been reported to have so many of the same comorbidities already known to be consequences of long-term untreated sleep apnea (eg., cardiovascular diseases, diabetes, kidney disease, hypertension.) One of the first steps for treating gout should be screening and diagnosis for sleep apnea, followed by treatment of the sleep apnea where indicated. I know from my own experience and the experiences of others that overcoming sleep apnea can prevent additional inflammatory gout flares immediately and completely. Effects #1 and #2 don't occur, and Effect #3 gradually reverses over several months of effective treatment for sleep apnea. More importantly, gout is an early warning of sleep apnea, which when heeded can lead to the early treatment of sleep apnea (which is readily treatable), thereby greatly reducing the risk for the development of sleep apnea's later developing life-threatening consequences. Detecting gout, even without clinical symptoms, by ultrasound or dual energy computed tomography leading to the diagnosis and treatment of sleep apnea can save lives along with saving joints.

[1] Choi HK, Niu J, et al, Nocturnal risk of gout attacks, Arthritis Rheumatol. 2015 Feb; 67(2): 555-62.
[2] Hasday, JD, Grum CM, Nocturnal increase of urinary uric acid: creatinine ratio. A biochemical correlate of sleep associated hypoxemia, Am Rev Respir Dis. 1987 Mar; 135(3): 534-8.
[3] Grum CM. Cells in crisis. Cellular bioenergetics and inadequate oxygenation in the intensive care unit, Chest. 1992 Aug; 102(2): 329-30.
[4] Ahmed SB, Ronksley PE, et al. Nocturnal hypoxia and loss of kidney function, PLoS One. 2011 Apr 29; 6(4): e19029.stigmas.

Potential Impact

How will an answer to your research question be used or help inform decisions for you or your group?

I am not a medical researcher. The publication of results of this research should provide enormous benefit for medical practitioners and the general public, as described in the answer to question 1.

Technical Experts and Stakeholders

Are there health care-focused, disease-focused, or patient-focused organizations or technical experts that you see as being relevant to this issue? Who do you think we should contact as we consider your nomination? This information will not influence the progress of your suggestion through the selection process, but it may be helpful to those considering your suggestion for further development.

1. Richard Johnson, MD, Chief of the Division of Renal Diseases and Hypertension at the University of Colorado in Denver. richard.johnson@ucdenver.edu
2. Daniel Gottlieb, MD. Director, Sleep Disorders Center VA Boston Healthcare System. gottlieb@bu.edu

3. John Sotos, MD. Cardiologist. sotos99@yahoo.com

Nominator Information

Other Information About You: (optional)

Please choose a description that best describes your role or perspective: (you may select more than one category if appropriate)

Patient/Consumer, self-taught student of the relationship between sleep apnea and gout

Please tell us how you heard about the Effective Health Care Program

Website search

May we contact you if we have questions about your nomination?

No.