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INSIDE

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Failing Doctors, Failing Hearts

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

Professor of Medicine, University of Kentucky;
Director, Sleep Disorders Center, Samaritan Hospital, Lexington

Dr. Phillips is a consultant for Cephalon, and serves on the speakers bureaus for Resmed and Respironics.

Synopsis: *Obstructive sleep apnea is associated with an increased risk of incident heart failure in community-dwelling middle-aged and older men, but not in women.*

Source: Gottlieb DJ, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure. The Sleep Heart Health Study. *Circulation* 2010 July 12; Epub ahead of print.

THIS REPORT IS FROM THE WELL-ESTABLISHED SLEEP HEART HEALTH Study (SHHS), now in its 15th year. For this report, the authors analyzed about 8.5 years of data from 4422 of the original cohort. All the participants included in this report had acceptable in-home polysomnograms (sleep studies) and were free of coronary heart disease or heart failure at baseline. As is true of most of the SHHS analyses, the apnea plus hypopnea indices (AHIs) were calculated based largely on oximetry (the criteria to score both apneas and hypopneas required at least a 4% fall in oxygen saturation). Coronary heart disease (CHD) was defined as the first occurrence of myocardial infarction, CHD death, or coronary revascularization procedure over the period of follow-up. Incident heart failure was simply defined as the first documentation of heart failure during this time. Because the people included in this report were part of a study designed to assess occurrence, risk, and outcomes of cardiac disease, the events reported are probably reasonably precise. The investigators also had extensive information about medications, lifestyle, and medical illness.

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The median AHI was 2.7 in women and 6.2 in men. Not surprisingly, increasing severity of obstructive sleep apnea (OSA) was associated with male sex, higher BMI, higher systolic blood pressure, lower HDL cholesterol, and higher prevalence of hypertension and diabetes. Although 24% of men and 11% of women had OSA that most clinicians would choose to treat (AHI of at least 15) on the baseline research polysomnogram, only about 19% of those with an AHI of 15 or higher had a physician diagnosis of OSA when asked about this 5 years after the research polysomnogram. Only 79 survey respondents (2.1%) reported any kind of treatment for OSA.

With regard to heart failure, there was a strong association of AHI with incident heart failure in men but not in women, even after adjusting for age, race, smoking, and BMI. Further adjustment for many relevant covariates did not affect this finding much. The higher the AHI, the greater the risk of incident heart failure; each 10-unit increase in AHI corresponded to an increased hazard ratio for heart failure of 1.13 for men.

On the other hand, the association of AHI with CHD was not strong, and was not statistically significant after adjustment for confounders, although it was significant for men younger than 70 who had an AHI of 15 or higher.

■ COMMENTARY

There are several relevant points about this study. The first is that the risk of heart disease associated with OSA found in this analysis is weaker than that reported in several previous clinic-based studies, and may be negligible for women. Does that mean that we should stop telling patients that untreated sleep apnea is a risk factor for heart disease? I don't think so. Remember, this study comes from a population-based cohort; many of these individuals were presumably asymptomatic. There is some evidence that the association of sleep disordered breathing with hypertension and other cardiovascular disease is stronger in individuals who report daytime sleepiness (the cardinal symptom of OSA) than in those who do not.[1] Patients who present with symptoms and have OSA on their sleep study are likely to be different (and at higher risk) than those who are asymptomatic and found incidentally on a population-based study. Randomized trials of CPAP efficacy might help to resolve this dilemma, but withholding CPAP therapy from sleepy patients with OSA over a long period of time is unethical because of the risk of driving accidents and the effectiveness of CPAP in relieving sleepiness. So, we are left with long-term observational trials of clinical populations. While patients who do not use CPAP are a poor control group, since they are also likely to be non-adherent in general, long-term observational studies comparing patients on CPAP therapy with untreated patients have consistently shown significantly increased cardiovascular mortality and morbidity in the untreated group.[2] And we do have randomized controlled studies of CPAP on blood pressure, demonstrating modest but significant reductions in blood pressure, even in non-sleepy people.[3] What I really wish these authors had done was to match the (very few) patients who were diagnosed with sleep apnea and who used CPAP with other members of the cohort with similar demographics and severity of illness to see if they fared better.

Another consideration is that the mean age of this cohort was 62; several studies have demonstrated that untreated OSA is more deadly in younger than in older people.[4] It's possible that this older cohort, perhaps because of survivor bias, had already outlived the worst that OSA could do.

One question that arises from this paper is whether it's "worth it" to treat OSA in women. This particular study, which focused on CHD and heart failure, did not find convincing evidence that untreated OSA is a risk for these conditions in women, and the risk was not strong for people older than age 70. On the other hand, CHD and heart failure are not the only adverse outcomes of OSA to consider. OSA also increases the risk of car crash[5] and hypertension, gender and age notwithstanding.

The finding of this study that surprised me most was the fact that only about 2% of these patients were treated for sleep apnea, although 24% of men and 11% of women met the diagnostic criteria (AHI of at least 15) at baseline. It's not clear where the ball is being dropped, but certainly some large part of this failure is lack of action on the part

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Questions & Comments
Please call **Paula Cousins**, Senior Managing Editor, at (404) 262-5488.

of physicians. This study adds convincing evidence that untreated OSA increases the risk of heart failure, a chronic and miserable condition, in middle-aged men. In this cohort, most of these prime candidates for CPAP treatment went untreated. We need to start taking sleep apnea to heart. ■

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β-blockers as Cardiopulmonary Agents: The Benefits May Not Be Limited to CVD

ABSTRACT & COMMENTARY

By Rahul Gupta, MD, MPH, FACP

Clinical Assistant Professor, West Virginia University School of Medicine, Charleston, WV

Dr. Gupta reports no financial relationship to this field of study.

Synopsis: *In a large, well-designed observational study of patients with COPD, treatment with β-blockers during a mean follow-up period of 7.2 years was found not only to reduce the risk of exacerbations, but also to improve survival.*

Source: Rutten FH, et al. β-blockers may reduce mortality and risk of exacerbations in patients with chronic obstructive pulmonary disease. *Arch Intern Med* 2010;170:880-887.

Chronic obstructive pulmonary disease (COPD) is a disease of epidemic proportions worldwide. In the United States, it causes more than 120,000 deaths each year, and is currently the fourth leading cause of mortality. Additionally, due to the chronic nature of the disease and frequent exacerbations in individual patients, there is resultant higher resource utilization compared with several other chronic illnesses. The natural history and prognosis as well as the etiology of acute exacerbations in patients with COPD are incompletely understood at this time. Therefore, while a number of factors such as infections and exposure to environmental pollutants may play a role in acute exacerbations of the disease, up to one-third of cases may not have a clear etiology.[1] Researchers believe some of these unknowns may be related to other medical conditions such as myocardial ischemia, heart failure, and pulmonary embolism.[1,2] Currently, only a few agents used in management of COPD have been proven to prolong survival (e.g., oxygen therapy). Furthermore, most clinicians tend to restrict the use of β-blockers in the management plan of COPD patients, sometimes including those with cardiovascular comorbidities, which may deprive these patients of the beneficial cardiovascular effects from these agents and may also result in some of the so-called COPD exacerbations.

Rutten at al conducted an observational cohort study using electronic data from 23 general practices in the Netherlands to evaluate the long-term effect of β-blocker use on survival and exacerbations in patients with COPD. The study included 2230 patients with mean age of 64.8 years followed for a mean of 7.2 years. Approximately 45% of the patients with COPD had cardiovascular comorbidities and two-thirds had cardiovascular disease, hypertension, or diabetes. Their results demonstrated that treatment with β-blockers may reduce the risk of COPD exacerbations (crude and adjusted hazard ratios for exacerbations were 0.73 [95% CI, 0.63-0.83] and 0.71 [95% CI, 0.60-0.83], respectively) and improve survival (crude and adjusted hazard ratios for mortality were 0.70 [95% CI, 0.59-0.84] and 0.68 [95% CI, 0.56-0.83], respectively) in patients with a COPD diagnosis. A subgroup analysis revealed that patients with COPD but without overt cardiovascular disease had similar results. Cardioselective and nonselective β-blockers did not substantially differ in their effects on COPD exacerbations. However, cardioselective β-blockers had larger beneficial effects on mortality than nonselective ones. In their comments, the authors note that reduction in risk of exacerbation of COPD by β-blockers cannot easily be explained by beneficial cardiovascular effects alone.

■ COMMENTARY

For decades, β-blockers were believed to worsen heart failure due to their negative inotropic effects. However,

a paradigm shift occurred when clinical trials provided evidence that β-blockers block the progressive negative impact of neurohormones (such as norepinephrine) on the failing heart and thus result in significantly positive clinical impact in the failing heart's pathophysiology. β-blockers have since become the standard of treatment as further research demonstrated that they can reduce the total mortality in patients with heart failure by 30%-40%.

Similar to the case of heart failure management, it is now emerging that in patients with COPD, several treatments used in comorbid diseases may have beneficial effects. In the past, observational studies have suggested that COPD patients treated with statins, angiotensin-converting enzymes, angiotensin receptor blockers, and β-blockers may have improved survival and reduced hospitalization from COPD exacerbations.[3,4] However, the present research by Rutten et al is the first observational study to demonstrate that long-term treatment with β-blockers may improve survival and reduce the risk of an exacerbation in patients with COPD.

There may be several reasons for this including the beneficial cardiovascular effects from β-blockers, such as lowering of heart rate, or improvement in heart failure or ischemic heart disease. There may also be additional, yet unproven pulmonary benefits.

But then we must not become too optimistic too soon. Observational studies such as this one by Rutten et al are subject to several limitations and therefore well-designed prospective, randomized controlled trials must be conducted before advocating a paradigm shift. Nevertheless, the important information from this study may be the fact that we may not need fear β-blockers as much as we currently do when developing a management plan for patients with COPD. Perhaps, we should consider widening the spectrum of patients with COPD in whom we use this group of drugs. ■

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Can We Diagnose Gout Without Needling Our Patients?

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD, MA

Chair, Department of Integrative Medicine,
Ross University School of Medicine,
Commonwealth of Dominica

Dr. Wilke reports no financial relationship to this field of study.

Synopsis: *Use of simply obtained historical, physical, and laboratory data can distinguish gout from other forms of arthritis in many patients and avoid joint aspiration.*

Source: Janssens HJ, et al. A diagnostic rule for acute gouty arthritis in primary care without joint fluid analysis. *Arch Intern Med* 2010;170:1120-1126.

The gold standard for diagnosing gout is identifying crystals of monosodium urate (MSU) in fluid aspirated from the affected joint. Despite this, we frequently diagnose gout without it. These researchers, who included primary care physicians and rheumatologists from the Netherlands, asked the question, "How valid is a diagnosis of acute gouty arthritis made by family physicians?" They then went a step further and developed a scoring rule to diagnose acute gout without an aspirate. This was a prospective diagnostic study. The subjects were 381 patients presenting consecutively to 93 family physicians (FPs) with the complaint of a single, acutely swollen, painful joint. The test was the FP's diagnosis of gout. There were no exclusion criteria. All patients were referred to the rheumatology department within 24 hours of presentation to the FPs' offices. At the specialist's office, the subjects were interviewed and examined, had blood drawn, and had the affected joint aspirated and examined for MSU crystals. If no other crystals (for instance, calcium pyrophosphate) were seen and if there was no evidence for a septic joint, the patients were followed for at least a year and completely reevaluated if there was a recurrence. The investigators were blinded to the FPs' diagnoses until they had completed their workups. The subjects averaged in age 57.7 years and were predominantly male (74.8%). MSU crystals were identified in 216 patients (56.7%). The sensitivity (SEN), specificity (SPE), positive predictive value (PPV), and negative predictive value (NPV) of the test are summarized in Tables 1 and 2 *(see page 125)*.

After performing univariate analysis and multivariate logistic regression, variables were identified that in-

Table 1. Presence or absence of MSU crystals and diagnosis.

Diagnosis	MSU crystals (+)	MSU crystals (–)	Total
Gout (+)	209 (TruePos)	119 (FalsePos)	328
Gout (–)	7 (FalseNeg)	46 (TrueNeg)	53
Total	216	165	381

Table 2. Sensitivity, specificity, and positive and negative predictive values.

SEN (TruePos/TruePos + FalseNeg)	209/216	97%
SPE (TrueNeg/TrueNeg + FalsePos)	46/165	28%
PPV (TruePos/TruePos + FalsePos)	209/328	64%
NPV (TrueNeg/TrueNeg + FalseNeg)	46/53	87%

dependently predicted a diagnosis of gout: male gender, previous patient-reported arthritis attack, involvement of the first metatarsophalangeal joint (MTP1), hypertension (HTN) or ≥ 1 cardiovascular disease (angina pectoris, myocardial infarction, heart failure, cerebrovascular accident, transient ischemic attack, or peripheral vascular disease), beer consumption, serum uric acid level > 5.88 mg/dL, erythrocyte sedimentation rate (ESR) > 20 for men or > 30 for women, and presence of tophus. These variables made up the "best model given the data" and were used to judge the performance of models based on easily obtained data. The last variable, tophus, was 100% specific for gout. The other variables were all statistically significant at the $P < 0.001$ level. The model that the investigators finally chose had two other variables, joint redness ($P = 0.002$) and onset within 1 day ($P = 0.42$), data easily obtained during a primary care visit. Beer consumption and ESR were dropped. Table 3 *(see above, right)* gives the point value for each variable.

When this scoring tool was applied to the population, a total score of ≤ 4 ruled out gout in almost all subjects, and a score ≥ 8 identified > 80% of patients with gout. Gout was present in 30% of those individuals who scored > 4 and < 8. The authors recommend that these patients should have joint aspiration.

Table 3. Gout scoring tool.

Variable	Points
Male gender	2
Previous patient-reported arthritis attack	2
Onset within 1 day	0.5
Joint redness	1
MTP1 involvement	2.5
HTN or ≥ 1 CVD	1.5
Serum uric acid level > 5.88 mg/dL	3.5

■ COMMENTARY

First the caveats: All of these patients presented with monoarticular arthritis. While this is the most common presentation for gout, it can be polyarticular, especially in the elderly. You will have to decide if the population in the eastern portion of the Netherlands is similar to yours. The authors did not show the raw data of the performance of their tool on the diagnosis of gout, so we are left to assume that they performed the math correctly. They reference their on-line calculator (www.umcn.nl/goutcalc), but it gives a risk score from 0.0 to 1.0 without guidance at what level you should act.

I think it is premature to adopt this diagnostic tool. It really should be vetted in a few more settings and populations first. Assuming it proves valid, it could benefit both patients and physicians. While it appears we are very good at identifying gout when we see it (97% sensitivity), we have too many false positives. We start these patients on treatment for a condition they don't have and which isn't completely benign. If the tool can readily and reliably differentiate between those patients who are very likely and very unlikely to have gout, we can begin appropriate therapy, and for those patients who fall in the middle, we can arrange for joint aspiration for a definitive diagnosis.

I like the idea of multiple data points to diagnose gout. Depending on limited data can be misleading. For instance, you might be tempted to dismiss gout in a man with a red MTP1 (i.e., podagra) and a serum uric acid level of 6.0, because the normal range for men is 2.5-8.0 mg/dL. However, the tool gives this patient a score of 9.0, indicative of gout. Considering the serum urate level in isolation will lead you astray. Gout can occur with normal uric acid levels,[1,2] and the vast majority of people with hyperuricemia do not develop gout.[3]

These researchers examined many candidate variables in the process of selecting the ones for their diagnostic score. Some of the items that weren't chosen (because they did not achieve statistical significance) include items that we generally consider to be risk factors: age, family history, diabetes mellitus, renal stones, recent joint trauma, obesity, and any alcohol consumption (although beer consumption was significant). They do not comment on this. ■

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Pharmacology Update

Dutasteride and Tamsulosin HCl Capsules (Jalyn™)

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Elliott and Chan report no financial relationship to this field of study.

THE FDA HAS APPROVED THE COMBINATION OF DUTASTERIDE (DUT) and tamsulosin (TAM) in a single capsule. Dutasteride is a 5-α reductase inhibitor and tamsulosin is an α-adrenergic antagonist. The combination is marketed by GlaxoSmithKline as Jalyn™.

Indications

DUT/TAM is indicated for the treatment of symptomatic benign prostate hyperplasia (BPH) in men with an enlarged prostate.[1]

Dosage

The recommended dose is one capsule taken daily 30 minutes after the same meal each day.[1] The capsule should be swallowed whole and not chewed or opened.

Each capsule contains dutasteride 0.5 mg and tamsulosin 0.4 mg.

Potential Advantages

The capsule provides two drugs for BPH with different mechanisms of action in a single capsule. Dutasteride reduced the risk of prostate cancer (relative risk reduction of 22.8%; 95% confidence interval [CI], 15.2-29.8) over a 4-year study period.[2]

Potential Disadvantages

Early-onset (i.e., first 6 months) ejaculation disorders appear more common with DUT/TAM (7.6%) than either alone (1.1% and 2.2%).[1] However the incidence was less than or equal to 0.1% at 19-24 months of therapy. DUT/TAM was primarily tested in Caucasians (88%) and the benefit in other ethnic populations, particularly African Americans, is not known.[1]

Comments

Dutasteride is an inhibitor of both type 1 and type 2 5-α reductase, in contrast to finasteride which is a type 2 inhibitor. Tamsulosin is a competitive inhibitor of α1A adrenergic receptors, which is predominately found in the prostate.[3] It is suggested that dutasteride prevents prostate growth that would occur with TAM monotherapy, thus maintaining the effect of the latter.

The efficacy of DUT/TAM was supported by a 4-year, randomized, double-blind, parallel group study (CombAT Study). Subjects with BPH, at least 50 years of age, serum PSA greater than 1.5 ng/mL but less than 10 ng/mL, International Prostate Symptom Score (IPSS) ≥ 12, and enlarged prostate (≥ 30 cc) were randomized to DUT/TAM (n = 1610), dutasteride alone (n = 1623), or tamsulosin alone (n = 1611). The primary endpoint was the change in IPSS. The changes at 24 months were -6.2 ± 7.14, -4.9 ± 6.81, and -4.3 ± 7.01 for DUT/TAM, DUT, and TAM, respectively. The mean differences were statistically significant between each monotherapy compared to the combination ($P < 0.001$). Difference was observed at month 9. These represent a 37%, 30%, and 26% decrease from baseline scores. There was also an improvement in maximum urine flow rate of 2.4 mL/sec for DUT/TAM, 1.9 mL/sec for DUT, and 0.9 mL/sec for TAM. Difference was observed by month 6. Sixty-six percent of subjects completed the 48-month visit. DUT/TAM was superior to TAM but not DUT in reducing the risk of acute urinary retention or BPH-related surgery.[4] However the combination was better than either monotherapy in time to first clinical progression of BPH (e.g., symptom deterioration) and change in IPSS. The superiority of DUT/TAM was observed from month 9 compared to TAM and month 3 compared to DUT.

Patient-reported quality of life and treatment satisfaction was in favor of DUT/TAM.[5] Drug-related adverse events were higher with DUT/TAM (28%) compared to DUT (21%) and TAM (19%); however, withdrawal rates were similar (6%, 4%, and 4%, respectively). In a post-hoc analysis among Asian men with moderate-to-severe BPH (n = 325), the combination achieved benefit over tamsulosin monotherapy but was not statistically better than dutasteride.[6]

Clinical Implications

BPH is a common condition in older men that leads

to lower urinary tract symptoms, urinary tract infection, and acute urinary retention. Pharmacotherapy includes an α-adrenergic receptor antagonist, 5-α reductase inhibitor, or a combination. The combination is generally more effective than monotherapy with either drug. Jalyn provides the combination of DUT and TAM in one capsule. ■

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CME Questions

39. Untreated obstructive sleep apnea (OSA) is associated with an increased risk of heart failure:
a. that is greater than the risk for coronary heart disease.
b. in women, but not in men.
c. that is greater for older men than for younger men.
d. in a dichotomous (all or nothing) way.

40. In the above study by Rutten et al, the long-term use of β-blockers in patients with COPD was associated with:
a. reduced rate of COPD exacerbations.
b. improved patient survival.
c. Both a and b are correct.
d. Neither a or b are correct

41. Choose the *incorrect* item. Statistically significant variables associated with gout are:
a. male gender.
b. involvement of the first metatarsophalangeal joint.
c. hypertension.
d. previous patient-reported arthritis attack.
e. onset within 1 day.

42. Using the gout risk score tool, a man with a previous episode of arthritis and a red MTP1 would have a score of:
a. 4.5
b. 5.5
c. 6.5
d. 7.5
e. 8.5

Answers: 39. a, 40. c, 41. e, 42. d.

CME Objectives

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville
Dr. Kuritzky is a consultant for Abbott, AstraZeneca, Boehringer Ingelheim, Daiichi, Sankyo, Forest Pharmaceuticals, Lilly, Novo Nordisk, Takeda.

Safety of testosterone replacement

Source: Basaria S, et al. Adverse events associated with testosterone administration. *N Engl J Med* 2010;363:109-122.

Of late, there has been a renaissance of interest in identification and management of hypogonadism in older men. This new enthusiasm is based upon a recognition that subnormal testosterone is both common and consequential. For instance, prevalence studies suggest that as many as 40% of healthy men older than age 50 have a subnormal morning total testosterone level. Subnormal testosterone is associated with changes in sexual function, mood, muscle mass, and central obesity. Observational data indicate that low testosterone is also associated with increased mortality. The advent of better-tolerated, easy-to-use testosterone replacement modalities (e.g., patches, gels, buccal tablets), has simplified the treatment approach, but the question about long-term testosterone safety is unanswered.

In the Testosterone in Older Men with Mobility Limitations study of senior men (n = 209; mean age, 74 years), subjects were treated with testosterone 1% gel to achieve mid-normal testosterone levels. The trial was discontinued early upon the recommendation by the Data and Safety Monitoring Board because of an increase in adverse events in the treatment group, including some serious events. For instance, there were 23 CV adverse events in the treatment group, compared with 5 in the placebo group.

The small size of the trial and the highly selected group (men with physical limitations) makes it difficult to generalize about the results. Nonetheless, clinicians should recognize that testosterone replacement may be associated with important adverse events. Larger, long-term studies will be necessary to establish the safety profile of testosterone replacement. ■

Is obesity a factor in asthma?

Source: Pakhale SM, et al. A comparison of obese and nonobese people with asthma: Exploring an asthma-obesity interaction. *Chest* 2010;137:1316-1323.

Population studies have shown that obesity is related to the incidence of asthma. Compared to non-obese subjects, the odds ratio per year for developing asthma among obese individuals is approximately 1.5, and increases as the degree of obesity increases. Although mechanisms through which obesity might contribute to incident asthma are poorly understood, several prospective studies have demonstrated the same relationship.

Of course, some persons who carry a diagnosis of asthma have been misdiagnosed. In this study by Pakhale et al, subjects diagnosed as asthmatic underwent formal pulmonary function testing to confirm their diagnosis. Overall, of 496 subjects, asthma was ultimately ruled out in 150 of them. Likelihood of misdiagnosis was increased especially in older males.

There was one subgroup of obese individuals among whom the likelihood of asthma misdiagnosis stood out: If an obese individual had had an urgent visit for respiratory symptoms in the past 12 months, the misdiagnosis of asthma was more than 4-fold greater than in non-obese persons.

Based upon this information, it is suggested that clinicians should consider performing objective confirmation of the diagnosis of asthma (as with pre- and post-bronchodilator spirometry), particularly among obese older males. ■

A new tool for treatment of plantar warts

Source: Gamil H, et al. Intralesional immunotherapy of plantar warts: Report of a new antigen combination. *J Am Acad Dermatol* 2010;63:40-43.

Plantar warts, most commonly found on the plantar surface of the feet but also seen on the hands and other sites, are often challenging to treat. Although available tools include destructive therapies (e.g., cryotherapy, bichloroacetic acid), topical immune modulators (e.g., imiquimod), oral agents (e.g., cimetidine, levamisole), and simple surgical excision, each of these modalities has limitations. Hence, new methods of intervention are sought.

Gamil et al investigated the use of intralesional measles/mumps/rubella vaccine (MMR, as used in standard childhood immunizations) in a pilot trial. Vaccine was injected once every 3 weeks for a maximum of three injections, in 23 subjects.

Although the duration of treatment was only 6 weeks (injections at time 0, 3 weeks, and 6 weeks), patients were followed for 9 months to evaluate for recurrence.

Complete clearance of warts occurred in 20 of 23 patients, 1 patient had partial clearance, and 2 had no response. Only 1 patient experienced recurrence over 9 months. Other than local pain during the actual process of injection, the only other reported adverse effect was a transient flu-like syndrome in 1 patient.

MMR is inexpensive and well tolerated, and intriguing as a novel immunomodulatory path for attacking plantar warts. ■

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