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INSIDE

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Alcohol Consumption and Mortality in Patients with CVD

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

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Dr. Karpman serves on the speakers bureau for Forest Laboratories.

Synopsis: *In patients with cardiovascular disease, light-to-moderate alcohol consumption is significantly associated with a lower incidence of cardiovascular and all-cause mortality.*

Source: Costanzo S, et al. Alcohol consumption and mortality in patients with cardiovascular disease: A meta analysis. *J Am Coll Cardiol* 2010;55:1339-1347.

Numerous published studies have revealed that ischemic cardiovascular events and/or all-cause mortality are significantly increased even in apparently healthy individuals who consume an excessive amount of alcohol and are significantly reduced in those individuals who regularly consume only small-to-moderate quantities of alcohol.[1-6] However, it should be noted that relatively few observational studies have evaluated the association between alcohol intake and secondary events including mortality in patients with cardiovascular disease (CVD), and the results in even these few studies have consistently revealed a reduction in the all-cause mortality risk in subjects who were light or moderate consumers of alcohol.[7,8]

Costanzo and colleagues extended the results of previous analyses[8] by evaluating more recent studies, which correlated alcohol intake by patients with established CVD with cardiovascular and/or overall mortality. They identified 54 studies but restricted their analysis to the results of only 8 major prospective studies that enrolled a total of 16,351 patients with a history of CVD. The meta-analysis on cardiovascular mortality revealed a J-shaped curve with a significant maximal protection (i.e., a significantly lower incidence of cardiovascular and all-

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cause mortality) when subjects consumed light-to-moderate amounts of alcohol in the range of approximate 5-25 g/day.

■ COMMENTARY

The 2006 Diet and Lifestyle Recommendations Scientific Statement from the American Heart Association Nutrition Committee clearly advises: "If you consume alcohol, do so in moderation (equivalent of no more than one drink for women or two drinks for men per day)."[9] This recommendation has been widely accepted and has been considered to be quite valid for patients with known CVD as well as for healthy individuals. Costanzo and colleagues have now clearly demonstrated that the same recommendation remains current and can be appropriately extended to CVD patients; however, due to the lack of controlled intervention trials, which are both difficult to perform and ethically questionable, cardiovascular patients who do not regularly consume alcoholic beverages should not necessarily be advised to initiate alcohol consumption, even though the benefits have been clearly demonstrated. On the other hand, heavy or binge alcohol drinkers, whether they have associated CVD or not, should be strongly advised to totally abstain or to at least decrease their alcohol consumption to no more than a moderate level of intake.

In summary, physicians should be aware that the regular intake of a light-to-moderate amount of alcohol, especially if it is consumed as part of a healthy lifestyle (i.e., increased physical activity, no smoking, etc.) in subjects who are following a healthy dietary regimen (i.e., decreased dietary fat intake, high consumption of fruit and vegetables), and who receive appropriate drug therapy, will help substantially diminish the level of cardiovascular and/or all-cause mortality risk to a level which is substantially lower than exists in either alcohol abstainers or heavy alcohol drinkers. ■

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

Another Argument for Moderation in All Things

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

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

Synopsis: *Being overweight or obese increases the risk of cirrhosis. In this study, excess body weight contributed to almost 20% of the cirrhosis-related hospital*

admissions and deaths, while alcohol contributed to almost 50%.

Source: Liu B, et al; and the Million Women Study Collaborators. Body mass index and risk of liver cirrhosis in middle aged UK women: Prospective study. *BMJ* 2010;340:c912.

This study is the result of a secondary data analysis from the Million Women Study (www.millionwomenstudy.org). The investigators set out to study the relationship between body mass index (BMI) and liver cirrhosis, and to determine whether alcohol or other factors affect this relationship. The Million Women Study is an ongoing prospective cohort study of 1.3 million women who were recruited through the National Health Service (NHS) in England and Scotland from 1996 to 2001. Participants completed questionnaires at entry to the study and every 3 or 4 years afterward. The questionnaires collected demographic, lifestyle, medical, and sociodemographic details. Once enrolled, study participants were followed through computerized health records by NHS number. During the period of follow-up for this study, both the cause of death and diagnoses on admission to hospital were coded by using ICD-10. Women who reported having had any type of liver disease (including viral hepatitis), cancer, or unknown BMI at recruitment were excluded from analysis.

The investigators estimated the risk of hospital admission with cirrhosis or death from cirrhosis for six categories of BMI (< 22.5 kg/m^2, 22.5 to < 25 kg/m^2, 25 to < 27.5 kg/m^2, 27.5 to < 30 kg/m^2, 30 to < 35 kg/m^2, and ≥ 35 kg/m^2) at recruitment and also, in those with a value > 22.5 kg/m^2, for each 5 unit increase. They set the reference group as women with a BMI between 22.5 and 25 kg/m^2. They used age as the underlying time variable and adjusted for alcohol intake, socioeconomic status, smoking status and amount smoked, and physical activity. They also examined the effect of adjustment for additional factors, such as use of hormonal therapies, parity, and year of birth.

They also examined the effect of BMI on the risk of subsequent hospital admission with or death from cirrhosis in relation to other factors that have been found to be associated with cirrhosis, including alcohol consumption, smoking, and diabetes. They estimated the proportion of hospital admissions with or deaths from liver cirrhosis in middle-aged women in the U.K. that could be attributed to BMI and to alcohol. They adjusted for age, region, socioeconomic status, smoking, and physical activity.

The final sample included 1,230,662 women. Nearly half (46%) of women in the study were at or below a healthy weight (BMI < 25 kg/m^2), 36% were overweight (BMI 25 to < 30 kg/m^2), and 18% were obese (BMI ≥ 30 kg/m^2). The mean BMI was 27.6 kg/m^2, and the mean age at recruitment was 56 years. Of the women included in these analyses, 77% reported drinking some alcohol. Among the drinkers, the mean reported alcohol consumption was about five and a half standard drinks a week. The proportion of women reporting drinking any alcohol and the amount they drank decreased with increasing BMI. The proportion of women who were current smokers and the proportion who reported doing strenuous physical activity more than once a week also decreased with increasing BMI. The proportion of women in the upper socioeconomic group decreased with increasing BMI. As expected, the proportion who reported being treated for diabetes increased with increasing BMI. In other words, the heavier a woman was, the less likely she was to be in the upper socioeconomic group, exercise, smoke cigarettes, or drink alcohol, but the more likely she was to have diabetes.

Over about 6 years of follow-up, 1811 women had their first cirrhosis-related hospital admission or death, and 421 of these women had cirrhosis recorded for the first time at death. The overall incidence of first hospital admission with or death from cirrhosis in this population was 1.2 per 1000 women over 5 years. Compared with the reference group (women with a BMI of 22.5 to < 25 kg/m^2), both the women who had a lower BMI and those with a higher BMI had a significantly greater relative risk of cirrhosis. (The authors chose not to do further analysis of the women whose BMI was < 22.5 kg/m^2 because they could not exclude the possibility that previous illness may have contributed to weight loss, and there were not very many women in this category). Among women who had a BMI of ≥ 22.5 kg/m^2, the estimated increase in the risk of cirrhosis was 28% for each 5 unit increase in BMI. Routine adjustment for socioeconomic status, alcohol consumption, smoking, and physical activity, in addition to age and recruitment region, did not alter the pattern of risks substantially.

The authors were also interested in learning if other factors, particularly alcohol consumption, interacted with body weight in affecting cirrhosis risk. They compared the effect of BMI on the relative risk of cirrhosis in categories of alcohol consumption, smoking, and diabetes. They found that the trend in the relative risk with increasing BMI did not differ significantly between drinkers with increasingly larger consumptions of alcohol. However, although the relative risk per unit increase in BMI did not vary by alcohol intake, the absolute risk did. In women drinking < 70 g alcohol per week (mean intake 0.4 drinks/day), the incidence of liver cirrhosis was 0.8/1000 over 5 years for those with BMI between 22.5 and 25 kg/m^2 and increased to 1.0/1000 in women with BMI of ≥ 30 kg/m^2. For women drinking ≥ 150 g per week (mean intake, 2.5 drinks per day) the risks of cirrhoses were 2.7/100 and 5.0/1000 for those of healthy weight

and those who were obese, respectively.

The relative risk of cirrhosis with increasing BMI did not vary between women who had diabetes and those who did not, but it was increased in women who were current smokers; smokers had relative risks of cirrhosis almost three times those of never-smokers.

■ **COMMENTARY**

Alcohol consumption is a well-known cause of liver cirrhosis, but recent increases in the prevalence of cirrhosis are unlikely to be driven by increased alcohol consumption alone. Obesity has been implicated as a contributing cause of cirrhosis.[1] These authors have strengthened the evidence that obesity and overweight cause liver cirrhosis, and have quantified the risk in middle-aged women. In a companion paper in the same issue of the *British Medical Journal*, Hart et al described a similar relationship in a large population of British men, and noted that "raised BMI and alcohol consumption are both related to liver disease, with evidence of a supra-additive interaction between the two."[2]

The likely mechanism is increased fat deposition within the hepatocytes and the development of fatty liver (hepatic steatosis) that occurs with obesity. This can lead to inflammation (non-alcoholic steatohepatitis) and subsequent liver fibrosis and cirrhosis.[3] People with a high alcohol intake and diabetes also have fatty livers, and hepatic steatosis in the presence of diabetes may increase the likelihood of progression to cirrhosis.[4] In addition to the association of alcohol, obesity, and diabetes with cirrhosis, the authors of this study found that the relative risks associated with increasing body mass were increased by smoking, but did not speculate on the mechanism.

Although the risk for cirrhosis posed by obesity appears to be less than half that posed by heavy alcohol consumption, it is clearly a substantial risk. And heaven forbid that you also smoke. ■

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Silent Pulmonary Emboli in Patients with DVT: Time to Screen?

ABSTRACT & COMMENTARY

By Joseph Varon, MD, FACP, FCCP, FCCM

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Dr. Varon receives grant/research support from and serves on the speakers bureaus for The Medicines Group and EKR Pharma.

Synopsis: *Asymptomatic pulmonary embolism is quite common among patients with deep venous thrombosis. In many instances in these patients, the pulmonary emboli are located within the central pulmonary arteries.*

Source: Stein PD, et al. Silent pulmonary embolism in patients with deep venous thrombosis: A systematic review. *Am J Med* 2010;123:426-431.

THIS STUDY WAS AIMED AT EVALUATING THE INCIDENCE of unsuspected or undiagnosed pulmonary embolism (PE) among patients with deep venous thrombosis (DVT). The primary question that the investigators were addressing was whether or not routine PE screening was necessary for those patients with documented DVT. To accomplish this task, the investigators conducted a systematic review of 28 published studies in PubMed through July 2009. These 28 studies were the result of a literature search that included more than 950 citations. The 28 studies contained specific raw data and detailed description of the methodology utilized to diagnose PE, and documented the absence of symptoms of PE. Criteria for diagnosis of a "silent" PE included the interpretation of a high-probability ventilation-perfusion lung scan, computed tomography (CT), pulmonary arteriography on the basis of either the prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) or non-PIOPED criteria and the absence of pulmonary symptoms and/or signs.

Of 5233 patients with DVT evaluated, 1655 (32%) had evidence of silent PE. Those patients with proximal DVT had a higher incidence of PE. Larger perfusion defects were noted in those patients that had DVT in the pelvic veins or thighs as compared with those with distal thrombi. Moreover, the incidence of recurrent PE was higher in those patients with silent PE (5.1%) as compared to those patients without silent PE (0.6%). A trend for an increased prevalence of silent PE was noted with aging.

Those patients younger than age 40 years had silent PE in 14% of the cases as compared to 22% in those aged 40-70 years, and 40% in those older than 70 years of age.

■ **COMMENTARY**

For decades, we have known that PE is commonly found in patients postmortem, in whom this clinical entity was undiagnosed or not suspected antemortem.[1] The main question has been: Should we look for PE in every patient with DVT even if they have no pulmonary signs or symptoms?[2] The fact is that the treatment of both DVT and PE is the same and conducting additional studies has cost and potential side effect issues.

This well-conducted systematic review is interesting because it shows a high prevalence of silent PE in patients with DVT. With this in mind, the rationale for conducting "additional" pulmonary work-up in patients with documented venous thrombosis (i.e., ventilation-perfusion lung scans, CT, or angiogram) is the fact that patients with DVT tend to have more recurrent PEs when the patients have a "silent" PE (as noted in this study) when compared to those with a first episode of non-silent PE.

That almost one-third of all patients with DVT have a silent PE moves forward the concept of considering pulmonary screening in this patient population. In addition, the decision to admit a patient with a documented DVT to a hospital instead of treating at home may be modified on the basis of these findings. ■

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How Much Physical Activity to Avoid Weight Gain?

ABSTRACT & COMMENTARY

By Rahul Gupta, MD, MPH, FACP

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

Synopsis: *Contrary to the current guidelines, in the long term, an average of approximately 60 min/day of moderate-intensity activity for women is required to be successful in maintaining a normal weight.*

Source: Lee IM, et al. Physical activity and weight gain prevention. *JAMA* 2010;303:1173-1179.

Obesity has become a public health crisis in the United States. In the past three decades, obesity prevalence has steadily increased. Not only does the economic impact of this current epidemic loom over us, but the present generation of Americans may for the first time have a shorter life expectancy than their parents if we are unsuccessful in controlling this epidemic. Research suggests that the total health care costs attributable to obesity and overweight will more than double every decade. It is estimated that by the year 2030, health care costs attributable to obesity and overweight alone could range from $860 to $956 billion, which would account for 15.8%-17.6% of total health care costs, or $1 of every $6 spent on health care.[1] Because we know that the majority of obese or overweight people who are successful in losing weight are not able to sustain that weight loss, it is a reasonable approach to avoid weight gain in the first place. Physical activity is clearly one method of preventing such weight gain. However, it is unclear at this time whether the 2008 federal guidelines recommending at least 150 min/week (7.5 metabolic equivalent [MET] hours/week) of moderate-intensity aerobic physical activity for individuals to obtain substantial health benefits is sufficient.[2,3]

In the current study, the authors conducted a prospective cohort study of 34,079 U.S. women (mean age, 54.2 years) consuming a usual diet from 1992 to 2007. Women were classified as expending < 7.5 , 7.5 to < 21, and ≥ 21 MET hours/week of activity at each time and change in body weight was measured at periodic intervals (21 MET is the equivalent of 420 min/week of moderate activity or 60 min/day). The researchers found that women gained a mean of 2.6 kg throughout the study period of 13.1 years. Only among women with a BMI of < 25 kg/m^2 was there an inverse dose-response relation between activity levels and weight gain. So, more physical activity in these women was associated with a lower weight gain. Compared with women expending ≥ 21 MET hours/week, those expending 7.5 to < 21 MET hours/week gained 0.11 kg, whereas those expending < 7.5 MET hours/week gained 0.12 kg. The difference in weight gain between these last two groups was not statistically significant. In other words, women who were successful in maintaining a normal weight and gaining < 2.3 kg over 13 years averaged approximately 60 min/day (420 min/week) of moderate-intensity activity throughout the study; those who gained significantly more weight averaged less physical activity, with no difference in weight gain between the two lesser active groups.

■ **COMMENTARY**

A decline in daily physical activity, including that during leisure time is clearly a major factor contributing to the current obesity epidemic. We know that physical activity is beneficial to health with or without weight loss. We also know that most people gain some weight as they age. However, the question of how much daily physical activity is required to prevent weight gain remains. In addition to the above mentioned federal guidelines, the Institute of Medicine (IOM) suggests that 420 min/week (60 min/day) of moderate-intensity activity may be recommended for individuals to avoid becoming overweight or obese.[4] The above study clearly supports the IOM recommendations and perhaps heralds that it may be time to revise the federal guidelines once again. However, it is also important to note the limitations of this study. Self reporting of results such as physical activity and body weight can be subject to individual bias. The current study was limited to middle-aged women and therefore may not apply to other groups.

However, it is important to remember that weight gain results from an imbalance between energy consumed and energy expended. Therefore, whereas any amount of physical activity is clearly better than none for the body, the prevention of weight gain or weight maintenance is dependent upon a number of factors including physical activity, healthy diet, and control of concurrent chronic illnesses. Nevertheless, this is a significant study and serves as a reminder that guidelines and recommendations must be revisited and updated periodically to suit the changing needs of our population. ■

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Pharmacology Update

Miconazole Buccal Tablets (Oravig™)

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 relationships to this field of study.

THE FDA HAS APPROVED A MICONAZOLE BUCCAL TABLET for the treatment of oropharyngeal candidiasis. This once-daily mucoadhesive buccal tablet provides slow release of the drug over the course of the day. The tablet is marketed by Strativa Pharmaceuticals as Oravig™.

Indications

Miconazole buccal tablets are indicated for the local treatment of oropharyngeal candidiasis in adults.[1]

Dosage

The buccal tablet should be placed to the gum region (with the round side facing the gum) once daily for 14 consecutive days.[1] It should be applied in the morning after brushing the teeth and placed against the upper gum just above the incisor tooth and held in place for 30 seconds to ensure adhesion. The tablets should not be crushed, chewed, or swallowed. Chewing gum should be avoided, but food and drink can be taken normally. The application site should be alternated between the right and left sides of the mouth.

Miconazole buccal tablets are supplied as 50 mg tablets.

Potential Advantages

Miconazole buccal tablet is applied once daily compared to five times daily for clotrimazole troches.

Potential Disadvantages

Some *Candida* strains show reduced in vitro susceptibility to miconazole.[1]

Comments

Miconazole is an azole antifungal agent with in vitro activity against *Candida albicans*, *Candida parapsilosis*, and *Candida tropicalis*. The efficacy of the buccal tablets for the treatment of oropharyngeal candidiasis was shown in two studies, one in HIV-infected patients and in patients who were receiving radiotherapy for head and neck cancer.[1,2] In both studies the infections were mainly caused by *C. albicans* (85% and 71%, respectively). In the first study, HIV patients with symptoms and microbiological documentation of oropharyngeal candidiasis were randomized to miconazole 50 mg daily for 14 days (n = 290) or clotrimazole troches 10 mg five times daily for 14 days (n = 287). Clinical cures (complete resolution of signs and symptoms) on days 17-22 were similar, 60.7% for miconazole and 65.2% for clotrimazole. The relapse rates (21-24 days after treatment completion) were also similar, 27.3% and 27.8%, respectively.

In the second study, adult patients who underwent radiation therapy for head and neck cancer with oropharyngeal candidiasis were randomized to miconazole buccal tablets (50 mg daily; n = 148) or miconazole oral gel (125 mg four times daily; n = 146) for 14 days. The complete response (complete disappearance of lesions) rates at day 14 were 50% for miconazole tablets compared to 43.8% for miconazole gel. The clinical relapse rates 14 days after the end of treatment were 18.9% and 12.5%, respectively. Patients with normal secretion responded better (100%) than those with reduced secretion (56.2%) or those with xerostomia (46.7%).[2] The adhesion of the tablet to the gum was reported as very good, as 92.2% adhered for 6 hours and 61.1% for 12 hours.[2] The tablets were generally well-tolerated with adverse events similar to the comparator; however, dysgeusia and ageusia were reported more frequently than the comparator (4.1% vs. 0% and 2.4% vs. 0.3%, respectively).

Clinical Implications

Oropharyngeal candidiasis is a common infection in immunosuppressed patients. The causative agent is generally *Candida albicans*. Oral fluconazole is considered the drug of choice,[3] although topical therapy is often adequate for initial episodes. These include clotrimazole troches, nystatin suspension, or pastille or miconazole mucoadhesive tablets. ■

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CME Questions

22. The incidence of cardiovascular and all-cause mortality is:

a. significantly lower in all patients who regularly consume a light-to-moderate quantity of alcohol.
b. not affected in CVD patients who regularly consume a light-to-moderate daily quantity of alcohol.
c. decreased in apparently healthy patients who regularly consume alcohol in any quantity.
d. not affected in apparently healthy patients who regularly consume a light-to-moderate daily quantity of alcohol.

23. In the study by Stein and coworkers, the prevalence of pulmonary embolism in patients with proximal deep vein thrombosis (DVT) was:

a. lower than in patients with distal DVT.
b. the same as in patients with distal DVT.
c. directly related to the presence of heparin antibodies.
d. was not affected by thrombolytics.
e. higher than in patients with distal DVT.

Answers: 22. a, 23. e.

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 and serves on the speakers bureaus of Abbott, AstraZeneca, Boehringer Ingelheim, Daiichi Sankyo, Forest Pharmaceuticals, Eli Lilly & Co., Novo Nordisk, and Takeda.

What aspect of HTN produces toxicity?

Source: Rothwell PM, et al. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. *Lancet* 2010;375:895-905.

A well-established body of epidemiologic literature supports a continuous graded risk between systolic blood pressure (SBP) and CV risk. This relationship has held constant whether one considers office BP, home BP, or ambulatory blood pressure monitoring (ABPM). Because BP is variable over time, it is unclear whether the toxicity of BP to the vasculature is more strongly associated with mean BP, maximum BP, pulse pressure (SBP − DBP), or BP variability. Circadian rhythm of BP has also been recognized to be particularly associated with adverse outcomes: ABPM subjects whose BP does not decline overnight (called non-dippers) have greatly increased CV risk, well beyond what would be expected simply by having a greater total number of hours of exposure to elevated BP.

Rothwell et al used a data set comprised of persons who had sustained a TIA in large clinical trials (n = 2006), including the UK TIA Trial and ASCOT. Visit-to-visit BP variability and maximum SBP were better predictors of adverse outcome than mean SBP. Similarly, persons with episodic HTN (normal BP on some occasions, elevated on others) were also at increased stroke risk, surpassing risk for stable BP.

It remains to be elucidated why these subgroups of individuals with BP variability have a greater risk burden. Although the associations between maximum SBP, BP variability, and episodic BP elevations were consistent, this does not establish causation. Perhaps the strongest cautionary message from this trial is that clinicians should not fall prey to false reassurance when they see a mixed BP response pattern including some BP measurements at goal and others elevated; such episodic elevations are consequential. ■

New short-course topical treatment for actinic keratoses

Source: Swanson N, et al. Imiquimod 2.5% and 3.75% for the treatment of actinic keratoses: Results of two placebo-controlled studies of daily application to the face and balding scalp for two 2-week cycles. *J Am Acad Dermatol* 2010;62:582-590.

Actinic keratoses (AKs) recently have been recognized as both a cosmetic and a dermatopathologic problem, since they are precursors to squamous cell carcinoma. Indeed, current literature suggests that AKs be considered squamous cell carcinoma in situ. AKs treatment includes cryotherapy, excision, chemical destruction (e.g., 5-fluorouracil, diclofenac), immune activation (imiquimod [IMQ]), and others. Because topical treatment courses are sometimes protracted, and induce unpleasant cutaneous inflammatory changes, clinicians desire simpler, gentler methods.

Swanson et al randomized patients with AKs on the face and scalp to IMQ or placebo (n = 479). IMQ was applied as pulse therapy: qd for 2 weeks, then no treatment for 2 weeks, then repeat (total = 14 days of treatment). Outcomes were measured at 8 weeks.

IMQ produced a 72%-82% reduction in AKs lesions; higher doses produced complete clearing in 59% (vs 6% with placebo). A companion article in the same journal showed similar clearance rates for a longer regimen (3-week treatment courses). This simpler regimen was well tolerated, and provides a quick and effective route for topical treatment of AKs. ■

Depression and sleep disturbance

Source: Van Mill JG, et al. Insomnia and sleep duration in a large cohort of patients with major depressive disorder and anxiety disorders. *J Clin Psychiatry* 2010;71:239-246.

Both anxiety and depression disorders have a strong association with sleep disturbance. The association between sleep and depression is bidirectional: Depression is often manifest by or leads to sleep disturbance, and persistent insomnia increases risk of depression.

Van Mill et al sought to elucidate further the relationship between sleep disorders and depression by analyzing subjects in the Netherlands Study of Depression and Anxiety cohort (n = 2619).

In this population of subjects (approximately three-fourths suffered from depression and/or anxiety), almost half scored at least 9 on the Insomnia Rating Scale (IRS; the same metric that was employed in the Women's Health Initiative), fulfilling criteria for clinically significant insomnia. Insomnia scores were related to both anxiety and depression, but worse for depression, and highest for comorbid depression and anxiety. Interestingly, even persons with depression or anxiety in remission had elevated scores on the IRS. The authors suggest that, based upon their data, inquiry into sleep status is valuable not only during both depression and anxiety, but even during periods of remission. ■

In Future Issues: Does Reporting Estimated GFR Improve Outcomes?