Job-Stressed Women Face Higher MI Risk

BY BRUCE JANCIN
FROM THE ANNUAL SCIENTIFIC SESSIONS OF THE AMERICAN HEART ASSOCIATION

CHICAGO – Women who report high psychological job strain have a 40% increased risk of cardiovascular disease, according to a large, 10-year prospective study. High job strain is defined by a demanding job, often involving time pressure, and coupled with low decision-making authority or opportunity for personal growth. But women with high job strain weren’t the only group at increased risk for acute MI and other cardiovascular events in this analysis of more than 17,000 working women participating in the Women’s Health Study. Those with active job strain defined as high-demand work featuring a high sense of control, based on Robert Karasek’s 14-item job strain model used in this study, had a 60% increase in total cardiovascular events compared with those reporting low job strain, Natalie Slopen, Sc.D., reported at the meeting.

This last point regarding the cardiovascular risks associated with job strain should be near and dear to hearts of female physicians. Many, perhaps most, physicians fit within the Karasek active job strain category, noted Dr. Slopen, a postdoctoral research fellow in the department of society, human development, and health at Harvard School of Public Health, Boston. The Women’s Health Study involves 17,415 female, mostly white, health professionals in their good health at an average age of 57 years at enrollment in what was initially a randomized, placebo-controlled clinical trial of vitamin E and aspirin. More than 200,000 women completed baseline interviews that included questions assessing psychological job strain.

JANUARY 2011 • CARDIOLOGY NEWS

Effects on the Eye

Advise patients to seek immediate medical attention in the event of a sudden loss of vision in one or both eyes while taking PDE5 inhibitors, including REVATIO. Such an event may be a sign of non-arteritic anterior ischemic optic neuropathy (NAION), a cause of decreased vision including permanent loss of vision, that has been reported postmarketing in temporal association with the use of all PDE5 inhibitors, including sildenafil, when used in the treatment of erectile dysfunction. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors. Physicians should also discuss the increased risk of NAION with patients who have already experienced NAION in one eye, including whether such individuals could be additionally affected by use of vasodilators, such as PDE5 inhibitors (see Adverse Reactions).

There are no controlled clinical data on the safety or efficacy of REVATIO in patients with retinal pigmentary, a minority whom have genetic disorders of retinal photoreceptor. Prescribe REVATIO with caution in these patients.

Hearing Impairment

Advise patients to seek prompt medical attention in the event of a sudden decrease or loss of hearing while taking PDE5 inhibitors, including REVATIO. These may be accompanied by tinnitus and dizziness, have been reported in temporal association to the intake of PDE5 inhibitors, including REVATIO. It is not possible to determine whether these events are related directly to the use of PDE5 inhibitors or to other factors (see Adverse Reactions).

Combination with other PDE5 inhibitors

Sildenafil® is also marketed as VAQUARA®. The safety and efficacy of combinations of REVATIO® with VAGARA® or other PDE5 inhibitors have not been studied. Inform patients taking REVATIO not to take VAQUARA or other PDE5 inhibitors.

Prolonged Erection

Use REVATIO with caution in patients with anatomical deformation of the penis (e.g., angulation, cavernosal fibrosis, or Peyronie’s disease) or in patients who have conditions, which may predispose them to priapism (e.g., sickle cell anemia, multiple myeloma, or leukemia). In the event of an erection that persists longer than 4 hours, the patient should seek immediate medical assistance. If priapism (painful erection greater than 6 hours in duration) is not treated immediately, penile tissue damage and permanent loss of potency could result.

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

• Hypertension (see Warnings and Precautions)
• Vision loss (see Warnings and Precautions)
• Hearing loss (see Warnings and Precautions)
• Priapism (see Warnings and Precautions)

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Safety data were obtained from the placebo-controlled clinical study and an open-label extension study in 277 treated patients with pulmonary arterial hypertension.

Doses 10 mg TID were studied.

The overall frequency of discontinuation in REVATIO-treated patients at the recommended dose of 20 mg TID was 3% and was the same for the placebo group.

In the placebo-controlled trial in pulmonary arterial hypertension, the adverse drug reactions that were reported by at least 3% of REVATIO patients treated at the recommended dosage (20 mg TID) were more frequent in REVATIO patients than placebo patients, are shown in Table 1. Adverse events were generally transient and mild to moderate in nature.

Table 1. REVATIO All Cause Adverse Events in % of Patients and More Frequent (> 1%) Placebo

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Placebo</th>
<th>REVATIO 20 mg TID</th>
<th>Placebo-Subtracted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epistaxis (3%)</td>
<td>1</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td>7</td>
<td>6</td>
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<tr>
<td>Flushing (4%)</td>
<td></td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Vision loss</td>
<td></td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Hearing loss</td>
<td></td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Syncope</td>
<td></td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Myalgia</td>
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<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Myopathy</td>
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<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Palpitations</td>
<td></td>
<td>3</td>
<td>3</td>
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<tr>
<td>Hot flush</td>
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<td>3</td>
<td>3</td>
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<tr>
<td>Urticaria</td>
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<td>3</td>
<td>3</td>
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<tr>
<td>Fatigue</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

not otherwise specified

At the recommended 20 mg TID, there was a greater incidence of some adverse events including flushing, diuretics, myalgia and visual disturbances. Visual disturbances were identified as mild and transient, and were predominately color vision, but also increased sensitivity to light or blurred vision. The incidence of retinal hemorrhage at the recommended sildenafil 20 mg TID dose was 1.4% versus 0% placebo and for all sildenafil doses studied was 1.2% versus 0% placebo. The incidence of eye hemorrhage at both the recommended dose and at the 10 mg TID dose was 0.7% versus 0% for sildenafil versus 1.4% for placebo. The patients experiencing these events had risk factors for hemorrhage including concurrent antiocoagulant therapy.
pin for primary prevention of cancer and cardiovascular disease. The study is now in the observational phase with 30 years of follow-up, during which 517 clinically verified nonfatal MIs, strokes, coronary revascularizations, and cardiovascular deaths have occurred. In a Cox proportional hazards model adjusted for age, race, socioeconomic status, and study drug assignment, the 3,529 women who reported high job strain (a baseline hazard of 4.5% increased risk of MI, a 40% increase in coronary revascularization, and a 40% increase in total cardiovascular events, compared with the 4,161 female health professionals with low job strain.

Women who reported high job strain at baseline had a 90% increased risk of myocardial infarction.

DR. SLOPEN

The 3,736 women who reported active job strain had a 60% increase in total cardiovascular events compared with the low job strain group.

The investigators also looked about job insecurity. At baseline, 19% of Women's Health Study participants indicated they were unsure about future job loss. Contrary to the study hypothesis, however, no independent association was found between job insecurity and subsequent development of cardiovascular disease.

An important clinical implication of this study is that it may be useful for physicians to ask about job stress as part of their total health assessment of women employed outside the home. Women with high job strain or active job strain can be counseled that there are data to support several beneficial inter-ventions, including maintaining a physically active lifestyle to help burn off psychological stress, engaging in social support networks to aid in coping with work strain, and reserving time every day – as little as 10-15 minutes – for some form of relaxation. It’s also important to let patients know that help is available outside the workplace; e-mail is a big of fender in this regard, according to Dr. Slopren.

The Women’s Health Study is funded by the National Institutes of Health. Dr. Slopren declared having no relevant financial disclosures.

CV, Arthritis

Markers Predict Cardiac Events

Both markers of rheumatoid arthritis severity and traditional markers of cardiovascular risk are independent predictors of future CV events in RA patients. Dr. Daniel H. Solomon, chief of the section of clinical sciences in the division of rheumatology, immunology, and allergy at the Brigham and Women’s Hospital, Boston, and his associates examined the relative importance of the two types of markers in predicting CV events using a large, longitudinal cohort of RA patients, CORRONA ( Consortium of Rheumatology Researchers of North America). Enrollment began in 2002, and patients were followed through 2006. For this analysis, 10,156 subjects were followed for a median of 22 months for the development of incident MI, stroke, or transient ischemic attack.

The study subjects’ mean age was 59 years, 80% were women, and 75% were postmenopausal. Median disease duration at baseline was 7 years. There were 29 MIs and 47 strokes or TIs during follow-up, for an event rate of about 4 per 1,000 person-years.

Six traditional markers of CV risk – hypertension, diabetes, hyperlipidemia, current tobacco use, known cardiovascular disease, and a family history of premature CV events – were important predictors of CV events during follow-up. In addition, seven markers of RA severity were strong, independent predictors of CV risk.

Moreover, the incidence of CV events escalated as the number of either type of risk factor increased. The incidence was 0 in patients with no CV risk factors and no markers of RA severity, and it rose to 7.5 per 1,000 person-years in patients with two or more CV risk factors and three or more markers of RA severity, the researchers wrote (Ann. Rheum. Dis. 2010;69:1920-5).

There was no specific support for this analysis. Dr. Solomon receives support from the National Institutes of Health, the Agency for Healthcare Quality and Research, the Arthritis Foundation, Abbot, and Agenen.

—Mary Ann Moon