

Treating the Whole Patient

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Collaboration and communication between psychiatrists, primary care doctors and other physicians are becoming increasingly critical, as both research and anecdotal data are lending empirical credibility to the interdependence of body and mind. Comorbid depression with major medical illnesses may be particularly dangerous, and evidence is accumulating that failure to address this depression can impede medical treatment and increase mortality.

"I'm not sure that people -- meaning consumers, mental health professionals and non-mental health professionals -- realize what the numbers are," David Kupfer, M.D., explained in an interview with *Geriatric Times*. "They're epidemic and scary. We're not talking about feeling somewhat down and mildly dysphoric, we're talking about major depression."

Kupfer, chair of University of Pittsburgh's department of psychiatry, recently moderated a conference titled "The Unwanted Co-Traveler: Depression's Toll on Other Illnesses." Sponsored by the National Institute of Mental Health (NIMH), the conference comprised specialists in cardiovascular disease, cancer, diabetes, HIV/AIDS, and Parkinson's disease (PD) and other neurological diseases.

Psychiatrists and primary care physicians "can learn a lot from each other," Kupfer continued. He believes that depression frequently is undertreated in patients with comorbid medical illness because of the mistaken belief that it is a normal response to the latter, particularly in the case of elderly patients. In fact, major depression does not occur in the majority of patients with other medical illnesses. However, when it does, neurovegetative symptoms associated with depression can substantially interfere with patients' ability to follow through with treatment recommendations. The following is a look at the latest research and treatment recommendations for depression that accompanies cardiovascular disease, stroke and PD.

Cardiovascular Disease

Estimates indicate that roughly one-fifth of post-myocardial infarction patients meet diagnostic criteria for major depression. Research indicates that the prevalence of depression among patients who have not had heart attacks but have angiographically documented coronary artery disease runs around 18% (Carney et al., 1987, as cited in Robinson and Krishnan, in press), compared to about 10% in the general American population. The risk of dying within six months is three to four times greater for depressed survivors of myocardial infarction (MI), as compared to their nondepressed peers (NIMH, 1999).

In another study, Canadian researchers found that the significantly higher risk of cardiac mortality at the one-year mark among depressed patients was largely independent of the severity of cardiac disease (Frasure-Smith et al., 1999). Equally, if not more, concerning are recent findings indicating that depression can actually foreshadow the development of heart disease (Moon, 2001).

"Depression is a chronic illness and contributes to chronic stress," Lawson Wulsin, M.D., coordinator of the family medicine and psychiatry residency training program at University of Cincinnati, told *GT*.

"We know that stress is taxing to the cardiovascular system in particular, because it can increase blood pressure, decrease heart rate variability and may suppress immune function in subtle ways that contribute to inflammatory processes, and cardiovascular disease is an inflammatory disease."

In addition, higher smoking rates among depressed individuals put them at higher risk of developing heart disease, said Wulsin, who presented findings suggesting the link between depression and subsequent heart disease at the American Psychiatric Association's 2000 annual meeting.

In a recent interview, Wulsin reiterated his recommendation that depressed patients over the age of 40 be referred for a full medical checkup to screen for potential cardiovascular problems: "Psychiatrists should be taking better cardiovascular histories of their depressed patients, and primary care [doctors] and cardiologists should be taking good histories of depression in their patients with heart disease."

Wulsin also explained that prophylactic use of antidepressants may be justified in patients with cardiovascular disease who have a history of major depression or a strong family history of the mood disorder. He added, however, that too many questions remain regarding the treatment of depression, and its effect on cardiovascular outcomes, to recommend that all patients with cardiovascular disease receive prophylactic antidepressant treatment.

Despite the high incidence of depression among patients with cardiovascular disease, information on how to safely and effectively treat such patients remains limited. Tricyclic antidepressants generally are not used, due to documented side effects that include cardiac conduction delays and orthostatic hypotension. To date, sertraline (Zoloft) has been shown safest and most effective in post-MI patients (Goodnick and Hernandez, 2000; Robinson and Krishnan, in press).

A number of studies have shown that the selective serotonin reuptake inhibitors (SSRIs) are safe and effective for depressed patients with ischemic heart disease, and this class of antidepressants is generally preferred by clinicians due to its more favorable side-effect profile. Still, when choosing an SSRI -- particularly for post-MI patients -- psychiatrists should take into account factors such as platelet activation, as well as the usual drug interaction caveats. Concerning the latter, University of Miami mood disorders director

Paul J. Goodnick, M.D., clearly remembers hearing about a patient who was put on paroxetine (Paxil), along with a β -blocker, digoxin and other medications by cardiac care unit staff after being hospitalized for chest pain. The patient, who was not being treated for depression, was released and then emergently re-hospitalized after interaction between the paroxetine (a potent 2D6 inhibitor) and the β -blocker significantly lowered his heart rate.

Stroke

An estimated 10% to 27% of American stroke patients experience major depression each year. That translates to between 60,000 to 162,000 people, three-quarters of whom are over the age of 65. An additional 15% to 40% will suffer depressive symptoms within two months of suffering a stroke.

If the emotional suffering inherent in depression were not incentive enough to treat the disorder, researchers have discovered that untreated depression in this population can seriously impede patients' chances of recovery. A growing body of research strongly indicates that depression in stroke patients leads to poorer outcomes, both in cognitive functioning (Kimura et al., 2000) and in the recovery of the ability to perform activities of daily living (ADLs) (Chemerinski et al., 2001).

"Patients tend to report that they're depressed because they've had a stroke," Robert Robinson, M.D., head of the psychiatry department at University of Iowa College of Medicine, said in an interview with *GT*. "Physicians in those circumstances will often just regard it as an understandable, reactive depression and not realize what a profound effect this depression has on [patients'] recovery and survival."

Assessing depression in a stroke patient can present unique clinical challenges. Stroke can cause apathy and/or crying spells, interfere with a patient's awareness of objectively observable neurovegetative signs, and impair their ability to express or describe emotion (Black, 1995).

If a patient's ability to process verbal or written language has not been impaired, a normal mental status exam can provide reliable and valuable diagnostic information when combined with a comprehensive interview and direct observation of depressive symptomatology. For patients whose language processing skills have been affected, Robinson explained that a presumptive diagnosis of depression generally is made in the presence of neurovegetative signs such as crying, withdrawal, sleep and/or appetite disturbance.

Robinson believes that when depressed stroke patients are treated, they are most likely to receive SSRIs, despite the demonstrated effectiveness and relative safety of the tricyclic antidepressant nortriptyline (Aventyl, Pamelor) in this patient group. In a placebo-controlled, double-blind study published last year (Robinson et al., 2000), nortriptyline bested fluoxetine (Prozac) in the treatment of post-stroke depression, improving recovery of ADLs and reducing anxiety symptoms.

Still, there are physicians "who just don't have any experience with these medications, even though they're effective," said Robinson. "In patients who can't take nortriptyline, citalopram [Celexa] may be a good idea," particularly for patients with cardiac conduction abnormalities. Robinson firmly believes that cardiovascular disease is not necessarily a contraindication for the use of tricyclics and said that if a stroke patient's electrocardiogram shows no conduction problems six to 12 months after an MI, he feels confident about prescribing nortriptyline. Regardless of which antidepressant he selects, Robinson believes that treatment should continue for a full year and said he bases this recommendation on research he is currently conducting that suggests depressed stroke patients may be at increased risk for mortality for up to five years following the stroke.

Parkinson's Disease

As many as two out of three Americans afflicted with Parkinson's disease may suffer from depression. While common in this population, depression can be hard to diagnose because some PD symptoms (such as psychomotor retardation, appetite disturbance and affective flatness) can mimic it. Depressed PD patients have higher rates of anxiety and are more likely to experience sadness without guilt or self-blame than depressed patients who do not have the disease.

Looking at phenomena such as sleep disturbance -- a chronic problem in PD patients -- in conjunction with feelings of hopelessness, worthlessness, anhedonia and suicidal ideation is a better way to assess depression in this population, according to William McDonald, M.D., professor of psychiatry and behavioral science at Emory University and director of the Fuqua Center for Late-Life Depression.

The SSRIs have been used safely and effectively to treat depression in patients with PD. An exception is patients taking selegiline (Eldepryl), an antiparkinson agent, in whom the combination may lead to serotonin syndrome.

Otherwise, McDonald told *GT*, "There's absolutely no reason not to give them a trial of antidepressant. My clinical experience tells me that they have great responses and you clearly do not worsen their Parkinson's symptoms...I think when you get into the area of medical comorbidity, [physicians can] be a little less willing to use medication for fear they'll make things worse."

The phenomenon known as off-period depression is another PD-related problem that can be successfully treated with medication, according to Kevin J. Black, M.D., assistant professor of psychiatry, neurology and radiology at Washington University School of Medicine. Off-period depression occurs when a dose of levodopa (Sinemet) or a dopamine agonist (e.g., pramipexole [Mirapex], pergolide [Permax], ropinirole [Requip], bromocriptine [Parlodel]) wears off. Black told *GT* it affects between 5% and 10% of patients with PD at some time during the course of their illness.

These patients are not otherwise depressed and their clinical presentation can be striking. Black recalled meeting one patient with a 10- to 15-year history of the disease who talked

of a wish to die; after taking a dose of levodopa 30 minutes later, all depressive signs vanished and were replaced by cheerful affect. Increasing the amount or frequency of levodopa doses can be of considerable help, said Black. Other alternatives include the addition of selegiline or catechol-O-methyltransferase inhibitors such as entacapone (Comtan), which enhance and extend the effects of levodopa.

Black has found electroconvulsive therapy (ECT) to be helpful in patients with PD with psychotic depression and with hallucinations that often occur in later stages of the disease. Black recommends that ECT be performed only twice per week in these patients due to an increased tendency to become confused after treatment.

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