Depression and Medical Illness

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INTRODUCTION

Researchers have found that the prevalence of major depression increases linearly as one moves from community to primary care to medically ill populations. Prevalence rates have been shown to be about 2% to 5% in community populations, 5% to 10% in primary care patients, and 6% to 14% in medically ill patients.[1] Depression is second only to hypertension as the most common chronic condition encountered in general medical practice.[2] Identification and effective treatment of co morbid depression is being increasingly considered an essential component of high-quality clinical care of patients with chronic medical illness. This is in response to a number of studies demonstrating the high prevalence of depression in the medically ill and the major adverse impact of affective illness on symptom burden, functional impairment, and self-management of illness.

DEPRESSION AND MEDICAL ILLNESS : INTERRELATIONSHIPS

There is a substantial body of literature documenting increased prevalence of depression in several chronic medical illnesses, including various forms of vascular disease (cardiovascular, cerebrovascular, or peripheral vascular), diabetes mellitus, and arthritis. Specifically, patients with cardiovascular disease appear to have approximately three times the risk for depression,[3,4] those with diabetes mellitus have two to three times the risk,[5] and those with arthritis seem to have 40% to 60% more risk for depression.[6]

Depression tends to amplify deleterious effects of medical illness and may even lead to increased mortality. The Systolic Hypertension in the Elderly Program found that depressive symptoms represented a significant risk factor for stroke, myocardial infarction (MI), and death.[7] One study[8] reported that 32% of patients with acute MI experienced depression in the first few weeks after the event and were at increased risk of mortality over 18 months. In a larger sample and at 5-year follow-up, the same group found up to four times higher rates of cardiac mortality in patients with depression.[9] Overall, these studies suggest that depression developing in the post-MI period is associated with a significantly higher risk of subsequent MI and death, with adjusted odds ratios for the latter in the range of 4 to 6.[8,9] Finally, a recent study found that elderly patients with and without baseline cardiac problems showed an increase in mortality if they suffered from sub-threshold, minor, or major depression.[10]

Similarly, patients with depression and diabetes mellitus are at increased risk for poorer adherence to diet and medication regimens, greater functional impairment, and higher healthcare costs than those without depression.[11] They suffer from higher rates of a variety of diabetes mellitus complications such as diabetic retinopathy, nephropathy, neuropathy, macrovascular complications, and sexual dysfunction than non-depressed patients with diabetes mellitus.[12]

Studies have also suggested that major depression in adults is a risk factor for the later development of two of the most common medical illnesses associated with shortened lifespan in adults - diabetes mellitus and coronary heart disease.[13] It has also been observed that depressed patients are three times as likely not to adhere to treatment for their medical illness as nondepressed patients.[14] Findings from an analyses of the Cochrane database suggest that recovery rates in medically co-morbid depressed patients being treated with antidepressant medications are three times higher than recovery rates in patients on placebo.

Cardiovascular Disease

Depression as a factor in heart disease has been studied extensively. It has been proposed that β blocker therapy causes a significant amount of depression; however, the "depressive mood" caused by these agents is generally not clinically significant enough to meet the criteria for major depressive disorder as specified by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).[15] The medical history of the patient also plays an important role in the development of depression after a myocardial infarction or other cardiac event, such as a coronary artery bypass graft.[16-18] Risk factors for development of depression after myocardial infarction include the presence of other debilitating medical conditions, previous major or minor depression, and type A personality.[19]

Platelet activation leading to thrombosis may be a factor in how depression is biologically related to increased mortality in cardiovascular disease. It has been hypothesized that elevated levels of serotonin in platelets in a depressed patient may be a factor in promoting thrombogenesis.[4,20] Other factors may include elevated platelet calcium levels[4] and the availability of nitric oxide (NO), formed by the enzyme nitric oxide synthase (NOS). NO inhibits platelet aggregation;[21] thus, inadequate production of NO has been hypothesized as a risk factor in development of coronary vasoconstriction.[22]

Psychological stress, including depression, may increase ventricular ectopy and subsequently increase the risk of ventricular fibrillation.[23] In addition; high-frequency heart-rate variation is markedly diminished in depressed patients due to decreased parasympathetic tone. This decrease in parasympathetic activity lowers the threshold for ventricular ectopy and ventricular fibrillation, leading to a higher potential for sudden cardiac death.[15,17,18, 24-28]

Due to the increased frequency of depression among patients with cardiac disease, as well as the increase in morbidity and mortality that depression causes in this patient population, treatment of depression in patients with cardiovascular disease is imperative. The question remains: which antidepressant is safest for the patient with cardiac disease? Treatment of depression in cardiac patients is complicated by concerns regarding effects of medications on heart rhythm, blood pressure and other cardiovascular functions. Although many agents have been shown in clinical trials to be relatively safe for patients without cardiac disease, only a small number of trials have thoroughly evaluated the use of antidepressants in patients with cardiac disease.

A few basic principles of treatment emerge from available results. No TCA should be used, as consequences of their use (increased heart rate, rate of orthostatic hypotension, and increased PR and QTc intervals) may be fatal. Although controlled data are available for the safety of fluoxetine and paroxetine in patients with IHD, there may be some questions with regards to their efficacy in this patient group. Bupropion has been shown in two studies to be safe, particularly to avoid causing orthostatic hypotension and to reduce premature ventricular contractions. Yet, the only antidepressant shown to be safe and effective in post-MI patients is sertraline.[29]

Diabetes Mellitus

Patients with depression have been shown to exhibit insulin resistance and decreased glucose tolerance.[30] Catecholamines appear to increase glucose levels in blood by blocking insulin release and increasing glucose uptake; they may also reduce sensitivity to insulin.[31] In contrast, increases in serotonergic function may increase sensitivity to insulin and reduce plasma glucose.[32]

Short-term administration of TCAs may lead to reduced fasting blood glucose while longer use increases baseline values, due to their catecholamine profile. They successfully treat depression but also lead to deterioration in glucose control. SSRIs such as fluoxetine and sertraline, improve both dietary compliance and HbA_{1c} levels in addition to reduction in severity of depression.[29]

Neurology

Depression is a common occurrence after a CVA (Cerebrovascular accident). The incidence of Post Stroke Depression may be as high as 50%.[33] Though the TCAs are effective specially nortryptyline the side effects may negate its use in these patients while the SSRI's like citalopram, sertraline and floxetine who have controlled data on efficacy and safety are preferred.[34]

The frequency of depression in Parkinson's disease has been estimated at 51%. This is expected due to the dopamine deficiency state in this disease. Risk factors for depression include the presence of akinesia, anxiety, and psychosis.[35] The TCAs have the most beneficial action both on depression as well as rigidity, akinesia and tremor. Though SSRIs are effective for depression they may worsen Parkinson's symptoms. Bupropion may have risk of psychosis and delirium.[36]

Depression may also be a symptom with dementia specially Alzheimer's disease and vascular types. Moclobemide, which is a RIMA antidepressant, is good for dementia with depression but the efficacy is best for sertraline, citalopram and paroxetine in double blind studies.[37]

Cancer

Depression estimates vary from 17%-25%. The symptoms of cancer and depression may overlap. Depression may precede, accompany and follow cancer. In terms of efficacy TCAs and SSRIs are similar but the latter may be preferred due to lesser side effects. Mirtazapine, a NaSSA antidepressant, may also be effective.[38]

SUMMARY

Depression is seen frequently in association with chronic medical illness and leads to increased morbidity, mortality and healthcare costs. Treatment with an antidepressant helps in improving depression and possibly the medical illness itself.

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