Depression in the physically ill patient

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Medical illness can become a psychological burden to some patients, leading to depression that significantly affects their outcomes and prognoses.

PHOTOLIBRARY

Depression and physical illness have been recognised as being closely linked since the early 1900s.[1] Despite this, the presence of depression in physically ill patients is often missed and, therefore, not treated appropriately.[2,3] There are several reasons why depression may not be diagnosed, including:

- difficulty differentiating depression from a patient's normal emotional response to physical illness
- difficulty distinguishing symptoms of depression from those of the physical disease itself
- difficulty distinguishing symptoms of depression from the side effects of treatment for the physical disorder.

The relation between depression and physical illness is complex.[4] The risk of depression is increased by many of the same factors that can lead to or aggravate physical diseases. These include smoking, poor diet, lack of exercise, obesity and hypertension. Depression is associated with:

- alterations in the metabolism of several important neurotransmitters – for example, serotonin, noradrenaline, dopamine, gamma-aminobutyric acid and glutamate
- changes in endocrine functioning – for example, cortisol and thyroid and growth hormones
- impairment of immunological status – for example, inflammatory processes and cell-mediated immunity.

These biological effects may, in turn, increase the risk of progression of diseases such as cardiovascular disease, metabolic syndrome, cancer and HIV infection.

Comorbid depression affects the outcome and prognosis of patients with a physical illness. This may be because of a delay in seeking treatment, a lowered rate of diagnosis and/or poor adherence to treatment, not only medications but also behavioural modifications and health-promoting activities. In turn, physical illness may directly affect a patient's brain and/or become a psychological burden, which could lead to the development of depression. Overall, these interactions lead to a poorer outcome of the medical illness and increased mortality, in addition to the burden of the depression itself.

Coexistence of depression with physical illness

The coexistence of depression with medical illness may occur for a number of reasons. Depression may be a direct consequence of the medical illness such as occurs with thyroid disease, Addison's disease or Cushing's disease. In these situations, the depressive syndrome results from the physiological effects of the hormonal changes. Depression may occur as a direct consequence of central nervous system disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease and stroke. In these cases it is most probably due to the effects of the disease process on the areas of the brain linked to mood regulation, such as the prefrontal cortex and the limbic region.

There may also be a biological basis for depression in some medical illnesses, such as heart disease, arthritis, chronic respiratory disease, gastric disease and malignancy, in which depression may share common risk or pathological factors. In susceptible patients, depression may be induced by certain medications, such as β-blockers, reserpine, steroid contraceptives, interferon, anticancer drugs and isotretinoin. A depressive state may occur after withdrawal of drugs such as alcohol, sedatives, hypnotics, cocaine or amphetamines, or a low mood may occur in the context of drug and alcohol intoxication and abuse.

More commonly, depression may develop as a psychological response to physical illness, particularly those associated with physical disability, poor physical health, chronic pain and low survival prognosis. In other words, there is a psychological reaction to having a medical illness or some experience of 'loss' associated with the illness. These losses include:

- those that may be obvious, such as

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continued

Table 1. Differential diagnoses of depression in physical illness

- Mood disorders due to a general medical condition
- Substance or drug-induced mood disorders
- Major depressive episode
- Adjustment disorder
  – with depressed mood
  – with mixed anxiety and depression
- Normal grief-like reaction
- Demoralisation

Table 2. *Diagnostic and Statistical Manual of Mental Disorders (DSM)*-IV criteria for major depression[5]

- Persistent depressed mood, sadness or irritability
- Loss of interest and pleasure in work, hobbies, sex, etc
- Loss of weight or appetite
- Insomnia or hypersomnia for most of the day
- Psychomotor agitation or slowing
- Fatigue or loss of energy
- Feelings of worthlessness or guilt that are excessive
- Poor concentration or decision-making
- Suicidal ideation that may lead to a specific plan or attempt

the loss of a bodily part – for example, amputation and mastectomy
- loss of functioning – for example, paralysis and impotence
- less apparent losses – for example, the loss of the sense of self, self-esteem and a purpose or role in life.

These psychological reactions may resemble, and may be viewed as, attenuated forms of grief. There is no relation between the extent of the physical illness and the severity of the psychological response. The emotional response is determined by the patient's perception of the meaning of his or her illness. An illness may be viewed as a threat to physical integrity, a confirmation of a patient's mortality and vulnerability, and/or a loss of sexuality. Past personal experiences with illness and death will influence how a patient reacts psychologically to his or her diagnosis and illness.

Differential diagnoses

Many biological and psychosocial causal factors can contribute to the syndrome or collection of symptoms and signs that are referred to as depression (Table 1). The disorder is classified as major depression if five or more of the criteria listed in Table 2 are present for most of the day on the majority of days for a minimum of two weeks.[5] If the patient meets three or four criteria over at least two weeks, the condition is minor depression and, in the presence of a physical disorder, is most appropriately referred to as an adjustment disorder with depressed mood. In this case the mood disorder is occurring in the context of a significant stressor(s), such as the impact of disability resulting from the illness or the attendant psychosocial consequences – for example, marital disharmony or loss of productivity.

Major depression indicates a greater likelihood of response to antidepressants, while supportive counselling and other psychotherapies may be more appropriate for minor depression, adjustment disorder and grief states. If the depression is secondary to a medical condition or drug, then addressing the underlying cause would be necessary.

It is also quite appropriate for patients to become emotional and upset after the diagnosis of an illness or trauma. The response may well be in keeping with the extent of the illness and their cultural background and personality. If the lowered mood is not persistent but fluctuates from day to day, is responsive to the environment and is not excessive, overwhelming or incapacitating, it is reasonable to view it as appropriate and a normal grief-like reaction. Individuals with such a reaction will respond to support, encouragement and an opportunity to express their fears and disappointments. Demoralisation – a loss of spirit or drive due to recurring or protracted suffering – may develop as a natural reaction to a severe and/or chronic illness.

Prevalence

The prevalence of depression in individuals with chronic medical conditions is higher than that of the general population and is up to 40% in those with some neurological conditions. A large US population-based study of more than 30,000 people used diagnostic interviews to identify prevalence rates of major depression for various medical conditions.[6] These included: depression rate of 7.9% for those with congestive heart failure, 8.0% with hypertension, 9.3% with diabetes, 9.3% with coronary artery disease, 11.4% with cerebrovascular accident, 15.4% with chronic obstructive pulmonary disease, 17.0% with end-stage renal disease and an average depression rate of 8.8% with any chronic condition. In addition, participants with two or more chronic illnesses were 2.6 times more likely to have major depression. These estimates are lower than those reported by other studies using screening instruments to detect depression that are not selective for major depression.[7] This high prevalence of depression in medically ill patients reported in a research study is in contrast to the relatively low rates of detection and treatment in clinical practice.

Assessment of depression in medically ill patients

Depression associated with physical illness warrants careful assessment. The key to detection is to consider its presence and make the appropriate enquiries, such as: 'How have you been feeling?', 'Have you been feeling sad, upset or miserable?', 'Has all this been getting you down?' or 'Do you sometimes feel like giving up?' It can be difficult to tease out the biological symptoms of depression (insomnia, anorexia, weight loss, lethargy and fatigue) from those that occur as a consequence of medical illness or treatments. Anxiety may also be present and this can amplify physical symptoms.

Some symptoms, such as a persistent and unresponsive lowered mood, a loss of interest, negative thinking, guilt, feelings of worthlessness and low self-esteem, are strongly suggestive of clinical depression.[8] It is important to carry out a risk assessment of all depressed patients and make enquiries about thoughts of wanting to die or any wishes to self-harm or end their lives. The presence of a suicide plan should always be taken seriously and psychiatric referral should be sought.

There may be a temporal relation between the onset or exacerbation of the physical disorder and the depression, or sometimes a depressive syndrome may antedate the onset of an illness. It may be difficult at times to distinguish a normal grief-like response to an illness from a depressive disorder that warrants clinical intervention.[9] Is the depth of the patient's despair closely linked to the course of the illness or is the patient consistently depressed despite improvement? Is he or she able to be cheered up by the presence of family and/or friends? Interviewing significant others can be helpful in gauging the emotional change in the patient since the illness began.

Several depression rating scales have been used in studies or the clinical care of physically ill patients to screen them for depressive illness. These include:

- observer-rated instruments such as the Hamilton Depression Rating Scale and the Composite International Diagnostic Interview (CIDI)/ CIDI-Short Form
- subject-rated scales such as the Beck Depression Inventory for Primary Care, the Hospital Anxiety and Depression Scale, and the 90-item Symptom Checklist.

The Depression in the Medically Ill Scale screening tool has been developed and validated in medically ill patients.[10,11] It excludes items related to physical illness and has compared well with the *Diagnostic and Statistical Manual of Mental Disorders (DSM)*-IV diagnostic criteria and clinicians' judgements of clinical depression.[5] The nine-item depression subscale of the Patient Health Questionnaire (PHQ-9) has also been found to be a valid, reliable screening and monitoring tool.[3,12] Such scales and simplistic 'ticking the box' approaches, however, should only be used for screening and should not take the place of an individualised evaluation and diagnostic formulation of the physical and psychosocial aspects of the patient's illness.

Somatisation refers to a patient's presentation with physical symptoms that are due to underlying psychological factors rather than having a medical cause. As such, the possibility of somatisation should be kept in mind when unusual or unexplained physical symptoms occur. It is important to avoid misattribution of physical symptoms to a new physical condition or an exacerbation of an existing physical disorder. Pain or unusual weakness can be a sign of an underlying psychiatric disorder, such as depression, or may be an expression of psychological distress where anxious and depressive states are manifest in a physical manner. This is commonly associated with a stress response, such as to a serious physical condition, where somatic symptoms can be frequently reported during the adaptation process and no organic cause can be identified. In these circumstances it is prudent to carefully assess patients for depressive symptoms.

It is important to exercise caution when patients present with possible somatisation and not be too rapidly dismissive of the physical symptomatology; patients should always be adequately assessed and investigated. A too hasty conclusion that a symptom is 'psychosomatic' can lead to a missed diagnosis with dire consequences; the presence of signs of depression does not necessarily exclude underlying physical disease. Often in these circumstances, referral of patients to an experienced psychiatric colleague can help tease out the psychological issues and either ensure appropriate investigation or minimise excessive investigation.

Reasons for treating depression

Depression in physically ill patients is associated with increased morbidity and mortality when compared with that predicted for the illnesses themselves. Major depression is associated with significantly increased use of health resources, lost productivity and functional disability.[6] Functional disability has been found to be higher in patients with both major depression and chronic medical conditions than in patients with either condition alone.[13] A further study found that a diagnosis of major depression in older medical inpatients was associated with poorer physical health and poor mental health in their informal caregivers.[14,15]

The presence of depression may impair a patient's ability to seek help and adhere to treatment for comorbid physical illness. A meta-analysis of 12 studies showed that depressed physically ill patients are three times more likely to be non-adherent to medical treatment than physically ill patients with no depression.[12] In addition, there is evidence that depression is a risk factor for cardiovascular disease, cerebrovascular disease and type 2 diabetes.

Depressed patients are less likely to have an adequate and appropriate diet, are

more likely to smoke and drink excessive alcohol, and are less likely to be physically active. Therefore, the treatment of depression in physically ill patients could significantly improve depressive symptoms in a wide range of physical diseases and is likely to improve patients' quality of life or even help him or her overcome the physical illness. Importantly, patients with depression due to medical conditions, particularly chronic, painful or incurable illness (for example, malignancy, AIDS, and brain or spinal cord injury), have a significantly increased risk of suicide and attempted suicide.

Management of depression

Management of depression consists of a comprehensive assessment and problem-based management plan that tailors a range of biological and psychosocial therapies to the needs of each patient. In most instances, the presence of a major depressive episode warrants treatment with an antidepressant. Occasionally, patients who are highly motivated may respond to expert psychotherapy, such as cognitive behavioural therapy or interpersonal psychotherapy, alone; however, if symptoms do not quickly respond then medication should be prescribed.

Antidepressant medication should be accompanied by supportive therapy, including an opportunity for patients to express their fears and their understanding of their illnesses, psychoeducation about depression and antidepressants and, if appropriate, reassurance.

How often medical outpatients should be seen will vary and must be tailored individually depending on the severity of symptoms and the presence of suicide risk. As a rule of thumb, most patients should initially be reviewed weekly to assess medication tolerability and to monitor their response to treatment. Once these are assured, treatment can be spaced to every two weeks then every four weeks. Longer gaps may be appropriate when a full remission of symptoms has been achieved.

Initiation of treatment must be followed by a continuation phase of treatment and a follow-up phase,[3] implementing treatment for at least six to 12 months for the first episode of major depression with the goal of achieving a full remission of symptoms. Treatment guidelines and algorithms for interventions used for depressive disorders are generally applicable to medically ill patients; these have been published elsewhere.[16]

Pharmacotherapy

Treatment should be aimed at treating or removing the underlying cause of depression. For example, if the depression is induced by a medication, discontinuation of the causal agent, if possible, may be all

that is required.

Treatment of the depression itself is otherwise warranted and medications should generally be considered for moderate-to-severe major depression. There have been well-controlled trials of pharmacotherapies, and the available antidepressant medications are effective for the treatment of depression in medically ill patients.[2] Further, Cochrane reviews have shown that various antidepressants are superior to either placebo or no treatment.[17] SSRIs are regarded as suitable first-line therapy, as shown by several double-blind randomised controlled studies demonstrating their effectiveness in various disorders, including cardiac disease, arthritis, stroke, diabetes, multiple sclerosis, dementia, Parkinson's disease, cancer and HIV infection.[2,18,19]

A systematic review of treatment of depression in patients with cancer recommended that pain and other reversible physical symptoms should be treated before or at the same time as specific antidepressant treatment was started.[20] Also, there are data that dual-acting antidepressants, those that influence both serotonin and noradrenaline, may have an advantage in patients experiencing comorbid chronic pain. However, there appears to be no conclusive evidence supporting the relative superiority of any one specific antidepressant over another or the superiority of one treatment modality over another.

Optimally, antidepressant choice should be based on key clinical variables such as the patient's physical state, depressive symptomatology, and past treatment response and the side effect profiles of medications. Switching to another antidepressant should be considered if there are intolerable side effects or there is an inadequate response after four weeks' therapy with an adequate dose.

Psychological therapies

Psychological therapies have been found to be effective in treating depression in patients with various physical illnesses, including HIV infection, cardiovascular disease, cancer and diabetes.[7,18,19] Psychological therapies studied have included interpersonal psychotherapy, cognitive behavioural therapy, stress management and problem-solving interventions. Such structured psychotherapies may also be suitable for patients with an adjustment disorder for which specific antidepressant treatment is not usually indicated.

Some studies have found lower rates of recovery and higher relapse rates in patients with comorbid depression compared with depressed patients with no medical illness.[7] They have suggested that collaborative treatments, including antidepressants, psychotherapy, education and case management, may be necessary to

overcome the risk of treatment recurrence or resistance in patients with comorbid depression. At any rate, most patients would benefit from a combined modality approach that includes both psychosocial and pharmacological treatments.

Principles of management for the GP

The GP plays a central role in the management of depression in the physically ill patient. It is likely that the GP has the patient's most complete physical and mental health information and therefore continuity of care that will facilitate optimal management. The GP is able to investigate medical problems that aggravate depression and can also co-ordinate both drug and psychological treatments for depression. If necessary, the GP can refer the patient to a psychiatrist if the depressive illness is severe, unresponsive to treatment, complex or atypical in nature, or if there is a possibility of a neuropsychiatric disorder, uncertainty about the diagnosis, a high risk of suicide or refusal to accept recommended advice or treatment.

When selecting an antidepressant, the potential for drug interactions should be carefully considered in depressed patients with medical illness because they are probably being treated with several other medications. With the SSRIs, serotonin syndrome may occur when they are co-administered with proserotonin compounds such as tramadol or sumatriptan. In addition, the dose of the antidepressant chosen should be carefully titrated, taking into account the changes in pharmacokinetics in physically ill patients due to renal or liver impairment or drug effects. Care should be taken to ensure that the treatment chosen does not aggravate the existing physical illness – for example, tricyclic antidepressants should not be given to patients with recent MI.

There are few studies of the treatment of depression in elderly patients with comorbid depression and physical diseases. Selection of an antidepressant requires even more care in elderly patients because of the potential for drug interactions and physical impairments due to both medical conditions and age-related changes. SSRIs are perhaps still the first choice of treatment but their side effects may be more problematic than in younger patients – for example, the syndrome of inappropriate antidiuretic hormone secretion resulting in hyponatraemia can occur occasionally, and may result in delirium and even death. Antidepressants are usually started at a lower dose in the elderly but should be gradually increased to the accepted therapeutic dose with close monitoring.[21]

Conclusion

Depression can be a risk factor for, or a consequence of, medical illness. Depression in medically ill patients is highly prevalent and can be associated with: greater morbidity and mortality rates; functional, social and occupational impairment; health risk behaviours; and higher health resource use and burden. Early detection and appropriate management of depression in patients with medical illnesses can improve outcomes and quality of life and prevent suicide. Unfortunately, most published practice guidelines for general medical care do not pay sufficient attention to psychiatric aspects.[22] With a growing recognition of the significance of depression in medically ill patients, it is hoped that future guidelines will include specific recommendations for diagnosis and active treatment of depression. MT

A list of references is available on request to the editorial office.

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References

1. Gillespie L. The clinical differentiation of types of depression. Guys Hosp rep 1929; 79: 231-233.
2. Benton T, Staab J, Evans DL. Medical co-morbidity in depressive disorders. Ann Clin Psychiatry 2007; 19: 289-303.
3. DeJesus RS, Vickers KS, Melin GJ, Williams MD. A system-based approach to depression management in primary care using the Patient Health Questionnaire-9. Mayo Clin Proc 2007; 82: 1395-1402.
4. Prince M, Patel V, Saxena S, et al. No health without mental health. Lancet 2007; 370: 859-877.
5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed (DSM IV). Washington, DC: American Psychiatric Association; 1994.
6. Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. Gen Hosp Psychiatry 2007; 29: 409-416.
7. Iosifescu DV. Treating depression in the medically ill. Psychiatr Clin North Am 2007; 30: 77-90.
8. Moorey S, Steiner H. Do depressive symptoms differ between medically ill and non-medically ill patients referred for psychological therapy? Comparing negative thoughts about the self in cancer and non-cancer patients. Behav Cogn Psychother 2007; 35: 283-291.
9. O'Keeffe N, Ranjith G. Depression, demoralisation or adjustment disorder? Understanding emotional distress in the severely medically ill. Clin Med 2007; 7: 478-481.
10. Hilton TM, Parker G, McDonald S, et al. A validation study of two brief measures of depression in the cardiac population: the DMI-10 and DMI-18. Psychosomatics 2006; 47: 129-135.
11. Wilhelm K, Kotze B, Waterhouse M, Hadzi-Pavlovic D, Parker G. Screening for depression in the medically ill: a comparison of self-report measures, clinician judgment, and DSM-IV diagnoses. Psychosomatics 2004; 45: 461-469.
12. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. Arch Intern Med 2000; 160: 2101-2107.
13. Schmitz N, Wang J, Malla A, Lesage A. Joint effect of depression and chronic conditions on disability: results from a population-based study. Psychosom Med 2007; 69: 332-338.
14. McCusker J, Cole M, Ciampi A, Latimer E, Windholz S, Belzile E. Major depression in older medical inpatients predicts poor physical and mental health status over 12 months. Gen Hosp Psychiatry 2007; 29: 340-348.
15. McCusker J, Latimer E, Cole M, Ciampi A, Sewitch M. Major depression among medically ill elders contributes to sustained poor mental health in their informal caregivers. Age Ageing 2007; 36: 400-406.
16. Ellis P; Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for Depression. Australian and New Zealand clinical practice guidelines for the treatment of depression. Aust N Z J Psychiatry 2004; 38: 389-407.
17. Gill D, Hatcher S. Antidepressants for depression in medical illness. Cochrane Database of Syst
Rev 2000; issue 4: CD001312.
18. Evans DL, Charney DS, Lewis L, et al. Mood disorders in the medically ill: scientific review and recommendations. Biol Psychiatry 2005; 58: 175-189.
19. Krishnan KR. Treatment of depression in the medically ill. J Clin Psychopharmacol 2005; 25: S14-S18.
20. Rodin G, Katz M, Lloyd N, Green E, Mackay JA, Wong RK. Treatment of depression in cancer patients. Curr Oncol 2007; 14: 180-188.
21. Kennedy GJ, Marcus P. Use of antidepressants in older patients with co-morbid medical conditions: guidance from studies of depression in somatic illness. Drugs Aging 2005; 22: 273-228.
22. Kilbourne AM, Daugherty B, Pincus HA. What do general medical guidelines say about depression care? Depression treatment recommendations in general medical practice guidelines. Curr Opin Psychiatry 2007; 20: 626-631.