



Elif Tatlıdil Yaylacı¹, Ayşe Gül Yılmaz Özpolat²

¹Numune Eğitim ve Araştırma Hastanesi, Psikiyatri Kliniği, ²Ankara Üniversitesi Tıp Fakültesi Psikiyatri AD, Ankara, Türkiye

Özet

Fiziksel hastalığı olan bireyler tedaviye uyumun azalması ve prognozun kötüleşmesi ile bağlantılı olarak depresyona daha yatkındırlar. Fiziksel hastalığı olan depresyon hastalarında yaşam kalitesi düşmekte, tıbbi morbidite ve mortalite artmakta, fonksiyonel kapasitenin azalması daha sık görülmekte, mesleki performans düşmekte ve rol fonksiyonlarında azalma olmaktadır. Ayrıca uzun hastane yatışları, fiziksel semptomların artması, tıbbi tedaviye uyumun azalması ve artmış sağlık giderleri ve sağlık sisteminin kullanımı da diğer sonuçlardır.

Anahtar Kelimeler

Depresyon; Fiziksel Hastalık; Tedavi

Abstract

People with physical illness are at an increased risk of depression, which is linked with a worse prognosis and reduced adherence to treatment. Medically ill patients with depression have reductions in quality of life, increased medical morbidity and mortality, increased functional disability, reduced occupational performance, and reductions in role functioning. Other implications of depressive comorbidity include prolonged hospital admission, amplification of physical symptoms, reduction in adherence to medical treatment, and increased medical costs and health care use.

Keywords

Depression; Physical Illness; Treatment

Introduction

In people with physical illness there is an increased risk of depression, which is linked with poor prognosis and reduced adherence to treatment. Physically ill patients with depression have reduction in quality of life, increased medical morbidity and mortality, increased functional disability, reduced occupational performance and reduction in role functioning. The other implications of depressive comorbidity include prolonged hospital admission, amplification of physical symptoms, reduction in adherence to medical treatment, increased medical costs and health care use [1].

When a person has both depression and chronic physical health problem, the functional impairment is likely to be greater than having depression or physical health problem alone [2].

Depression is approximately two to three times more common in patients with a chronic physical health problem than in people who have good physical health and it occurs in about 20% of people with a chronic physical health problem [2].

Medical in-patients are more likely to have depression than are out-patients. The factors contributing to an increased risk of depression in physical illness are listed in Table 1 [3].

Table 1. The factors contributing to an increased risk of depression in physical illness

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|--|
| Biological |
| Hormonal, nutritional, electrolyte or endocrine abnormalities |
| Effects of medication |
| Physical consequences of systemic and/or intracerebral disease |
| Psychological |
| Sense of loss associated with serious medical illness |
| Effects on body image, self-esteem, sense of identity |
| Impaired capacity to work and maintain relationships |

The physical problems could be under diagnosed in psychiatric patients. The patients with physical illness and depression have poorer levels of functioning and higher levels of mortality and morbidity compared to the patients with similar illnesses but without depression [4].

The physically ill patients with depression use more medical health care resources than those without, both for assessment and treatment. For example, the frequency of a patient's attendance at a medical out-patient clinic is better predicted by how he is depressed than his underlying medical condition [4]. In primary care settings, the patients with cardiac disease, stroke, diabetes, asthma, and many other chronic medical conditions have poorer outcomes, more frequent use of costlier health services, and greater morbidity and mortality rates when the person also suffers from depression [5].

This article outlines the assessment of depression in the patients with physical illness, explores some of the diagnostic issues involved and reviews the treatment options available.

Relationship between depression and physical illness

The comorbidity of depressive and physical illnesses may be understood in a number of different, potentially overlapping ways. First and commonly, the physical condition causes the depressive illness. This may be owing to a presumed direct biological mechanism, especially if the disease involves the endocrine or central nervous systems [3]. Many drugs used for the treatment of physical illness may have depressive side-effects. In a comprehensive list over 100 drug treatments reported as causing depressive illness. Examples of drug treatments with depressive side-effects are shown in Table 2 [3]. Second, the

Table 2. The drugs causing depressive side-effects

| |
|--|
| Corticosteroids |
| Beta-blockers, digoxin, calcium channel blockers |
| Aminophylline, theophylline |
| Non-steroidal anti-inflammatory drugs |
| Cimetidine |
| Metoclopramide |
| Levodopa, methyl dopa |
| Isotretinoin |
| Interferon α |

physical problems develop or increase owing to depressive illness. The depressive illness contributes to other alterations in health-related behaviors, including poor compliance with medications, diet, exercise and utilization of health care services. Dinan has suggested that, the increased risk of coronary artery disease and reduced bone mineral density in patients with depression is caused by increased activation of the hypothalamic-pituitary-adrenal axis causing hypercortisolism [6]. Third, the depressive and physical illnesses may have a common cause, such as bereavement or stress triggering stroke and depression [7]. Finally, the depressive illness may be coincidental or unrelated to the physical problem, as both physical and psychiatric conditions are common in the general population. Depression pre-dates the medical illness in up to 25% of patients with comorbid depression, and it is associated with an increase in somatic complaints [7].

Specific Disorders

Although a person can develop depression in association with almost any physical illness, some diseases are more likely to lead to depression than others.

A-Neurological Disorders

Parkinson's Disease

The most commonly cited prevalence of depression in Parkinson's disease (PD) is between 40% to 50% of all PD cases. While the elderly have an overall elevated risk of depression (11%) compared to the general population (7%), there is a considerably enhanced risk of depression in PD. Depression in PD has adverse effects on the quality of life of Parkinson's patients which is one of the most disabling aspects of the disease [8]. Depression is also associated with worsened motor function and increased disease severity that directly impacts the daily life. The amotivational syndrome of Parkinson's disease may be difficult to distinguish from depressive illness, and the additional symptom of anhedonia is helpful in differential diagnosis [9].

Epilepsy

Mood disorders in patients with epilepsy remain unrecognized and often treated incorrectly. The precise diagnosis and effective therapy are very important because of high suicide rate. The incidence of suicide in people with epilepsy is at least five times higher, than in the general population. The incidence of depressive disorders in epileptic patients is 30% to 70% during their life time. Depression may have a stronger influence on the quality of life than do the signs of epilepsy [10].

Multiple Sclerosis

The depressive syndromes associated with multiple sclerosis (MS) occur throughout the natural history of the disease, including very mild forms of MS. Reports of the lifetime risk for major depressive disorder (MDD) in MS populations have ranged from 27% to 54% [11].

The association of depression with the duration of MS is also unclear. Although no correlation was found in most of the studies, some reported a greater risk of depression in the first year after diagnosis [12] and in patients younger than 35 [13]. The quality of life is significantly lower among depressed MS patients than among non-depressed control patients with MS, even when controlling the factors such as level of neurologic disability and fatigue. There is also evidence that depression decreases adherence to treatment regimens for MS, and that adherence improves with treatment of depression [14].

Dementia

Depression is common in dementia, with prevalence more than 20%, causing distress, reducing quality of life, exacerbating cognitive and functional impairment, increasing mortality, and increasing carer stress and depression. Treatment of depression is therefore a key clinical priority to improve the well-being, quality of life and the level of function of the patients with dementia [15].

Depression has been reported to be more common in vascular ones than Alzheimer's dementia, unrelated to the level of cognitive impairment, and occurring at any stage of disease. The presentation will often be atypical and should be considered for patients showing a sustained change of the behaviour [16].

B-Cardiovascular Disorders

The symptoms of depression and the diagnosis of major depressive disorder carry a 3.5 to 6.6-fold increased adjusted relative risk of death in 6 and 18 month follow-up of patients with myocardial infarction. In these patients the predominant mode of death is a sudden cardiac death [17]. Yesilbursa et al compared depression and anxiety levels of patients admitted for acute coronary syndrome with patients followed for stable coronary artery disease in outpatient clinics and control group was without coronary artery disease. They used Geriatric Depression Scale, Beck Depression Inventory, Beck Anxiety Inventory, State and Trait Anxiety Inventory(STAI 1 and STAI 2) for comparison and they found that all test scores were significantly higher in acute coronary syndrome [18].

Mild to moderate depression occurs in approximately one-third of the patients following a coronary bypass surgery but may remit within weeks to months. The depressive symptoms are present in almost 30% of the patients with coronary artery bypass graft after surgery, but the presence of depression in the early postoperative period is not correlated with depression at 12 month follow-up. Depression at this later point is associated with increased mortality at 10 year follow-up [19].

C- Endocrine Disorders

Diabetes Mellitus

Depression occurs in approximately 30% of the patients with type 1 and type 2 diabetes [20]. Numerous studies have confirmed that the course of depression in patients with diabetes is more severe, and the relapses of depression episodes are more frequent, especially in patients with unbalanced diabetes [21]. A group of risk factors was specified directly resulting in the occurrence of a severe depression episode in the course of diabetes, including past depressive episode, degree of intensity of symptoms of diabetes, and past cardiovascular surgeries [22].

Hypothyroidism

The psychiatric symptoms include depressed mood, apathy, im-

paired memory and concentration. Hypothyroidism may also contribute to treatment refractory depression. Subclinical hypothyroidism may produce depressive symptoms and cognitive deficits, although these tend to be less severe than those produced by overt hypothyroidism [23].

Furthermore the lifetime prevalence of depression in patients with subclinical hypothyroidism is approximately two times than the general population. These patients display a lower response rate to antidepressants and a greater likelihood of responding to T3 augmentation than euthyroid patients with depression [24].

Cushing's Syndrome

Most patients with Cushing's syndrome experience fatigue, and depressed mood was reported approximately in 75%. Of these, approximately 60% experience moderate or severe depression [25].

The presence of depressive symptoms was significantly associated with older age, female gender, higher pretreatment 24 hour urinary cortisol levels, a more severe clinical condition and absence of pituitary adenoma [26].

D-Malignancies

Many neurovegetative symptoms of depression can be caused by cancer or side effects of treatment. Given evidence about the bidirectional relation between fatigue and depression in cancer patients, and the finding that inflammatory cytokines may cause both depression and the cancer "sickness syndrome", many clinicians include all neurovegetative symptoms as indicators of depression in patients with advanced disease [27].

The highest rates of depression are seen in patients with cancers of the pancreas, oropharynx and breast [28]. A past history of depression is probably the single greatest risk factor for current major depression in patients with advanced cancer. The others include younger age, poor social support network, poor functional status, and pain [29]. Additionally, depression in cancer patients is associated with decreased adherence to treatment, prolonged hospital stay, and reduced quality of life [30]. However in some cases of malignancies such as prostate carcinoma after radical prostatectomy although erectile disfunctions arise no depression symptomatology is observed among patients [31].

E-HIV Infection

Depressive spectrum disorders seem to be the most common psychiatric manifestations of HIV disease [32]. Major depressive disorder is more prevalent among HIV-infected individuals than in the general population, with estimated prevalence rates varying widely from 2% to 30%, but lower rates of depression are found among patients who had not progressed to AIDS [33]. MDD in HIV infected patients may be a primary consequence of central nervous system effects of HIV, a reaction to the stigmatization and emotional consequences of the diagnosis and coping with a serious medical illness, or a combination of these factors, thus constituting a heterogeneous group of affective disorder. Depression in HIV-positive patients might, however, influence the immune response and depression might lead to a progression of HIV disease and an increase in mortality rate [34].

Diagnosis of depression in physical illness

Screening, diagnosing, and managing depression in a primary

care setting is cost-effective and crucial to the overall health and well-being of all patients in primary care. Most people who complete suicide make contact with primary care health services in the days or months before their death. Approximately 20% of them make contact with primary care providers in the week before suicide and approximately 40% make contact within the month before suicide [35].

Depression is more difficult to diagnose in the patients with a physical illness. The biological symptoms of depression include anorexia, weight loss, sleep disturbance, lethargy and psychomotor retardation, all of which may equally be due to the physical illness [2].

It is particularly important that the assessment focuses on the cognitive symptoms of depression. The somatic symptoms are used to support the diagnosis of major depression if they are severe and disproportionate to the medical illness, and temporally related to the affective cognitive symptoms of depression. Three cardinal affective symptoms were suggested that help to differentiate depression from non-depression in medical patients are depressed mood, morning depression and hopelessness. Inappropriate guilt, feeling punished, lowered self-esteem and suicidal ideation are reported less frequently by the patients with depression in a medical rather than a psychiatric setting [3].

It is also important to consider the other potential causes of low mood in the patients with physical illness. These include the normal and understandable emotional reactions to physical ill health. The psychological symptoms of depression are common particularly in hypoactive delirium, which is often referred as a depressive illness for psychiatric assessment [36]. Differentiating between the two conditions is relevant to allow early treatment and avoid potential increased confusion resulting from the anticholinergic side-effects of antidepressant therapy. In organic affective disorders such as hypothyroidism, it is important to treat the underlying physical condition appropriately and then to reassess mood before considering antidepressant medication [37].

Many diagnostic tools and scales for depression rely heavily on the presence of somatic symptoms, including insomnia, loss of appetite, anergia and reduced libido to confirm a diagnosis. However, the somatic symptoms associated with depression are also present in many physical illnesses frequently, causing uncertainty about their attribution to either depression or the physical illness. In a similar way, the social symptoms of depression, including withdrawal and impairments in role functioning, may occur in both depression and physical illness, making them unreliable as markers of depression in medically ill patients. The diagnosis of depression in medically ill patients therefore relies more heavily on the symptoms of psychological distress, including preoccupation with guilty themes and failure, impairments in self-esteem, and an inability to derive joy from previously enjoyed activities [1].

Treatment of depression in physical illness

Collaborative care by primary care physicians and psychiatrists has been shown to improve adherence to treatment and symptoms in patients with major depression [38]. The successful treatment of depression by this collaborative care model may reduce patient's perception of physical symptoms, reduce incapacity as a result of those symptoms, improve efficacy of medical interventions, and improve the patient's compliance with medical treatment [39].

The biopsychosocial approach is particularly relevant here. As with any patient with depression, treatment should always involve supportive and problem-solving strategies, education, support for family members and opportunities to discuss social difficulties [40].

The main potential benefit of considering a purely psychotherapeutic approach to treatment is the avoidance of drug interactions or side-effects exacerbating the physical problems. Specific psychological therapies such as problem-solving, cognitive behavioral therapy (CBT) or interpersonal therapy (IPT) may be used as an alternative or adjunct to antidepressant medication for mild depressive disorders in those with physical illness. Of these, CBT has been the most frequently applied. The intrinsic acknowledgement of physical symptoms within the theoretical framework is particularly useful, and CBT is now well incorporated by health psychologists into cardiac rehabilitation and chronic pain programs [1].

Mohr et al demonstrated improvements in both disability and fatigue with CBT for depression in patients with multiple sclerosis [41]. In a recent study by Markowitz et al the patients with type 1 diabetes received 10 to 12 sessions of CBT. There was a clinically meaningful decrease in the depression severity, demonstrated improvements in diabetes self-care and possible improvement in glycemic control [42]. The telephone-delivered interpersonal therapy intervention showed potential to reduce depressive and psychiatric symptoms among HIV-infected persons in the rural areas in USA [43]. In a study by van Schalk et al, IPT for late-life depression in general practice was found superior to usual care both by the patients and the physicians [44]. The antidepressants should be considered whenever symptoms of depression persist, despite treatment of the underlying medical condition or brief psychotherapeutic interventions. The threshold for prescribing antidepressants is generally higher in this patient group because of the risk of metabolic complications and/or drug interactions. The choice of the drug depends on the physical illness of the patient and medications already prescribed, influenced as in usual practice by response to previous treatments. Unfortunately, data on the use of antidepressants in physically ill patients is lacking. Extra care must be taken in prescribing antidepressants to this group because of side effects, possible impact on the liver and kidneys, and the risk of drug interactions [7].

Because of increased sensitivity to side-effects in those with medical illness, treatment may need to be introduced at a lower dose before cautiously increasing this. Dividing out the dose may also improve tolerance. The anticholinergic side-effects of the tricyclic antidepressants have been a particular problem for patients with physical illness [45].

No absolute contraindication is reported for ECT. With continuing advances in the use of ECT, it is now relatively safely in cardiac, pregnant and elderly patients. However, it is wise to proceed cautiously in patients with increased intracranial pressure, a recent intracranial bleeding or myocardial infarction, cerebral or aortic aneurysm, acute respiratory tract infection and in patients at risk of complications from a general anaesthetic [37]. Given the accumulating evidence showing that depression associated with chronic physical illness has a detrimental effect on morbidity and mortality, health professionals will continue to be encouraged to actively seek such at risk people. The list summarizes implications of our findings for mental health care provision.

- Care needs to be taken when asking about possible depression

in chronic disease.

- Concerns regarding medication ‘masking’ the problem and adding to the tablet burden might be improved by increasing access to services such as brief psychological interventions (such as IAPT) at the time of referral.
- Integrating chronic disease and mental health services (such as in collaborative care models) may help reduce the stigma of depression and the burden of extra appointments.
- Unmet expectations following psychotherapy may be prevented by discussing the role of brief interventions (such as IAPT) to increase understanding.

Conclusion

People with chronic physical illness hold a range of beliefs about depression which may help explain some under-detection in primary care. An understanding of patients’ reasons for presenting or not disclosing distress may assist in identifying subgroups of patients with different management needs, facilitate the targeting of GPs’ time and therapeutic efforts, and guide more individualised care (46).

Competing interests

The authors declare that they have no competing interests.

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