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Clinical Pearl

Recognition and Treatment of Depression

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Scope of the Problem

Major depressive disorder is a prevalent illness associated with considerable morbidity, mortality, and pervasive impairment in psychosocial functioning [1-4]. Approximately 16 percent of the adult population will experience an episode of depression in their lifetime [5]. Depressive disorders are linked to a high disease burden [6] with tremendous socioeconomic sequelae [7]. According to a World Health Organization study, by the year 2020 depression will be the disease associated with the second greatest number of disability-adjusted life years worldwide [6]. And yet, major depression remains underrecognized and undertreated with less than a quarter of those suffering from depression receiving adequate treatment for the disorder [5].

Signs and Symptoms of Major Depression

According to the Diagnostic and Statistical Manual, 4th Edition (DSM-IV) [8], an episode of major depression is defined as 5 or more of the following symptoms occurring nearly all day every day for at least 2 weeks:

- Depressed mood,
- Markedly diminished interest or pleasure in activities,
- Significant weight loss (when not dieting), or weight gain, or change in appetite,
- Insomnia or hypersomnia,
- Psychomotor agitation or retardation,
- Fatigue or loss of energy,
- Feelings of worthlessness or guilt,
- Diminished ability to think or concentrate,
- Recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt [8].

To meet DSM-IV criteria for an episode of major depression, 1 of the 5 symptoms must be either depressed mood or diminished interest. These symptoms must cause clinically significant stress or impairment in functioning and cannot be directly attributable to another medical condition.

Epidemiology of Major Depressive Disorder

Major Depressive Disorder (MDD), characterized by 1 or more episodes of major depression, affects approximately 1 out of 6 individuals. The rates of depression in women are disproportionately high: twice as many women as men are diagnosed with

this illness. This finding has been replicated in many countries around the globe, suggesting that this represents a "true" disparity and not a spurious effect of reporting bias (as had been hypothesized initially) [9]. Although MDD can have its onset at any age, the average age of an individual experiencing a first episode of MDD is approximately 22. Fifty percent of affected individuals experience a first episode before age 40. MDD is a heritable condition, with a 2- to 3-fold increase in risk among first-degree relatives of affected individuals. Interestingly, offspring of adults with MDD often initially present with anxiety disorders in childhood or adolescence and then develop MDD symptoms in adulthood [10].

Sequelae of Major Depressive Disorder

MDD is a serious medical condition characterized by high mortality rates (4-15 percent die by suicide) [11] and significant morbidity. MDD leads to loss of productivity in the workplace, impaired interpersonal relationships, and difficulty meeting life goals. If untreated, an episode of MDD tends to last about 1-2 years. More than half of individuals with a single episode of MDD will go on to have subsequent episodes [12]. Serial episodes of MDD, not surprisingly, erode families, lead to downward social mobility, and contribute to long-term disability.

Treatment Strategies for Depression

Despite the gravity of this illness, there are many treatment options available to individuals suffering from MDD.

Pharmacotherapy

The most commonly prescribed medications for depression are the selective serotonin reuptake inhibitors (SSRIs). These compounds include fluoxetine (Prozac and others), sertraline (Zoloft and others), paroxetine (Paxil and others), and citalopram (Celexa and others). SSRIs are characterized by relatively benign side effect profiles, few drug-drug interactions, and once-daily dosing. The most common side effects are headaches, gastrointestinal distress, and sexual dysfunction.

Other commonly prescribed medications include tricyclic antidepressant (TCAs) such as desipramine (Norpramin), nortriptyline (Pamelor) and amitriptyline (Elavil), and monoamine oxidase inhibitors (MAOIs) such as phenelzine (Nardil) and tranylcypromine (Parnate). TCAs and MAOIs are excellent antidepressants but require more careful monitoring and supervision. Side effects include dry mouth, orthostatic hypotension, urinary retention, cardiac conduction delays, and (in the case of MAOIs) life-threatening hypertensive crises.

Finally, many psychiatrists and primary care physicians have found that the so-called "mixed" or "dual agonist" agents such as bupropion (Wellbutrin), venlafaxine (Effexor), and duloxetine (Cymbalta) provide an alternative for individuals whose depressions do not respond to the serotonergic medications such as SSRIs or who have historically responded to a combination of serotonergic and noradrenergic medications in the past but prefer to take a single pill. Side effects from these medications tend to be a combination of those seen with SSRIs and TCAs and vary with neurotransmitter receptor affinities.

It is difficult to demonstrate differences in *efficacy* among these agents because of unique individual responses. Thus, the choice of a medication for a patient usually depends on prior history of response/nonresponse and side effect profiles of individual agents. It is important to remember that antidepressant effects often do not appear until 4-8 weeks after reaching a therapeutic dose, while unwanted side effects tend to emerge immediately. Unless forewarned about the delay in response, patients may stop taking a medication prematurely or refuse to take a high enough dose to bring about recovery. Physicians can preempt nonadherence by prefacing treatment with a clear explanation about expected response time and by scheduling a follow-up appointment 4-6 weeks after initiation of treatment to evaluate the need for dosage adjustment.

Psychotherapy

Depression-specific psychotherapies are also excellent treatments for depression. Unfortunately, most psychotherapies do not target specific disorders and have not been tested in randomized clinical trials. Detractors of psychotherapy have questioned its theoretical value, and insurance companies have ceased to reimburse for many of these treatments. Nevertheless, there are several psychotherapies that have been evaluated in rigorous clinical trials and have demonstrated efficacy as treatments for MDD. These individual treatments (indeed, they are all individual therapies) include cognitive behavioral therapy (CBT), interpersonal psychotherapy (IPT), cognitive behavioral analysis system of psychotherapy (CBASP), and psychodynamic-interpersonal therapy (PI) [13]. Depression-specific psychotherapies have demonstrated efficacy both as monotherapy and as adjuncts to medication.Other psychotherapies such as psychoanalysis, group therapy, and supportive psychotherapy have not been systematically evaluated as treatments for MDD.

Other Treatment Strategies for Depression

One of the most powerful treatments for depression is electroconvulsive therapy (ECT). Although much maligned by popular accounts (eg, *One Flew Over the Cukoo's Nest*), ECT is an effective option for selected patients [14]. Because ECT is a cumbersome procedure to conduct in outpatient settings, it is typically reserved for severely depressed or refractory patients. Phototherapy with high energy (lux) light boxes is clearly effective for individuals prone to seasonal MDD and may be used to prevent MDD in individuals who have recurrent winter depressions. Implantable vagus nerve stimulators and transcranial magnetic stimulators have attracted attention as potential treatments for refractory depression, although the efficacy of these therapies has not been clearly established.

Depression: An Illness, Not a Weakness

Perhaps the most important message about MDD—for both health care professionals and patients—is that depression is an illness, not a personal weakness or failing. Like many other medical conditions, MDD is a biologic process that interacts with life circumstances (similar to diabetes mellitus) and responds to proper treatment. It is heritable, serious, and associated with both death and poor functioning. As physicians, we should routinely consider MDD as part of our differential diagnosis in patients

with multiple somatic complaints, vague feelings of malaise, or the specific constellation of complaints listed in the criteria above.

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