Clinical Update

The Active Management of Depression

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Primary care clinicians are ideally positioned to serve as the central health care providers for patients with major depression.

While family physicians play a leading role in caring for patients with major depression, the quality of that care that could be greatly improved. A 1997 to 1998 survey of a national sample of adults with depressive or anxiety disorders revealed that 83% of these patients visited a health care provider.[1] Of this total, 84% were treated by primary care clinicians, compared with 16% who were treated by mental health professionals. However, about 90% of those cared for by mental health professionals received treatment that met criteria for adequacy outlined in treatment guidelines, compared with 19% of those cared for by primary care professionals.

A critical role for family physicians is to integrate treatment of depression with that of other conditions, especially in light of the association of depression with a variety of chronic diseases. The Institute of Medicine has concluded that depression is strongly associated with the occurrence of, and death following, myocardial infarctions.[2] In diabetes, depression is associated with a 2% increase in glycosylated hemoglobin levels[3] and can predict occurrence of diabetic complications. Additionally, chronic illnesses may, in themselves, exacerbate depression several fold.

Primary care clinicians are ideally positioned to serve as the central health care providers for patients with major depression. These physicians have many attributes that support this role, including their longitudinal relationship with patients, response to undifferentiated problems, frequent use of the biopsychosocial model, and ability to integrate care of mental and medical conditions. However, challenges in fulfilling this role also exist, including difficulties in recognizing patients with major depression, developing an adequate diagnostic initial assessment, implementing effective short- and long-term treatment and management strategies, and integrating care of depression with that of other conditions affecting patients.[4] This article will review each of these challenges.

Recognition of Major Depression

DeGruy has eloquently described the barriers to recognition and management of mental disorders in primary care, including infrequent use of diagnostic criteria, concern regarding treatment effectiveness, availability of time and resources, the presence of other pressing clinical problems, and issues of third-party reimbursement and other organizational concerns.[4]

Family physicians and their patients often do not recognize somatic symptoms as originating from depression. In one study, primary care physicians correctly identified 94% of depressed patients presenting with psychological complaints, but they failed to recognize the psychiatric nature of somatic complaints in about half of the patients. This finding is of concern because 83% of depressed patients presented with somatic complaints.[5]

The attribution patients assign to their problems can also contribute to lack of recognition. In one general practice study, patients' attributions were classified as somatizing (5%), psychologizing (23%), normalizing (48%), or no predominate attribution (24%).[6] For example, patients in this study might attribute fatigue to anemia (somatizing), emotional exhaustion (psychologizing), or being over-extended (normalizing). The likelihood of a missed diagnosis in patients who met criteria for depression or anxiety was strongly associated with attribution: Physicians diagnosed 72% of psychologizing patients accurately, but they reported a

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Screening for depression

TABLE 1

Outpatient adults

- Over the past 2 weeks, have you felt down or hopeless?
- Over the past 2 weeks have you felt little interest in doing things?

A positive response to either question should be followed by a more in-depth interview to confirm or refute the diagnosis.

Postpartum women (Edinburgh Postnatal Depression Scale)

1. I have been able to laugh and see the funny side of things
__ As much as I always could (0)
__ Not quite so much now (1)
__ Definitely not so much now (2)
__ Not at all (3)

2. I have looked forward with enjoyment to things
__ As much as I ever did (0)
__ Rather less than I used to (1)
__ Definitely less than I used to (2)
__ Hardly at all (3)

3. I have blamed myself unnecessarily when things went wrong
__ Yes, most of the time (3)
__ Yes, some of the time (2)
__ Not very often (1)
__ No, never (0)

4. I have been anxious or worried for no good reason
__ No, not at all (0)
__ Hardly ever (1)
__ Yes, sometimes (2)
__ Yes, very often (3)

5. I have felt scared or panicky for no very good reason
__ Yes, quite a lot (3)
__ Yes, sometimes (2)
__ No, not much (1)
__ No, not at all (0)

6. Things have been getting on top of me
__ Yes, most of the time I haven't been able to cope at all (3)
__ Yes, sometimes I haven't been coping as well as usual (2)
__ No, most of the time I have coped quite well (1)
__ No, I have been coping as well as ever (0)

7. I have been so unhappy that I have had difficulty sleeping
__ Yes, most of the time (3)
__ Yes, sometimes (2)
__ No, not very often (1)
__ No, not at all (0)

8. I have felt sad or miserable
__ Yes, most of the time (3)
__ Yes, quite often (2)
__ No, not very often (1)
__ No, not at all (0)

9. I have been so unhappy that I have been crying
__ Yes, most of the time (3)
__ Yes, quite often (2)
__ No, only occasionally (1)
__ No, never (0)

10. The thought of harming myself has occurred to me
__ Yes, quite often (3)
__ Sometimes (2)
__ Hardly ever (1)
__ Never (0)

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correct diagnosis in only 17% of somatizing patients, 15% of normalizing patients, and 31% of patients with no predominate attribution.

Initial Diagnostic Assessment

The United States Preventive Services Task Force suggests that primary care physicians screen for major depression. The Task Force recommends using 2 simple questions about mood and anhedonia (Table 1) that are generally as effective as longer instruments.[7] The Patient Health Questionnaire-9 (PHQ-9) or the longer Prime-MD can be used for further evaluation of patients who respond positively to either question, thus helping to both confirm the diagnosis of depression and measure severity.[8,9] Other instruments include the Beck Depression Inventory,[10] the Zung scale,[11] and the General Health Questionnaire.[12] These tools take longer to administer, are not specific in measuring the criteria for major depression, and do not measure severity well.

In family practices, pregnant and postpartum women represent a special population at increased risk for depression.[13] About 5% of middle class women and up to one quarter of low income women experience postpartum depression.[14] In about half, onset of the depressive disorder occurs before delivery.[15] Women who have previously suffered postpartum depression are at high risk, as are those with histories of depression or premenstrual dysphoric disorder. The Edinburgh Postnatal Depression Scale is a useful 10-item self-report instrument available in Spanish and English (Table 1).[16,17] Similar instruments have not been developed for pregnant women.

A patient who responds positively to the 2 screening questions in Table 1 or to another screening approach should be further evaluated to confirm the diagnosis of major depression. Many primary care clinicians do this through unstructured history taking. Others use an instrument such as the previously discussed PHQ-9. This tool offers an advantage because it provides a reliable symptom assessment, measures severity, and can be repeated over time to evaluate therapeutic response.[8]

The physician should consider bereavement and substance abuse as possible causes of depression; bereaved patients who continue to meet criteria for major depression at 2 months often benefit from treatment. By that time, the sadness, poor concentration, and other symptoms associated with normal grief are no longer constant and occur in waves brought on by memories. Conversely, persons also suffering from depression report these symptoms as enduring and autonomous.[18]

The primary care physician also should inquire about agitation and symptoms of anxiety disorders. These are experienced by 85% of depressed patients; 50% have comorbid anxiety disorders.[19-21] Identification of such comorbidity is helpful in determining treatment, evaluating response, and managing patients over the long term. The Prime-MD, available in multiple languages, is also useful for screening for both anxiety and substance abuse, which can complicate both the recognition and treatment of comorbid depression.[9]

Sexual function is often affected by depression. The physician should inquire about sexual arousal, erection or lubrication, and orgasm during the initial assessment.[22] Approximately 50% of women and 40% of men with major depression report sexual-arousal problems, and 15% to 20% report orgasm problems during the month prior to diagnosis.[23] Further questioning can assess whether this dysfunction is caused by another disorder (eg, diabetes) or whether it is part of the depressive syndrome. This provides a baseline for later assessment of side effects and treatment effectiveness, and it communicates to the patient that the physician will be attentive to this area. In discussing sexual function with depressed patients, it may be helpful to tell patients that a study of the effectiveness of treatment of depression with selective serotonin reuptake inhibitors (SSRIs) found that patients reported modestly improved sexual function with treatment.[24]

Management of Major Depression

The acute management of the patient with major depression includes patient education, shared decision-making regarding a treatment modality, supportive counseling, and treatment-specific counseling.[25] Education and counseling should extend over the initial weeks of treatment and be combined with monitoring response, identifying and managing any treatment-emergent side effects, and adjusting medications. Long-term management goals include attaining full remission of symptoms, assisting the patient to return to full functional status, integrating depression care with the treatment of other chronic illnesses, maintaining or tapering pharmacologic treatment, and monitoring for and preventing relapse or recurrence.

Education

Education should help patients understand and accept the diagnosis, reduce any stigma they or their families might attach to major depression, and build increased adherence to subsequent treatment.[26] It might be helpful to provide a brief explanation of the biologic basis of depression (including biochemical changes in brain function and "chemical imbalances" of serotonin and other neurotransmitters). Explaining pharmacotherapeutic effects (if medication is desired) as mechanisms to help rebalance brain chemistry further emphasizes the biologic basis of depression and decreases any perceptions that depression is a result of moral or character weakness. This educational message should also stress that antidepressants are not habit-forming or addictive, are not "uppers" or "downers," and are not tranquilizers. The physician also should convey a positive prognosis but note that several weeks and, possibly, adjustments in treatments, may be required. For patients choosing antidepressants, the McArthur Foundation Initiative has identified 7 key educational messages (Table 2).[27]

Counseling

Patients often benefit from counseling regarding sleep, exercise, and substance use. Many patients with depression experience early morning awak-

ening. Those with agitated depression also often experience delayed sleep onset associated with worry. Providing the patient with information on basic sleep hygiene, exercise, and encouraging abstinence from or moderation in consumption of alcohol might all help.[28-30] Additionally, sleep disturbances can indicate the possibility of comorbid disorders. A report that a patient fears going to sleep because of nightmares suggests posttraumatic stress disorder.

For some patients, counseling by the family physician or through referral may be a helpful treatment adjunct. Often depressed patients have deficient coping mechanisms and need assistance in developing strategies to resolve issues in their life. Principles used in cognitive behavioral therapy might be helpful in patient education and counseling.[31] These include problem-solving strategies to resolve stressful concerns and cognitive techniques to identify and correct distorted or maladaptive thought patterns.[29]

As patients respond to depression treatment, an additional component of primary-care-based counseling should target reinvolvement with pleasurable social and physical activities. This may simply involve identifying activities the patient enjoyed prior to the onset of depression but has since stopped, and focusing on the steps required to reactivate these interests.

Shared decision-making with regard to treatment will improve subsequent patient adherence.[27] Treatment options include psychotherapy, particularly cognitive behavioral therapy, pharmacotherapy, and electroconvulsive therapy. The latter should be considered for severely depressed patients, particularly persons with few social supports who are at significant risk of suicide.[25]

Cognitive behavioral therapy and other psychotherapies can show effectiveness equal to that of pharmacotherapy, although response usually lags by a month to 6 weeks compared with that attained by pharmacotherapy.[32] For moderately to severely depressed patients, pharmacotherapy is the treatment of choice in part because of its more rapid onset of action.[25]

Pharmacotherapy

Pharmacotherapy, most often in the form of an SSRI, is the treatment of choice for depression as a result of patient preference, insurance coverage limitations, or time constraints. In choosing an antidepressant, the family physician should be guided by effectiveness and potential for drug–drug interactions and for both short-and long-term side effects.[33]

Tricyclics, the SSRIs, and other newer antidepressants offer similar efficacy.[34] While efficacy assesses outcome under ideal treatment conditions, the primary care physician is more concerned with effectiveness, defined as the proportion of patients started on an antidepressant during routine clinical practice who attain lasting benefit. Effectiveness includes consideration of patients who discontinue treatment because of side effects or drug–drug interactions, as well as those who do not obtain adequate therapeutic response. Since about 25% of patients discontinue SSRIs because of side effects, this is an important concern.[24] Few studies have been conducted comparing the effectiveness of antidepressants.

Drug–drug interactions are mediated predominately by the cytochrome P450 isoenzymes responsible for drug metabolism in the liver.[35-37] The 2D6 isoenzyme is responsible for 50% of drug metabolism in the liver; the 3A4 isoenzyme is responsible for another 30%.[38] As a clinical example of the importance of such inhibition, codeine requires 2D6-mediated metabolism to become morphine and is ineffective for pain in many patients who are prescribed a 2D6 inhibitor. Patients receiving such agents also can have a 300% to 400% increase in blood levels of previously stable ß-blockers. Paroxetine and fluoxetine, the two SSRIs that strongly inhibit the 2D6 isoenzyme, cause clinically significant interactions; fluoxetine is also a moderate inhibitor of the 3A4 isoenzyme.[35] Because of the number of potential drug–drug interactions through these isoenzymes, physicians must check for interactions before prescribing these medications or adding other new medications in patients already receiving these agents. This also is a consideration for patients who might require additional medications acutely, for instance in response to a cardiac or other emergency.

Side effects of concern include gastrointestinal effects, particularly nausea, and central nervous system (CNS) effects, including anxiety and agitation, sleep disturbance, and tremor. When these occur, they often decrease rapidly over the first 1 to 3 weeks. If severe, they can be managed by a temporary dosage decrease. For patients with significant CNS side effects, altering the timing of the daily dose might provide relief from daytime somnolence or agitation or from nighttime insomnia.

Long-term side effects of concern include weight gain and sexual dysfunction. While other SSRIs have low rates for weight gain, paroxetine causes a weight gain of more than 7% (about 10 lbs for a patient of average weight) in 20% to 25% of patients.[39] Some element of sexual dysfunction,

most often delayed orgasm, is estimated to occur in 30% to 40% of individuals receiving SSRIs.[40,41] Management options include delaying dosage of agents with a half-life of about 24 hours (escitalopram, citalopram, sertraline).[42] For instance, an individual who usually takes one of these agents in the morning may delay a day's dose until after engaging in sexual intercourse in the evening. While open-label studies support augmentation, particularly with bupropion or buspirone, the few small randomized double-blind trials available suggest that positive results should be interpreted with caution.[43] Alternatively, patients may benefit from sildenafil[44] or a switch to a non-SSRI antidepressant.

While management of side effects presents one option, the best clinical approach may be to select an agent with minimal side-effect potential. In double-blind randomized trials, escitalopram, a new SSRI treatment option, was demonstrated to require treatment termination in less than 5% of recipients at its usual dose of 10 mg, a rate no different from that of placebo.[45] In contrast, rates of 15% to 30% have been reported for other SSRIs and newer antidepressants at the time of their initial release.

Adjusting Treatment

One recent primary care trial examined the effectiveness of 3 SSRIs: fluoxetine, sertraline, and paroxetine. At the time this study was designed, citalopram was not in common use. While about 75% of patients attained remission, only 40% to 50% of patients were maintained on the first prescribed agent.[24] Additionally, about 20% of depression "treatment resistance" resulted because patients did not fill their prescriptions or adhere to treatment.[46] For patients who do not respond within the first month, increasing the dosage is appropriate.[47] About 25% of patients respond to this adjustment.[48] For patients who do not respond, reassessment of the diagnosis, as well as assessment of potential psychiatric comorbidities and suicidal ideation, is indicated. For nonresponders, and for those with intolerable side effects, switching to a second SSRI is a reasonable next step.[49] About 50% of patients switched to a second agent respond.[50] For those who do not respond, the primary care physician might consider a second medication switch or psychiatric consultation.

Further treatment adjustment is indicated for patients who experience partial response. This might take the form of augmentation with psychotherapy[51] or with another agent.[52] Lithium and thyroid hormone (often as 25 to 50 mg T3 daily) are the most frequently used options, although stimulants, other antidepressants, and atypical antipsychotics are all of value in some patients.[48,49,53]

When indicated, treatment should be discontinued by tapering the dose over several weeks to months, depending on the duration and severity of past episodes. Patients should be educated to be alert for recurrence. They should also be monitored for recurrence and restarted on full-dose therapy if this occurs. If patients stop therapy abruptly, the likelihood of withdrawal symptoms (agitation, irritability, dizziness, ataxia, nausea, paresthesias, sleep disturbances) is highly related to the half-life of the SSRI.[39] For paroxetine, which has the shortest half-life, withdrawal is frequent; the extended release preparation does not decrease the likelihood of withdrawal. Withdrawal symptoms are infrequent (< 2%) for sertraline, citalopram, and escitalopram, and they do not occur with fluoxetine.

Duration of Treatment

A major challenge in family practice is maintaining patient adherence to treatment for the recommended interval to prevent relapse and to avoid recurrence in those with a history of prior episodes. In one study, 25% to 33% of primary care patients stopped depression therapy within 1 month and over 40% within 3 months. Additionally, 62% failed to inform their physicians.[54] Depression also adversely affects compliance with treatment of comorbid medical conditions; in one meta-analysis, depression increased noncompliance 3-fold.[54]

For the first lifetime episode, the recommended

Key messages for patient education about depression TABLE 2

- Antidepressants work only if taken every day
- Antidepressants are not addictive
- Benefits from medication appear slowly over several weeks
- Continue antidepressants even after you feel better
- Mild side effects are common and usually improve with time
- If you are thinking of stopping the medication, call your physician first
- The goal of treatment is compete remission, but this sometimes takes several medication adjustments

duration of treatment is 6 to 9 months (4 to 6 months after recovery).[55] Longer therapy is appropriate for those with comorbid anxiety disorders, severe initial symptoms, difficulty in attaining therapeutic response, deficient social support, or a history of substance abuse, as well as for older adults. For patients with 3 or more previous episodes, long-term maintenance therapy is recommended.[55] For those with even one past episode, extended maintenance therapy might be beneficial. Maintenance therapy should be at the full dose required to attain initial response. In one study, only about 20% to 30% (depending on the treatment) experienced recurrence over 3 years if maintained at full dose, compared with 70% maintained at half the initial treatment dose, and 78% of those receiving placebo.[56] For women who have previously suffered from postpartum depression, postpartum prophylaxis can be very effective. In one randomized trial, 62.5% of women on placebo experienced recurrence compared with only 6.7% of those receiving prophylaxis.[57]

Practice Strategies to Improve Care

A number of primary care investigators have demonstrated the value of practice management and quality improvement techniques to increase the portion of patients who achieve and maintain response to depression therapy. These studies share an approach of "active management" to promote adherence to treatment guidelines.[58-63] For instance, Simon and colleagues demonstrated the value of initial and monthly phone contact.[64]

Active management techniques include the following:

- Initial and ongoing patient education and counseling, as discussed above
- Patient involvement and agreement in treatment choice
- Initial phone contact to assure the prescription has been filled and initial dose taken
- Periodic contact to inquire about adherence, treatment response, side effects, and to answer patient questions
- Adjustment of therapy for those not responding adequately by 4 to 6 weeks
- Establishment of a collaborative relationship with a psychiatrist for consultation and telephone advice

Additionally, primary care clinicians may find it helpful to add depression to their medical record preventive health maintenance flow chart, especially for patients with any past history of depression. Using the PHQ-9 can be beneficial in providing both the patient and physician with an objective measure of monitoring response and remission.

Conclusions

Effective and available treatments can have a major beneficial impact on patients with depression. To be maximally effective, primary care clinicians must actively manage the care of their depressed patients, using screening strategies to recognize depression in addition to targeted educational messages and active follow-up to improve treatment adherence. Long-term maintenance treatment prevents further recurrences in those who have already experienced multiple episodes. Choice of treatment should be guided by patient preference. For pharmacologic agents, selection should be based on effectiveness, likelihood of side effects and resultant premature discontinuation, and potential for drug–drug interaction. The majority of individuals with depression are managed solely in primary-care settings. With adequate treatment, remission of symptoms, significant improvement in quality of life, and return to full function at home and at work can be attained. ■

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