Q&As

Depression

Cutting Through the Confusion

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One in six Canadians will, at some point, suffer from a major depression. The lifetime prevalence is higher in women (10% to 25%) than in men (5% to 10%).[1,2] This disparity may be explained, in part, by the fact that men are less likely to seek out a physician's opinion for health-related problems.

Many depressed patients go unrecognized because they fail to seek help or present with concern about somatic symptoms. Of those who are identified as suffering from a major depressive disorder, most do not achieve full remission with the first antidepressant agent chosen.[3-6]

Joe's case

Joe, 42, presents with a variety of somatic symptoms, including:

- headaches,
- abdominal pain, and
- chest wall pain.

He has had difficulty sleeping for the past few months. His energy level is reduced and he gave up playing house league hockey this year because he'd lost interest in it.

He hasn't noticed any change in his mood, but admits to having a shorter temper and is a bit more irritable lately. He attributes this to difficulty getting along with his new boss.

Q *Do patients have to feel sad to be suffering from major depression?*

A At the time of a periodic health exam, asking patients whether they have had a recent mood change or a loss of interest in things can be an efficient screen for depressive illness. A positive response to either question should result in a more detailed inquiry of symptoms associated with depression (Table 1).[7] In the absence of depressed mood, the diagnosis of major depression is often overlooked.

Long-term followup studies suggest depression is a chronic, recurring illness. Only 20% of patients diagnosed with a major depressive disorder fully recover within 15 years of the original diagnosis.[8] The longer depression remains untreated, the more difficult it is to bring under control.

Depression in adolescents and in the elderly tends to be more persistent and often more difficult to treat. Major depression occuring in association with other significant psychiatric or medical comorbidity poses a greater treatment challenge. Every depressed patient should also be evaluated for suicide risk.

Q How do you select an antidepressant?

A First-line antidepressant agents include:

- selective serotonin reuptake inhibitors (SSRIs);
- serotonin noradrenaline reuptake inhibtors (SNRI), such as venlafaxine;
- noradrenaline dopamine modulators (NDM), such as bupropion; and
- noradrenaline and specific serotonin antagonists (NaSSa), such as mirtazapine.

Each of these classes has different modes of action and different side-effect profiles (Table 2). One useful strategy for selecting an antidepressant agent is to match the patient's associated symptoms with the side-effect profile of the drug.

Q What if there's a poor response to the antidepressant chosen?

A The goal of therapy is to treat symptoms to full remission. Incompletely treated depression leads to a higher burden of illness over the long term. When there is no response to the initial treatment, the diagnosis should be reconsidered to be sure that bipolar illness isn't the underlying problem. When a partial response is achieved with the initial agent, there are a variety of options to achieve a full remission.

1. Raising the dose of the index drug seems a reasonable first choice, assuming the drug is well-tolerated and has shown a partial response at the starting dose.
2. Switching to a second antidepressant in the same or different class should be considered if there was no response to the index antidepressant.
3. Combination or augmentation strategies are other safe and effective alternatives (Table 3).

Specific psychotherapeutic strategies have also been shown to improve treatment outcomes. The effect is greater when used in combination with antidepressant medication. Cognitive behavioural and interpersonal therapies have the greatest evidenciary base.[9,10] The presence of a supportive environment with a care provider whom the patient trusts is no doubt an important precondition to enhancing treatment response.

Consultation with a psychiatrist should be considered if:

- the diagnosis is in doubt,
- the patient is suicidal,
- the presenting symptoms are quite severe,

Table 1

Screening for major depression

If patient has depressed mood or loss of interest, continue screening for:

- Sleep disturbance
- Appetite disturbance
- Loss of energy
- Difficulty concentrating
- Feelings of worthlessness
- Psychomotor retardation
- Suicidal thoughts

Diagnose major depression when 5 or more symptoms present; must also include one of the following for at least 2 weeks:

- Depressed mood
- Loss of interest in activities
- Symptoms present most of the day, nearly every day
- Symptoms interfere with daily functioning

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- there is comorbidity with other serious mental disorders, or
- the patient has failed to respond to treatment.

Q How do you know if the patient is in full remission?

A Regular monitoring of the treatment response will allow the physician to determine whether patients are maintained in full remission. This means treating patients until they are feeling "normal" again. The 7-Item Hamilton Rating Scale for Depression (HAMD-7) assessment tool can be quite helpful for monitoring response to treatment (Table 4) and takes the physician only three minutes to complete.

Once full remission is achieved, patients should be periodically reassessed to assure remission is maintained and medication is being tolerated and taken as prescribed.

Table 2

First-line antidepressants

Agent	Class	Usual dose (mg/day)	Side-effects
Fluoxetine	SSRI	20-40	Anxiolytic effects, possible weight gain, possible sexual dysfunction
Fluvoxamine	SSRI	100-200	Anxiolytic effects, possible weight gain, possible sexual dysfunction
Paroxetine	SSRI	20-40	Anxiolytic effects, possible weight gain, possible sexual dysfunction
Sertraline	SSRI	50-200	Anxiolytic effects, possible weight gain, possible sexual dysfunction
Citalopram	SSRI	20-40	Anxiolytic effects, possible weight gain, possible sexual dysfunction
Venlafaxine	SNRI	75-225	Anxiolytic effects, possible weight gain, possible sexual dysfunction
Bupropion	NDM	150-300	Possible weight loss
Mirtazapine	NaSSa	15-45	Anxiolytic effects, prevents insomnia, possible weight gain

SSRI: Selective serotonin reuptake inhibitor
SNRI: Serotonin noradrenaline reuptake inhibitor
NDM: Noradrenaline dopamine modulator
NaSSa: Noradrenaline and specific serotonin antagonist

One in six Canadians will, at some point, suffer from a major depression.

Q How long should treatment last?

A
- The patient should be advised to stay on antidepressant medication for at least six months after full remission is achieved. (Note: The dosage at which full remission was achieved should be the maintenance dose.)
- Patients who have had a previous episode of major depression should be treated for at least a year.
- Patients who have experienced more than two episodes of major depression should be treated indefinitely.
- Adolescent depressions and geriatric depressions often require longer treatment courses to prevent relapse. Dx

Table 3

Augmentation/combination strategies

Level I evidence for:

- Lithium (600-900 mg/day) + TCA
- Triiodothyronine (T3) (25-50 µg/day) + TCA
- Mirtazapine (15-45 mg/day) + SSRI
- Mirtazapine (15-45 mg/day) + SNRI

Level II evidence for:

- Olanzapine (5-15 mg/day) + SSRI
- Risperidone (1-2 mg/day) + SSRI

Level III evidence for:

- Bupropion (100-300 mg/day) + SSRI
- Bupropion (100-300 mg/day) + SNRI
- Desipramine (25-75 mg/day) + SSRI
- Trazodone (50-150 mg/day) + SSRI

TCA: Tricyclic antidepressant
SSRI: Selective serotonin reuptake inhibitor
SNRI: Serotonin noradrenaline reuptake inhibitor

References

1. Weissman MM, Bland RC, Canino GJ, et al: Cross-national epidemiology of major depression and bipolar disorder. JAMA 1996; 276(4):293-9.
2. Canadian Network for Mood and Anxiety Treatments: Guidelines for the diagnosis and pharmacological treatment of depression. Cameron McCleery Productions Ltd., Toronto, 1999, pp. 6-8.
3. Kennedy SH, Lam RW, Cohen NL, et al: Clinical guidelines for the treatment of depressive disorders. Can J Psychiatry 2001; 46(Suppl 1):38S-58.
4. Ferrier IN: Treatment of major depression: Is improvement enough? J Clin Psychiatry 1999; 60(Suppl.6):10-4.
5. Parikh SV, Lesage AD, Kennedy SH, et al: Depression in Ontario: Undertreatment and factors related to antidepressant use. J Affect Disorders 1999; 52(1-3):67-76.
6. Druss BG, Hoff RA, Rosenheck RA: Underuse of antidepressants in major depression; prevalence and correlates in a national sample of young adults. J Clin Psychiatry 2000; 61(3):234-7.
7. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition. American Psychiatric Association, Washington, 1994, p. 327.
8. Kiloh LG, Andrews G, Neilson MD: The long-term outcome of depression. Br J Psychiatry 1988;1(53):752-7.
9. Keller MB, McCullough JP, Klein DN et al: A comparison of nefazadone, the cognitive behavioural-analysis system of psychotherapy, and their combination for the treatment of chronic depression. N Eng J Med 2000; 342:1462-70.
10. Reynolds CF, Miller MD, Pasternak RE, et al: Treatment of bereavement-related major depressive episodes in later life: A controlled study of acute and continuation treatment with nortriptyline and interpersonal psychotherapy. Am J Psychiatry 1999; 156(2):202-8.

Table 4

7-Item Hamilton Rating Scale for Depression (HAMD-7)

1. Depressed mood (sadness, the blues, weepy)
2. Feelings of guilt (self-criticism, self-reproach)
3. Interest, pleasure, level of activities (work and activities)
4. Tension, nervousness (psychologic anxiety)
5. Physical symptoms of anxiety (somatic anxiety)
6. Energy level (somatic symptoms)
7. Suicide (ideation, thoughts, plans, attempts)

Most depressed patients who meet criteria for major depressive disorder will score between 10 and 15 prior to initiation of therapy.

Each item is scored from 0-4

A total score ≤ 3 indicates full remission

A total score of ≥ 4 indicates non/partial response

Take-home message

Treating depression

- When selecting a first-line antidepressant, match the patient's symptoms with the side-effect profile of the drug.
- If there is no response to initial treatment, options include raising the dose, switching to another drug in the same or different class, or using combination/augmentation strategies.
- The HAMD-7 can be used to assess full remission.