What Should GPs Know?

Remission in Long-term Depression

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Major depressive disorder is a highly prevalent, often episodic, progressive disorder affecting approximately 15% to 20% of the general population. Most individuals experience recurrent episodes that heighten vulnerability to relapse. With each overt episode, the symptoms progress in severity, duration, and refractoriness to treatment. Today, the prevalence of depression represents a rapid trajectory of increase when compared to prevalence estimates as recent as three decades ago.

An apparent paradox has emerged in the management of the depressed patient. Although clinical research has demonstrated that different classes of antidepressants produce excellent short-term efficacy outcomes, the long-term naturalistic outcome of this illness remains rather disappointing. Many modifiable deficiencies in the management of the depressed patient have been hypothesized to be at the root of this problem. These deficiencies include:

Joan's case

Joan, 34, acknowledges a confluence of depressive symptoms. She denies any suicidal ideation or history of hypomania. This current depression is in the context of work-related stressors, such as mounting work expectations, and interpersonal conflicts with her boss.

She is not currently receiving any medication. She tells you that, five years ago, she experienced an index ambulatory depression, which was treated with a conventional antidepressant. She is asking to be reinitiated to this treatment. She is also inquiring about psychotherapeutic opportunities to assist her ability to cope at work.

1. **Which antidepressant would you select?**
2. **How long should she stay on antidepressant therapy?**
3. **What are key messages to communicate with her in psychoeducation about long-term antidepressant therapy?**

For a followup on Joan, go to page 89.

- under-recognition of depression;
- failure to employ evidence-based treatment in its management;
- failure to identify and manage comorbidity;
- ineffectual therapeutic paradigms (*i.e.*, brief treatment trials, insufficient dose); and
- failure to treat to full symptomatic remission.

What about remission and response rates?

Most first-line antidepressants available in Canada achieve response rates of 60% to 70%. In most studies, response is defined as a baseline reduction of ≥ 50% on a continuous efficacy measure, such as the Hamilton Depression (HAMD) rating scale. Although response has been the efficacy benchmark in academic settings, it falls short of being practical in naturalistic settings.

Remission is defined as a HAMD-17 score ≤ 7, which denotes full abatement of symptoms, and suggests a qualitatively better outcome. An adverse outcome implies a response to an antidepressant, but failure to achieve full remission. The HAMD-7 is a briefer, less complicated scale that defines remission as a score ≤ 3. It has been established that ongoing, sub-threshold depressive symptoms prospectively predict overt affective return and functional impairment. These symptoms also increase the risk for chronic illness, suicidal behaviour, and comorbid medical disorders.

Failure to achieve full remission after an index episode of depression strongly predicts a

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Table 1

Recurrence vulnerability factors

- Multiple episodes
- Early relapse after medication
- Psychotherapeutic medication discontinuation
- Comorbidity
- Older age of onset
- Presence of psychosis

A followup on Joan

An antidepressant that was proven effective in Joan's prior depression should be selected. However, the antidepressant may not be as adequately effective; this does not imply the medication has lost efficacy, but it could reflect an increasing complexity of the depression.

Minimum therapy of approximately one to two years is recommended, with lengthier therapy contingent on the trajectory of response. Joan should be informed about key issues in psychoeducation, such as the expected time course of efficacy, careful review of adverse events, clarification of serious vs. non-serious events, and which side-effects would be expected to abate over time.

Fears of dependency and the notion that medications are mood-controlling are unsettling concepts to patients. These fears should be discussed openly, with clarification of any myths or distortions. The family's attitude towards the disease and treatment should also be probed.

In the case of female patients of reproductive age, the safety of antidepressants around pregnancy matters should be discussed.

chronic course of illness. Furthermore, it has been hypothesized that there is a six-month window of therapeutic opportunity. Failure to achieve full remission in the first six months after treatment initiation may be the precursor of a subsequent chronic course. This failure also suggests the velocity of symptom change in antidepressant-treated depression is dependent on illness duration. Therefore, treatment avenues with the greatest prophylactic therapeutic potential should be considered.

How long should patients stay on therapy?

Once patients have benefited from depression-specific psychotherapy (*i.e.*, cognitive behavioural therapy), the clinician should estimate the duration of this modality of treatment. One needs to recognize that depression is a chronic, relapsing illness. Each new episode is associated with an increased risk of future episodes, which are typically longer in duration, often more severe in intensity, and more recalcitrant to treatment. It behooves clinicians to prevent episodes, if possible.

A period of at least six months of ongoing treatment is recommended after a mild index episode of remittent depression. Lengthier treatment would be suggested for persons who cluster "recurrence vulnerability factors" (Table 1). Treatment is recommended for two to five years, but may continue indefinitely, as required by each specific case. It should be pointed out that, although longer therapies are recommended, in the absence of compliance enhancement strategies (*i.e.*, psychoeducation), it is unlikely most patients will adhere to these foregoing recommendations.

Maintenance efficacy is available for all commercially available antidepressant agents. Unfortunately, there is a paucity of multi-year trials with any treatment intervention. It should be noted that dosing in maintenance therapy is similar to acute dosing, assuming the patient has tolerated the medication. Dx

Take-home message

What is important to realize about the treatment of depression?

- Psychoeducation is of utmost importance to promote patient compliance to therapy.
- There is a six-month window of therapeutic opportunity to achieve full remission of depression.
- Depression is a chronic, relapsing illness. Each subsequent episode is typically longer and more severe than the last, more recalcitrant to treatment, and is associated with an increased risk of future episodes.
- Patients' outcomes should be routinely monitored with scales like the HAMD-7.

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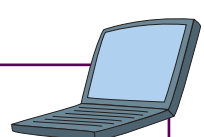

1. Depression and Bipolar Support Alliance: *www.dbsalliance.org*
2. Canadian Psychiatric Association on Treatment of Depressive Disorders: *www.cpa-apc.org*