When Is Pharmacotherapy Initiation Beneficial in Patients With Depressive Disorders?

Abstract: *Psychotherapy and pharmacotherapy are the most common treatments utilized in patients diagnosed with depressive disorders. Their efficacy in remitting symptoms and restoring patients to baseline functioning has been established throughout the literature; however, questions still remain on whether pharmacotherapy is necessary in all patients and if used, when initiation is most beneficial. Current guidelines recommend initiating only psychotherapy in patients with mild depression and advancing to pharmacotherapy as appropriate. Evidence-based literature has shown pharmacotherapy to have a significant and independent treatment effect in depressive disorders compared with psychotherapy. Combination treatment with both modalities has also shown to be beneficial for remitting depressive symptoms in this patient population. Therefore, treatment should be individualized for each specific patient based on severity of disease, history of depression and response to treatment, cost of treatment, and patient preference.*

Keywords: depression; pharmacotherapy; psychotherapy; initiation

Major depressive disorder (MDD) ranks as the 11th greatest cause of disability and mortality in the world according to the World Health Organization.¹ It is diagnosed in patients who have experienced at least 1 major depressive episode and have no history of mania or hypomania. As the prevalence of this condition continues to grow, clinicians are continually searching for the most effective treatment strategies for these patients. Both psychotherapy and pharmacotherapy are utilized to help patients achieve remission from their symptoms and restore baseline psychologic functioning. These treatment

patients diagnosed with depressive disorders.²⁻⁴ Findings regarding the appropriate initiation and comparative efficacy of pharmacotherapy, psychotherapy, and a combination of the 2 treatment modalities will be discussed in this article.

Options for Treating Depression

Psychotherapy options in the treatment of depression include cognitive-behavioral therapy (CBT), interpersonal psychotherapy (IPT), behavioral activation, problem-solving therapy,

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options are often initiated based on the severity of a patient's depression according to clinician-administered depression rating scales. Currently, there is variability in the literature as to when pharmacotherapy should be started in

psychodynamic psychotherapy, and supportive psychotherapy.⁵ These therapies aim at identifying and correcting maladaptive beliefs that may be contributing to the patient's depressive symptoms.

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Treatment with medication is an alternate option for patients suffering from depressive symptoms. There are a wide variety of pharmacotherapy options available to treat depression but selective serotonin reuptake inhibitors (SSRIs) are used most commonly because of their efficacy and relatively tolerable side effect profile.⁶ These agents increase the amount of serotonergic activity in the brain, which often leads to improvement in depressive symptoms due to the restoration of preexisting chemical imbalances. All SSRI agents have similar efficacy in the treatment of depression, therefore choice should be based on cost, side effect profile, and clinician experience.⁷ Other agents used in the treatment of depression include serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, atypical antidepressants, and monoamine oxidase inhibitors.

Psychotherapy and pharmacotherapy are often used in tandem to effectively treat depression. Each treatment modality has its benefits and barriers to success. Psychotherapy requires a greater time commitment from both the health care professional providing the therapy and the patient themselves. Because patients respond differently to the various types of psychotherapy as well as the various clinicians delivering the therapy, a trial of more than one type of therapy or provider may be necessary to achieve the greatest benefit. Psychotherapy also requires commitment to scheduled visits on a consistent basis. Pharmacotherapy requires adherence to the medication as well as toleration to the side effects associated with prolonged use. Cost is a factor to consider with both treatment modalities.

Current Guideline Recommendations

The 2009 National Institute for Health and Care Excellence (NICE) guidelines for the treatment of depression in adults recommends initiating pharmacologic treatment for 3 categories of patients: those who have a past history of moderate or severe depression, patients with an initial presentation of

subthreshold depressive symptoms that have been present for at least 2 years, or patients with mild depressive symptoms that persist after other interventions.⁶ The guidelines do not recommend routinely using pharmacotherapy for patients with subthreshold or mild depression, due to the poor risk-benefit ratio associated with medication in these types of patients. Instead, they recommend utilizing psychosocial intervention such as CBT, interpersonal therapy, and behavioral activation.

For patients with persistent subthreshold depressive symptoms or mild-to-moderate depression who have not benefited from the psychosocial therapy, the guidelines recommend initiating an antidepressant. When medication is initiated, the NICE guidelines suggest using an SSRI as a first-line option. They also recommend utilizing the antidepressant in combination with high-intensity psychological intervention, either CBT or IPT, for patients with more moderate to severe depression.

An update to these guidelines is set for September 2017, which will further provide recommendations in managing patients diagnosed with depression.

Psychotherapy Versus Pharmacotherapy: Comparative Efficacy

Research has been conducted to determine the comparative efficacy of psychotherapy and pharmacotherapy in the treatment of depression. A meta-analysis reviewing psychotherapy versus combination of psychotherapy and pharmacotherapy was conducted in patients with depressive symptoms.² The study, reviewing 19 different trials, showed there was a statistically significant difference in symptom improvement between psychotherapy and combination treatment. Therefore, the authors concluded adding pharmacotherapy to psychotherapy has an added independent and cumulative effect on depression.

Another meta-analysis reviewed the literature regarding the addition of

psychotherapy to baseline pharmacotherapy treatment for depressive disorders in adults.³ The analysis provided insight as to whether psychotherapy has an effect independent of medication therapy. The study reviewed 25 different trials and found a small but statistically significant effect in favor of adding psychotherapy to pharmacotherapy alone. In a subgroup analysis of the study, the increased effect was not found in patients with dysthymia (those experiencing depressive symptoms for longer than 2 years). Additionally, the review found that treatment dropout rates were significantly lower in the combined treatment group versus the pharmacotherapy alone cohort.

A third systematic review analyzed the effects of adding psychotherapy to pharmacotherapy for depressive disorders.⁴ The study found no significant differences between the effects of medication and psychotherapy when initiated as single interventions in the outpatient primary care population. Results did show, however, that medication was significantly more effective than psychotherapy alone for patients with dysthymia, further supporting the findings from the aforementioned meta-analysis.³ The study also found combination treatment, using both psychotherapy and pharmacotherapy, was significantly more effective than pharmacotherapy alone in outpatient treatment and in patients with dysthymia, treatment-resistant depression, and those with impaired cognitive function.

An interesting clinical dilemma has also been presented in the literature regarding the actual effect of antidepressant medication as compared with placebo. A meta-analysis presenting findings on this phenomenon was published in 2010.⁸ The study reviewed 6 different placebo-controlled trials to assess whether patients responded to true drug effects or merely the placebo effect of taking a pill. The meta-analysis looked at studies that utilized the Hamilton Depression Rating Scale (HDRS), which determines the severity of a patient's depression. The results presented in the analysis found that true

drug effects were nonexistent among patients experiencing mild to moderate baseline symptoms (an HDRS score <25). However, for patients with an HDRS score >25, categorized as very severe symptom baseline score, medication treatment effect was statistically superior to placebo counterparts.

Pharmacotherapy Initiation

Once a medication has been initiated for a patient, it is important to provide them with the necessary information to be successful with treatment. Most antidepressant medications require a few weeks to develop their full antidepressant effect. It is also important to instruct the patient on proper adherence to the medication and possible side effects associated with treatment. Long-term side effects associated with SSRIs can include gastrointestinal disturbances, weight gain, sexual dysfunction, and sleep disturbance.⁹ Counsel the patient on the risk of abruptly stopping pharmacologic treatment, because discontinuation without tapering can often lead to undesirable symptoms and suicidal behavior. Patients should also be aware that these medications are not addictive, which can help alleviate fears to begin medication therapy.

Conclusion and Recommendations

Current guidelines and evidence-based literature suggest depressive symptoms should be treated on an individual patient level. The NICE guidelines recommend beginning with psychotherapy for patients with mild depressive symptoms because of the

poor risk-benefit profile associated with pharmacotherapy. The guidelines recommend adding pharmacotherapy to psychotherapy when these depressive symptoms are more moderate-to-severe or are chronic in nature. They recommend beginning with an SSRI as the pharmacologic agent of choice.

Literature demonstrates pharmacotherapy has an independent, statistically significant effect for patients with major depressive disorder and that patients with severe and/or chronic depression may benefit more from utilizing pharmacotherapy as a first-line option, compared with psychotherapy alone. However, evidence-based literature suggests that pharmacotherapy is not necessary for initial therapy in all patients. Psychotherapy alone is efficacious in many patients with subthreshold or mild depression and combination treatment with psychotherapy and pharmacotherapy is more effective and results in greater adherence to therapy than either modality alone when treating patients with moderate to severe depression. Thus, an individualized approach to therapy based on symptom severity, history of depression and response to treatment, cost of treatment, and possible side effects associated with treatment should be employed to determine whether to initiate psychotherapy, medication, or a combination.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. **AJLM**

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