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Volume 20 (Issue 3) **March 7, 2016**

PHARMACOLOGIC TREATMENT OPTIONS FOR ADULT PATIENTS WITH MAJOR DEPRESSIVE DISORDER

Depressive disorders are major health issues and is associated with significant morbidity, mortality, and costs to society and health care systems. The economic burden associated with this disease state was $83.1 billion in 2000. Depressive disorders include major depressive disorder (MDD), dysthymia, and subsyndromal depression, including minor depression. Major depressive disorder is the most prevalent depressive disorder. Several treatment approaches can be used to effectively manage patients with MDD. This issue of *CLIPs* provides a review of pharmacological treatment options for adult patients with MDD. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at CHIPOR@samford.edu.

Qaseem A, Barry M, Dansagara, et al. Nonpharmacologic versus pharmacologic treatment of adult patients with major depressive disorder: a clinical practice guideline from the American College of Physicians. *Ann Intern Med.* 2016;164:350-359.

Introduction

- The lifetime prevalence of MDD is 16% and approximately 8 million ambulatory care visits occur each year with a primary diagnosis of MDD.
- MDD is defined as “depressed mood or loss of pleasure or interest along with other symptoms, including significant change in weight or appetite, insomnia or hypersomnia, psychomotor agitation or retardation nearly every day, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, indecisiveness or decreased ability to concentration and recurrent thoughts of death, or suicide, that last for at least 2 weeks and affect normal functioning”.

Treatment characteristics of depression

- Treatment for depression is classified in three phases: acute (6-12 weeks), continuation (4 to 9 months), and maintenance (≥1 year).
- Relapse is defined as the “return of depressive symptoms during the acute or continuation phase” and is considered a part of the same depressive episode.
- Recurrence is defined as “the return of depressive symptoms during the maintenance phase” and is considered a new episode.
- Response to therapy is typically defined as a ≥50% reduction in severity, as measured by appropriate tools.

Guideline focus

- The purpose of the American College of Physicians guideline is to summarize and grade evidence for the comparative effectiveness and safety of nonpharmacologic treatments and SGAs (second generation antidepressants, including serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, bupropion, mirtazapine, nefazodone, and trazodone) alone or in combination for MDD.
- Outcomes assessed included benefits in response (defined as a ≥ 50% improvement in HAM-D scores), remission (often defined as a HAM-D score ≤ 7), speed of response, speed of remission, relapse, quality of life, functional capacity (as assessed by various scales), reduction of suicidality, or reduction of hospitalization.
- Overall adverse reactions were assessed as well.
- This review will discuss only pharmacologic therapy (i.e., FDA approved drug products and complementary / alternative medicine).

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Table 1: SGAs versus pharmacologic therapies

Intervention	Finding	Quality of Evidence	Result
SGA vs. Omega-3 Fatty Acids (Monotherapy)			
1 clinical trial	Overall discontinuation rates	Low quality	No difference in overall discontinuation rates of treatment
SGA vs. Omega-3 Fatty Acids (Combination therapy)			
2 clinical trials	Overall discontinuation rates	Low quality	No difference in overall discontinuation rates
SGA versus SAMe (Monotherapy)			
1 trial	Overall discontinuation rates	Low quality	No difference in overall discontinuation rates
SGA versus St. John's Wort (Monotherapy)			
9 trials	Overall discontinuation rates	Moderate quality	Increased risk for discontinuation and discontinuation due to adverse events (non-statistically significant)
8 trials	Overall discontinuation rates	Moderate quality	Increased risk of overall adverse events
4 trials	Overall discontinuation rates	Low quality	No difference in serious adverse events
Switching to other SGAs			
1 trial	Overall response	Moderate quality	No difference in response when switching from 1 SGA to another (bupropion vs. sertraline or venlafaxine and sertraline vs. venlafaxine)
1 trial	Remission rates	Low quality	No difference in remission (bupropion vs. sertraline or venlafaxine and sertraline vs. venlafaxine) or depression severity (venlafaxine vs. citalopram) when switching from 1 SGA to another.
Augmenting with another SGAs			
1 trial	Response / remission rates	Low quality	No difference in response or remission for augmentation of citalopram with bupropion compared with augmentation with buspirone. Augmenting with bupropion decreases depression severity more than augmentation with buspirone. No difference in suicidal ideas and behavior or serious adverse event. Moderate quality evidence indicates discontinuation due to adverse events was lower with bupropion than with buspirone.

Overall Findings

- Rates were similar when comparing different SGA therapies with the exception of the following: increased functional capacity for SGA + cognitive behavioral therapy (CBT) combination vs. SGA monotherapy; increased remission for SGA + IT combination therapy vs. SGA monotherapy; increased response for SGA + acupuncture combination therapy vs. SGA monotherapy; and increased response for SGA vs. omega-3 fatty acids monotherapy.
- SGAs are associate with constipation, diarrhea, dizziness, headache, insomnia, nausea, sexual adverse events, and somnolence.
- Increased rates of discontinuation rates observed with SGA vs. acupuncture; increased discontinuation of treatment and discontinuation of treatment due to adverse events with SGA vs. St. John's wort and increased discontinuation of treatment due to adverse events with SGA vs. exercise.
- Recommendation: Clinicians should select between CBT or SGA. Discourage use of St. John's wort because of lack of purity standards.