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Depression as a Factor in Nonadherence in Schizophrenia

To the Editor: We read with interest the article by Kane and Correll¹ on optimizing treatment choice in schizophrenia to improve adherence, which suggested that long-acting formulations of antipsychotics can be a very powerful strategy in helping to ensure that patients benefit from the medication they have been prescribed. The authors discussed nonadherence, which may be related to patient factors, treatment characteristics, or the overall medical condition of the patient. To provide further insight into this issue, herein we discuss comorbid depression as a potential cause for nonadherence in schizophrenia.

Psychiatric comorbidities are common among individuals with schizophrenia, and it is estimated that comorbid depression occurs in 50% of these patients.² Additionally, a recent study³ revealed that patients with nonaffective psychosis have high levels of worry (67.7%) and low levels of self-esteem (62.1%). Further, patients' preferred treatment targets were feeling happier (63.2%), worrying less (63.1%), and increasing their self-confidence (62.1%).³ On the basis of these results, depression and subthreshold depression in schizophrenia might have an even higher prevalence than has been estimated. Indeed, a systematic review⁴ assessed the reasons for nonadherence to antipsychotics, categorizing them into intentional or unintentional. Depression is one of the main reasons for unintentional nonadherence, which exacerbates symptoms of schizophrenia.⁴ Since depression may impact cognitive functions, energy, and motivation, it may also affect patients' willingness and ability to adhere to their treatment.⁵ Thus, clinicians should pay attention to comorbid depression as a factor in nonadherence in schizophrenia.

Furthermore, second-generation antipsychotics (SGAs) may have a direct effect on depressive symptoms in patients with schizophrenia.² Recent network meta-analysis of placebo-controlled and head-to-head randomized controlled trials in adults with acute symptoms of schizophrenia revealed that SGAs significantly reduced depressive symptoms compared with placebo.⁶

Long-acting injectable (LAI) preparations of the SGAs have all demonstrated superiority over placebo and are comparable to their oral counterparts in terms of safety and tolerability.⁷ Therefore, we recommend using LAI SGAs for patients with schizophrenia and comorbid depression.

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