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ABOUT COVER

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Difference between treatment-resistant schizophrenia and clozapine-resistant schizophrenia

Ping-Tao Tseng, Mu-Hong Chen, Chih-Sung Liang

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Abstract

We read the impressive review article “Clozapine resistant schizophrenia: Newer avenues of management” with great enthusiasm and appreciation. The author believes that preventing clozapine resistance from developing may be the most effective treatment strategy for patients with clozapine-resistant schizophrenia (CRS), and optimizing clozapine treatment is a key component. Disentangling the differences between treatment-resistant schizophrenia and CRS is important for studies addressing treatment strategies for these difficult-to-treat populations.

Key Words: Treatment-resistant schizophrenia; Clozapine; Clozapine-resistant schizophrenia; Ultra-resistant schizophrenia; Ultra-treatment-resistant schizophrenia; Super-refractory schizophrenia

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Core Tip: A diagnosis of clozapine-resistant schizophrenia (CRS) is made after administering an adequate trial of clozapine and excluding “pseudo-resistance” in patients who have been diagnosed with treatment-resistant schizophrenia (TRS). Disentangling the differences between TRS and CRS is important point for studies addressing treatment strategies for patients with CRS.

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TO THE EDITOR

We read the impressive review article by Chakrabarti[1] with great enthusiasm and appreciation. The author suggests that clinicians need newer treatment approaches that go beyond the evidence for patients with clozapine-resistant schizophrenia (CRS). The author believes that preventing clozapine resistance from developing may be the most effective treatment strategy for patients with CRS, and optimizing clozapine treatment is a key component. Although this suggestion is new and insightful, we would like to discuss the differences between treatment-resistant schizophrenia (TRS) and CRS.

Treatment Response and Resistance in Psychosis (TRRIP) Working Group has suggested that CRS is a subspecifier of TRS[2]. A valid diagnosis of CRS needs to be based on: (1) Administering an adequate trial of clozapine; (2) Excluding the possibility of nonadherence to clozapine (*i.e.*, pseudo-resistance); and (3) Blood levels of clozapine ≥ 350 ng/mL. The TRRIP Work Group also recommend a minimum dose of 500 mg/d for patients who cannot undergo the blood test for clozapine concentration[2]. In the review article[1], the recommended adequate dose of clozapine is 200 to 500 mg/d, which may be low for patients with CRS.

Besides, when pooling available evidence for the management of CRS, we need to include studies that specifically addressing patients with a valid diagnosis of CRS. For example, Chakrabarti[1] cited a study by Masoudzadeh and Khalillian[3] who compared three interventions for patients with TRS, namely, clozapine, electroconvulsive therapy (ECT), and combined clozapine and ECT. In this study, a 40% reduction in the Positive and Negative Syndrome Scale scores was observed in patients who were treated with only clozapine[3]. It is clear that the study by Masoudzadeh and Khalillian[3] had included patients with TRS not CRS. Therefore, this study could not be considered as a CRS study.

FOOTNOTES

Author contributions: Tseng PT and Chen MH designed research; Chen MH and Liang CS performed research; Tseng PT and Liang CS analyzed data; Tseng PT wrote the letter; and Chen MH and Liang CS revised the letter.

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