World Journal of Psychiatry

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World J Psychiatry 2022 August 19; 12(8): 1102-1104

DOI: 10.5498/wjp.v12.i8.1102

ISSN 2220-3206 (online)

LETTER TO THE EDITOR

Difference between treatment-resistant schizophrenia and clozapine-resistant schizophrenia

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Specialty type: Psychiatry

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Chakrabarti S, India; Khan MM, India; Patten SB, Canada; Pivac N, Croatia

Received: September 4, 2021
Peer-review started: September 4, 2021
First decision: November 8, 2021
Revised: November 19, 2021
Accepted: July 11, 2022
Article in press: July 11, 2022
Published online: August 19, 2022

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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

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.

Citation: Tseng PT, Chen MH, Liang CS. Difference between treatment-resistant schizophrenia and clozapine-resistant schizophrenia. *World J Psychiatry* 2022; 12(8): 1102-1104
URL: https://www.wjgnet.com/2220-3206/full/v12/i8/1102.htm
DOI: https://dx.doi.org/10.5498/wjp.v12.i8.1102

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.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

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S-Editor: Wang JJ
L-Editor: A
P-Editor: Wang JJ

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