Research Report

Annals of Pharmacotherapy
1–7

DOI: 10.1177/10600280231201708
journals.sagepub.com/home/aop
Sage

Comparison of the Effectiveness and Safety of Clozapine Between Once-Daily and Divided Dosing Regimen in Patients With Treatment-Resistant Schizophrenia

Thanompong Sathienluckana, PharmD[1], Thaksin Jansing, PharmD[1], Supakan Srisuriyakamon, PharmD[1], Aunchalee thonkhunthod, PharmD[1], Parsiri Sangsuwanto, PharmD[1], Pholphat Losatiankij, MD[2], and Suttha Supanya, MD, FRCPsychT[2]

Abstract

Background: Clozapine is the most effective antipsychotic with respect to the incidence of discontinuation and is indicated for treatment-resistant schizophrenia. Although the recommendation for clozapine administration is divided dosing, once-daily dosing of clozapine is commonly prescribed in many countries. However, there is currently no clinical data comparing all-cause discontinuation between the 2 methods of administration of clozapine. **Objectives:** To compare the all-cause discontinuation and safety of clozapine administration between once-daily and divided dosing regimens. **Methods:** This was a retrospective cohort study. Participants were patients with treatment-resistant schizophrenia who had received 300 to 600 mg/day of clozapine for at least 3 months. Data were collected from outpatient medical records at Somdet Chaopraya Institute of Psychiatry. Eligible patients were classified into 2 groups: once-daily dosing and divided dosing. The primary outcome was the all-cause discontinuation rate between groups. The duration of the study was 2 years. **Results:** One hundred eighteen patients were included and analyzed in this study (once-daily dosing group: n = 58; divided dosing group: n = 60). There was no significant difference in all-cause discontinuation between the 2 groups (odds ratio 1.03; 95% confidence interval: [0.28, 3.79]: $P = 1.00$), or adverse events between groups. **Conclusion and Relevance:** In patients with treatment-resistant schizophrenia, there were no significant differences in effectiveness or safety between once-daily and divided dosing of clozapine. Further prospective studies with larger sample sizes are required to confirm these findings.

Keywords

clozapine, treatment-resistant schizophrenia, once-daily dosing, divided dosing

Introduction

Schizophrenia is an often long-term, progressive, and severe psychiatric disorder that impairs many aspects of functional outcomes, including social and vocational. Approximately one-third of patients with schizophrenia do not respond to antipsychotic drugs and are described as having treatment-resistant schizophrenia. Treatment-resistant schizophrenia is defined as failure to respond to an adequate dose and duration of treatment with at least 2 antipsychotic drugs.[1] Clozapine is the most effective antipsychotic with respect to the incidence of discontinuation in treatment-resistant schizophrenia. Therefore, clozapine is considered the gold standard for treatment-resistant schizophrenia.[1-3]

In addition, clozapine may reduce all-cause mortality in patients with schizophrenia and improve other outcomes, including hospitalization and functioning, compared with other antipsychotics.[4-6] However, clozapine has several adverse drug reactions (such as sedation, tachycardia, orthostatic hypotension, sialorrhea, and weight gain) and also has several black box warnings, such as agranulocytosis, seizure, and myocarditis. Therefore, the appropriate use of clozapine is essential to achieving better outcomes for patients with schizophrenia.[7]

[1]Faculty of Pharmacy, Siam University, Bangkok, Thailand
[2]Somdet Chaopraya Institute of Psychiatry, Bangkok, Thailand

Corresponding Authors:
Suttha Supanya, Somdet Chaopraya Institute of Psychiatry, 112 Somdet Chao Phraya Rd, Khlong San, Bangkok 10600, Thailand.
Email: suttha.supanya@hotmail.com

Pholphat Losatiankij, Somdet Chaopraya Institute of Psychiatry, 112 Somdet Chao Phraya Rd, Khlong San, Bangkok 10600, Thailand.
Email: attii2517@hotmail.com