JOURNAL OF HEALTH SCIENCE AND PREVENTION
http://jurnalfpk.uinsby.ac.id/index.php/jhsp
ISSN 2549-919X (e)

The Effectivity of Olanzapine and Diazepam Therapy in Schizophrenic Patients with Agitating States

Nevi Sulvita Karsa[1*], Sonny T Lisal[2]
[1)]*Pshyciatry Specialist Education Program, Hasanuddin University, Makassar, Indonesia*
[2)]*Department of Psychiatry, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia*
nevi.sulvita@umi.ac.id

DOI: http://doi.org/10.29080/jhsp.v8i1.1052

Received : October 2023, Accepted : April 2024, Published : April 2024

Keywords

Olanzapine; Diazepam; Schizophrenia; Agitation

Abstract

In the management of acute agitation in schizophrenia patients, the efficacy of antipsychotic medications, such as olanzapine has been widely studied. This study aimed to investigate the effectiveness of adding diazepam to olanzapine therapies in reducing agitation in schizophrenia. The research was conducted on a sample of patients diagnosed with schizophrenia in an agitated state. The study employed a pre-post-test design with non-randomized group selection, comprising two groups: olanzapine, olanzapine and diazepam. The Positive and Negative Syndrome Scale-Excited Component (PANSS-EC) was utilized to measure agitation symptoms. The results indicated a significant reduction in PANSS-EC scores in all groups from before therapy to the third day of therapy. In conclusion, combination therapy with antipsychotics and diazepam may be considered in the management of agitation in schizophrenia patients. Further research involving larger samples and exploring additional variables is recommended to enhance our understanding of this treatment approach.

Introduction

Schizophrenia is a complex mental disorder with various phenotypic expressions. Its prevalence reaches 0.46% worldwide and has a significant impact on social burden and human productivity [1,2]. In Indonesia, the prevalence of severe mental disorders including schizophrenia continues to increase, therefore an effective management modality for schizophrenia becomes very crucial [3]. Agitation which is often associated with psychotic problems is one of the symptoms which requires immediate treatment to prevent the occurrence of undesirable consequences. Pharmacological management of acute agitation has an important role in dealing with this situation. Common medications for acute agitation include first- and second-generation antipsychotics, as well as benzodiazepines [4,5].

Second-generation antipsychotics such as olanzapine are one of the options for agitation which can also repair cognitive function, positive symptoms, and negative symptoms, and decrease neuroleptic side effects compared to first-generation antipsychotic medications. However, sometimes the initial dose of antipsychotics may not be sufficient to control agitation, the addition of benzodiazepines becomes an important consideration for the management of this condition. Benzodiazepines such as diazepam are the drug of choice to appease patients with acute agitation. Several studies have assessed that administering diazepam injection along with atypical antipsychotics may provide improvement in agitated patients [6]. However, side effects such as pain at the injection site can sometimes cause thrombophlebitis. Therefore, this study aimed to investigate the difference in the effectiveness of olanzapine in combination with diazepam tablets in overcoming agitation in schizophrenia patients. This study aims to provide deeper insights into the use of these medications in the agitation management of schizophrenic patients, which will hopefully improve the understanding and clinical practice in treating patients with this mental disorder.

Methods

This study is an observational analytical study with a pre-and post-test design. The study was conducted in September-November 2022 in the Psychiatric Emergency Room of Dadi Psychiatric Hospital Makassar South Sulawesi. The study population consisted of all schizophrenia patients who experienced agitation or restless rowdiness in the Psychiatric ER of Dadi Psychiatric Hospital. The sample for this study was selected using the Consecutive Sampling method, where all patients who met the research criteria were included until the required number of samples was met. The minimum sample size is 10 for each group. Inclusion criteria for participation in this study are patients diagnosed with schizophrenia based on PPDGJ III criteria, aged between 18 and 55 years, having PANSS-EC score of > 20 or if any of the symptom items showed a score above 3, and receiving olanzapine therapy, either with or without the addition of diazepam, and willing to participate in this study. The exclusion criteria involved patients with a history of other drug abuse in the past 6 months and patients with a history of organic mental disorders. The data collected are primary data obtained directly from the research subject. The research instrument consists of an informed consent sheet and a PANSS-EC scale. Any patients who met the inclusion criteria were put into the study group, and the identity of the sample was recorded. Informed consent is given to the family or research subject. PANSS-EC scores were measured before patients received therapy and on day 1, day 2, and day 3 after receiving therapy. Changes in PANSS-EC scores were compared between the two therapy groups. Data collected from this study will be processed using statistical software, SPSS 23.0 and Microsoft Excel. The results of data processing will be presented in the form of tables, and diagrams, as well as correlation values and their significance. Before conducting this research, an ethical clearance was first obtained from the Commission for Ethics for Biomedical Research in Humans, Faculty of Medicine, Hasanuddin University. The confidentiality of the identity of the research subject is also maintained to ensure that this study doesn't cause any harm to any party. Variables in this study included independent variables such as olanzapine and diazepam treatment, dependent variables of improvement in agitation symptoms, controlled variables were schizophrenia diagnosis, and random variables were age and education level of patients. Operational definitions used include the definition of schizophrenia as a severe mental disorder with certain characteristics, the definition of PANSS-EC as an instrument of measurement of agitation symptoms, the definition of clinical symptom improvement as a decrease in PANSS-EC scores, and the definition of drug doses used in the therapy group. Authors in this research ensure that this research complies with all applicable ethical and regulatory procedures. Hopefully, the results of this study can provide benefits for all parties involved by the benefits of the research mentioned earlier.

Results

Table 1 shows the characteristics of subjects who received olanzapine monotherapy, there are 2 participants (20%) aged 17-25 years, 4 participants (40%) aged 26-35 years, 2 participants (20%) aged 36-45 years and 2 participants (20%) aged 46-55 years, while in the group received combination of olanzapine and diazepam therapy consist 2 participants (20%) aged of 17-25 years, 4 participants (40%), aged 26-35 years, and 4 participants (40%) aged 36-45 years old.

Table 1. The characteristics of the subjects that obtained olanzapine monotherapy and a combination of olanzapine and diazepam

Characteristics		Therapy (Olz+Diaz) n = 10	Control (Olz) n = 10
Age	17-25 years old	2 (20%)	2 (20%)
	26 – 35 years old	4 (40%)	4 (40%)
	36 -45 years old	4 (40%)	2(20%)
	46-55 years old	0	2 (20%)
Educational status	Elementary School	3 (30%)	2 (20%)
	Junior High School	3 (30%)	2 (20%)
	Senior High School	4 (40%)	6 (60%)

Table 2 shows a comparison of PANSS-EC values in subjects treated with olanzapine monotherapy versus a combination of olanzapine and diazepam, which showed a significant difference in PANSS-EC values before therapy until the first day (P value of 0.035) as well as PANSS-EC values on the second day to the third day (P value of 0.015).

Table 2. Comparison of PANSS-EC Values in subjects treated with olanzapine monotherapy versus a combination of olanzapine and diazepam

Group		Mean	P Value
Panss ec before 1st day of therapy	Olz	1,2	0,035
	olz+ Diaz	2,6	
Panss ec in the 1st and 2nd day	olz	2,0	0,143
	olz+ Diaz	1,6	
Panss ec in the 3rd and 4th day	olz	0,8	0,015
	olz+ Diaz	2,1	

In the group treated with olanzapine monotherapy, there was a decrease in PANSS-EC values from before therapy to the third day of therapy by 4, while in the group of olanzapine and diazepam combination, there was a decrease in PANSS-EC values by 6.3, as can be seen in Figure 1.

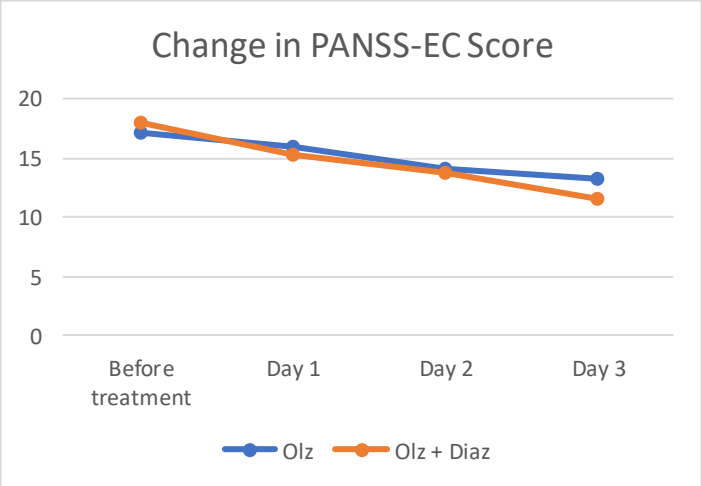

Figure 1. Change in the Value of PANSS-EC in subjects with olanzapine monotherapy versus a combination of olanzapine and diazepam

Discussion

Agitation is a major problem in acute schizophrenia and is an emergency that requires immediate intervention. To prevent harm to patients, doctors, nurses, and other subjects around the patient. Agitation patients used to be treated by restraint, but this treatment is associated with many negative impacts including frightening and traumatic experiences for the patients that potentially affect the future cooperation between the patient with health workers, thus more appropriate pharmacological interventions are needed to create more effective agitation management. In this study, researchers examined the effectiveness of adding diazepam tablets in schizophrenic subjects in agitated states receiving olanzapine therapy. The average dose of olanzapine received by subjects in this study was similar to the olanzapine dose in daily clinical practice (10-20 mg/day) [4,6,7,8]. Table 1 and Table 2 show the differences in decreased PANSS-EC values in subjects given combination therapy of olanzapine and diazepam tablets compared to those treated with olanzapine alone. There was a significant difference in PANSS EC values before therapy to the first day, where subjects with combination therapy of olanzapine and diazepam tablets experienced a decrease in PANSS EC values of 2.6 which was significantly greater compared to patients given olanzapine alone that only experienced a decrease in PANSS EC of about 1.2. This finding is in line with previous research that also supports the effectiveness of antipsychotics and benzodiazepine combination therapy in dealing with agitation [4].

Figure 1 shows the change in PANSS-EC values in patients receiving olanzapine alone versus olanzapine and diazepam combination therapy. Both groups experienced a decrease in Panss EC from before the therapy to the third day of therapy. Subjects receiving a combination of diazepam tablets and olanzapine experienced a more significant decrease in PANSS-EC values compared to those receiving olanzapine monotherapy. This finding possibly can be caused by the mechanism of olanzapine which also works as a histaminergic that can cause sedation effect and control agitation combined with diazepam which works by increasing the affinity of GABA to GABA-A receptors which is one of the large inhibitory neurotransmitters in the central nervous system, therefore creating a rapid effect in controlling agitation in schizophrenic patients. [7,8,9,10]. Diazepam tablets also have the advantage of being easily obtained in remote areas with low prices. In general, this study proved that combination therapy of olanzapine and diazepam tended to be more effective in reducing symptoms of agitation in schizophrenic patients

compared to olanzapine monotherapy. These results support the use of more comprehensive treatment strategies in managing agitation in schizophrenic patients.

Conclusion

From the results of this study, it can be concluded that therapy with olanzapine combined with diazepam tablets successfully showed a significant decrease in PANSS-EC scores, indicating improvement in symptoms of agitation in schizophrenic patients. The results of this study provide a basis for mental health practitioners to consider the use of combination antipsychotic therapy with diazepam tablets as an option in the treatment of agitation in schizophrenia patients. Further studies involving larger samples can provide a deeper understanding of the effectiveness of these therapies. In addition, future research may explore other variables that may affect the effectiveness of therapy, such as the duration of treatment and possible side effects. All this is expected to improve agitation management in schizophrenic patients.

References

1. Dilip V. Jeste, M.D, Jeffrey A. Lieberman, M.D, David Fassler, M.D, et al. 2013. Schizophrenia Spectrum and Other Psychotic Disorders. Diagnostic And Statistical Manual Of Mental Disorders. Hlm. 87-120
2. Kaplan, Sadock, Grebb. 1994. Skizofrenia. New York Medical Center. Hlm. 699- 744
3. Nurmiati Amir. 2017. Skizofrenia. FKUI. Hlm. 184-220
4. Zeller, Scott. Citrome Leslie.2016. Managing Agitation Associated with Schizophrenia and Bipolar disorder in the emergency Setting in Western Journal of Emergency Medicine Vol XVII No.2.Department of Psychiatric Emergency Services, Oakland, California.
5. Wilhelm,S *et al*. 2008. Use of Antipsychotics and Benzodiasepin in patients with psychiatric emergencies : Result of an observational Trial. BMC Psychiatry. Germany https://doi.org/10.1186/1471-244X-8-61
6. Wilson, M.et al. 2012. The Psychopharmacology of Agitation: Consensus the American Associztion for Emergency Psychiatry Project BETA Psychopharmacology Workgroup. Western Journal of Emergency Medicine Vol XIII. https://doi.org/10.5811/westjem.2011.9.6866
7. Walther s,et al. 2014 Rapid Tranquilization of Severely Agitated Patients With Schizophrenia Spectrum Disorders A Naturalistic, Rater-Blinded, Randomized, Controlled Study With Oral Haloperidol, Risperidone, and Olanzapine. Journal of Clinical Psychopharmacology https://doi.org/10.1097/JCP.0000000000000050
8. Walther s,et al. 2014 Rapid Tranquilization of Severely Agitated Patients With Schizophrenia Spectrum Disorders A Naturalistic, Rater-Blinded, Randomized, Controlled Study With Oral Haloperidol, Risperidone, and Olanzapine. Journal of Clinical Psychopharmacology
9. Miller J. 2021.Managing acute agitation and agresion in the world for drug shortages. The Mental Health Clinician is a publication of the College of Psychiatric and Neurologic Pharmacist
10. Hsu W-Y, Huang S-S, Lee B-S, et al. 2010. Comparison of intramuscular olanzapine, orally disintegrating olanzapine tablets, oral risperidone solution, and intramuscular haloperidol in the management of acute agitation in an acute care psychiatric ward in Taiwan. J Clin Psychopharmacol. 30:230–234