Jurnal Riset Kesehatan Poltekkes Depkes Bandung

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

Analysis of Creatinin Phospokinase (CPK) enzyme activity for determining te cut off duration of antipsychotic drug therapy

Analisis Aktivitas Enzim Kreatin Fosfokinase untuk Penentuan Cut Off Lama Terapi Obat Antipsikotik

Ruri Khoyimah[1*], Ani Riyani[1], Nani Kurnaeni[1], Rohayati Rohayati[1]
[1]Program Studi Sarjana Terapan, Jurusan Teknologi Laboratorium Medis, Poltekkes Kemenkes Bandung, Cimahi, Indonesia
*Email: khoyimahruri@gmail.com

ABSTRACT

Background: *Schizophrenia is a mental disorder affecting thoughts, emotions, and behavior. Antipsychotic therapy is the main treatment; however, it may cause neurological side effects, including Neuroleptic Malignant Syndrome (NMS). Creatine Phosphokinase (CPK) is commonly used as a biomarker for detecting NMS.*
Objective: *To evaluate the relationship between the duration of antipsychotic therapy and CPK enzyme activity and to determine the cut-off value of therapy duration associated with increased CPK levels in patients with schizophrenia.*
Methods: *This cross-sectional study used secondary data from 43 schizophrenia patients treated at the West Java Provincial Mental Hospital between January and September 2024. Samples were selected using purposive sampling. Inclusion criteria were patients receiving single or combination antipsychotic therapy, while patients with heart disease or muscle disorders were excluded. Spearman correlation analysis was used to assess the relationship between therapy duration and CPK activity, and Receiver Operating Characteristic (ROC) analysis was performed to determine the cut-off value.*
Results: *No significant relationship was found between the duration of antipsychotic therapy and CPK enzyme activity (p = 0.311). ROC analysis identified a therapy duration cut-off at 19–20 days, although its predictive value was weak (Asymp. Sig = 0.237).*
Conclusion: *There was no significant relationship between the duration of antipsychotic therapy and CPK enzyme activity in patients with schizophrenia. Although a therapy duration cut-off of 19–20 days was identified, further studies with larger samples are needed.*

Keywords*: antipsychotic drug therapy duration, creatine phospokinase (CPK), skizophrenia*

ABSTRAK

Latar Belakang: Skizofrenia merupakan gangguan mental yang memengaruhi pikiran, emosi, dan perilaku. Terapi utama skizofrenia adalah antipsikotik, namun penggunaannya dapat menimbulkan efek samping neurologis, termasuk Neuroleptic Malignant Syndrome (NMS). Creatine Phosphokinase (CPK) digunakan sebagai biomarker untuk mendeteksi NMS.
Tujuan: Mengetahui hubungan durasi terapi antipsikotik dengan aktivitas enzim CPK serta menentukan nilai cut-off durasi terapi yang berisiko meningkatkan kadar CPK pada pasien skizofrenia.
Metode: Penelitian cross-sectional ini menggunakan data sekunder dari 43 pasien skizofrenia di Rumah Sakit Jiwa Provinsi Jawa Barat periode Januari–September 2024. Sampel dipilih dengan teknik purposive sampling. Kriteria inklusi meliputi pasien yang menerima terapi antipsikotik tunggal maupun kombinasi, sedangkan pasien dengan penyakit jantung atau gangguan otot dikecualikan. Analisis hubungan dilakukan menggunakan uji korelasi Spearman, sedangkan analisis Receiver Operating Characteristic (ROC) digunakan untuk menentukan nilai cut-off.

https://doi.org/10.34011/juriskesbdg.v18i1.2863

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

Hasil: Tidak terdapat hubungan bermakna antara durasi terapi antipsikotik dan aktivitas enzim CPK (p = 0,311). Analisis ROC menunjukkan nilai cut-off durasi terapi pada hari ke-19 hingga 20, namun kekuatan prediksinya lemah (Asymp. Sig = 0,237).
Kesimpulan: Tidak terdapat hubungan bermakna antara durasi terapi antipsikotik dan aktivitas enzim CPK pada pasien skizofrenia. Meskipun diperoleh nilai cut-off pada hari ke-19–20, penelitian lebih lanjut dengan jumlah sampel lebih besar masih diperlukan.

Kata kunci: Kreatin Fosfokinase (CPK), lama terapi obat antipsikotik, skizofrenia

INTRODUCTION

Mental disorders are a global health problem that continues to increase annually. According to WHO data from 2022, approximately 24 million people worldwide suffer from schizophrenia. In Indonesia, the 2018 Basic Health Research (Riskesdas) showed that the prevalence of schizophrenia reached 6.7 per 1,000 people, up from 1.7 per 1,000 in 2013. In West Java Province, the number of schizophrenia sufferers reached 22,489, and according to data from the West Java Provincial Mental Hospital in 2023, 47.5% of patients treated for mental disorders were schizophrenic. [1]

Schizophrenia is a mental disorder that can affect an individual's thoughts, feelings, and behavior, and is often characterized by difficulty distinguishing between reality and delusions. [2] One of the main therapies for treating this disorder is the use of antipsychotic drugs, which are divided into two groups: typical (first-generation) and atypical (second-generation) antipsychotics.[3] Antipsychotic therapy can be given as monotherapy or in combination.[4] Although effective in reducing psychotic symptoms, the use of these drugs carries the risk of causing neurological side effects, both acute and chronic. Previous research has shown that the most common neurological side effect experienced by schizophrenia patients is Extrapyramidal Syndrome (EPS), which is characterized by tremors, rigidity, uncontrolled muscle contractions, seizures, or abnormal body postures.[5] In addition, the use of typical antipsychotics may lead to Neuroleptic Malignant Syndrome (NMS), a potentially life-threatening neurological emergency. Although relatively rare, NMS remains associated with a high mortality rate, and its incidence may increase along with the growing population of patients with psychotic disorders.

One of the laboratory parameters that plays a role in detecting SNM iscreatine phosphokinase (CPK) enzyme activity, which can increase due to skeletal muscle damage or muscle metabolic disorders.[6] Increased CPK enzyme activity has been associated with the use of antipsychotic therapy, as shown in a study by Grunder et al. (2019), who reported that CPK enzyme activity can increase within five days to one year after antipsychotic drug use.[7] In addition, a study conducted by Hein Bokern et al. (2020) found that clozapine antipsychotic therapy was associated with increased CPK enzyme activity.[8] Currently, CPK enzyme activity testing in schizophrenia patients at the West Java Provincial Mental Hospital is only performed based on clinical indications, according to a doctor's request. Initial laboratory tests for inpatients generally only include routine hematology and random glucose, without routine monitoring of CPK enzyme activity.

Although several studies have reported increased CPK enzyme activity during antipsychotic use, to date, no study in Indonesia has specifically analyzed the relationship between duration of antipsychotic therapy and CPK enzyme activity and determined a cut-off value for therapy duration as a basis for clinical monitoring. Furthermore, at the West Java Provincial Mental Hospital, CPK testing is still indicative and not routinely performed. The lack of local data on patterns of CPK increase based on duration of therapy creates a scientific and clinical gap in the development of guidelines for monitoring antipsychotic side effects. Therefore, this study was conducted to evaluate the relationship between duration of antipsychotic therapy and creatine phosphokinase enzyme activity and to determine a cut-off value for therapy duration that

https://doi.org/10.34011/juriskesbdg.v18i1.2863

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

can be used as a basis for consideration in the clinical monitoring of schizophrenia patients.

METHODS

Study design

The study was conducted using a cross-sectional approach using medical record data from schizophrenia patients at the West Java Provincial Mental Hospital. The relationship between the duration of antipsychotic therapy andCreatine phosphokinase (CPK) enzyme activity was analyzed, and a cut-off value for the duration of therapy that can be used in clinical monitoring was determined. Data collection was conducted at the West Java Provincial Mental Hospital from October to November 2024.

Data source and sampling procedure

The data used comes from the medical records of patients undergoing antipsychotic therapy between January and September 2024. The population in this study were patients diagnosed with schizophrenia and receiving antipsychotic therapy at the West Java Provincial Mental Hospital. The study sample consisted of 43 patients, selected using purposive sampling based on the following inclusion criteria: (1) Mental Hospital patients diagnosed with schizophrenia, (2) undergoing single or combination antipsychotic therapy, and (3) having CPK enzyme activity data recorded in medical records (January–September 2024). Patients with a history of heart disease or muscle disorders that could affect CPK enzyme activity were excluded from this study.

Variables of the study

To minimize the influence of confounding variables, data on antipsychotic type and treatment regimen were recorded and descriptively analyzed as part of the subject characteristics. Medication dosage information was also obtained from medical records and considered during result interpretation, although no separate quantitative dosage analysis was performed due to study design limitations and incomplete secondary data. These variables were recognized as potential factors influencing CPK enzyme activity and were considered in interpreting the relationship between therapy duration and CPK levels.

Measurement and instruments

This study used patient blood samples analyzed for CPK enzyme activity. CPK enzyme activity was measured using a Cobas C111 chemistry analyzer with specific Cobas reagents. To ensure the accuracy of the results, quality control was performed using PCCM Level 1 and PCCM Level 2 prior to testing the patient samples.

Data collection

Data were collected from patient medical records, including demographic information, antipsychotic therapy history, and CPK enzyme activity. CPK enzyme activity was measured using a kinetic photometry method, where the rate of NADPH formation is measured photometrically and the results are proportional to the CPK enzyme activity in serum. Blood sampling was performed according to standard laboratory procedures with proper serum processing to obtain accurate results.

Ethical considerations

This research has received approval from the Ethics Committee of the West Java Provincial Mental Hospital under Decree No. 16/KEPK/EC/XII/2024. All patient data used in the study will be kept confidential and used solely for scientific purposes. Patient identities are not included in the research data to maintain privacy and comply with medical research ethical standards.

https://doi.org/10.34011/juriskesbdg.v18i1.2863

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

Data analysis

The collected data was analyzed using SPSS software. A normality test was first performed to determine the data distribution. If the data were normally distributed, a correlation analysis was performed using the Pearson correlation test; if not, the Spearman correlation test was used. Furthermore, to determine the cut-off value for antipsychotic therapy duration, a Receiver Operating Characteristic (ROC) analysis was performed. The results of this analysis were used to evaluate whether therapy duration could be an indicator of increased CPK enzyme activity in schizophrenia patients.

RESULTS

Table 1. Patient Characteristics Based on Gender, Therapy Type, and CPK Value

Variables	Category	n	%
Gender	Male	30	72
	Female	13	28
	Total	43	100
Types of Antipsychotic Therapy	Combination of two atypical antipsychotics	21	49
	Combination of typical and atypical antipsychotics	19	44
	Single atypical antipsychotic	3	7
	Total	43	100
CPK Value	Normal	11	26
	Abnormal	32	74
	Total	43	100

Based on Table 1, 43 schizophrenia patients underwent antipsychotic therapy at the West Java Provincial Mental Hospital. Thirty patients (72%) were male, while 13 patients (28%) were female. The combination of antipsychotics used varied, with 21 patients (49%) using a combination of two atypical antipsychotics, 19 patients (44%) using a combination of a typical and an atypical antipsychotic, and 3 patients (7%) using a single atypical antipsychotic. Measurement of creatine phosphokinase (CPK) enzyme activity showed a range of values between 48 U/L to 8,250 U/L, with a median of 804 U/L and a mean of 1,889 U/L. Of the 43 patients, 32 patients (74%) had CPK enzyme activity exceeding the normal limit (>300 U/L for men and >200 U/L for women), while 11 patients (26%) had CPK enzyme activity within the normal range.

Table 2. Statistical Test Results of the Relationship between Duration of Antipsychotic Therapy and CPK Enzyme Activity

Analysis	Parameter	Value	p-value
Normality test (Kolmogorov–Smirnov)	Statistics	0.257	<0.05
Normality test (Shapiro–Wilk)	Statistics	0.668	<0.05
Spearman correlation (duration of therapy vs CPK)	Coefficient (ρ)	0.078	0.311
ROC Analysis	AUC	0.379	-
	95% CI AUC	0.201 – 0.558	-
	Cut-off point	Day 20	-
Cut-off duration of therapy (based on Youden Index)	Youden Index (J)	0.068	-
	Sensitivity	0.250	-
	Specificity	0.182	-

Based on Table 2, after conducting normality tests using the Kolmogorov-Smirnov and Shapiro-Wilk methods, the results showed that the CPK data distribution was not normal ($p < 0.05$). Therefore, a correlation analysis was performed using the Spearman test. The test results showed a correlation coefficient of 0.078 with a p-value of 0.311.

Receiver Operating Characteristic (ROC) analysis was performed to determine the cut-off value for duration of therapy associated with increased CPK enzyme activity. The

https://doi.org/10.34011/juriskesbdg.v18i1.2863

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

analysis showed an area under the curve (AUC) of 0.379 with a p-value of 0.237. Based on the Youden index, the identified cut-off point for duration of therapy was between days 19 and 20.

DISCUSSION

The results of this study indicate that the majority of schizophrenia patients undergoing antipsychotic therapy experienced increased creatine phosphokinase (CPK) enzyme activity. Of the 43 patients, 74% had CPK levels above the normal limit, while 26% were within the normal range. This finding is consistent with previous research suggesting that antipsychotic use can lead to increased CPK enzyme activity due to certain side effects, such as neuroleptic malignant syndrome or drug-induced myopathy.[6,9] The mechanism of increased CPK enzyme activity is related to the blockade of dopamine receptors in the nigrostriatal pathway which causes neuromuscular disorders, including dystonia and rigidity, which ultimately triggers the release of CPK into the blood.[10]

The distribution of patients by gender shows that there are more males than females, with percentages of 72% and 28%, respectively. This is consistent with research.Bawean and Thristy in 2023 found that schizophrenia is more common in men than in women.[11] Hormonal factors and differences in drug metabolism are thought to contribute to this difference.[12] In addition, men tend to have greater muscle mass than women, which may lead to differences in baseline CPK enzyme activity before and after therapy.[13]

In this study, the correlation analysis between the duration of therapy and CPK enzyme activity using the testSpearman's test showed no significant relationship (p-value = 0.311). The correlation coefficient of 0.078 indicates a very weak relationship between the two variables. This result differs from Kristina's (2006) study, which found that CPK enzyme activity was higher in patients using atypical antipsychotics such as clozapine and olanzapine compared to conventional antipsychotics.[14] This discrepancy could be due to differences in study design, sample population, or measurement methods.[15] Another study by Maren et al (2017) also showed that increased CPK enzyme activity was more frequently found in patients receiving long-term antipsychotic therapy, especially in patients with a history of neuromuscular disorders or extrapyramidal side effects.[16]

ROC analysis was performed to determine the cut-off value.off the duration of therapy associated with increased CPK enzyme activity. The results showed that the AUC value was 0.379 with a p-value of 0.237, which means that the duration of therapy is not a strong predictor for increased CPK enzyme activity. However, based on the Youden index, the optimal cut-off point for the duration of therapy was found on days 19 and 20. These results indicate that although the relationship between duration of therapy and CPK enzyme activity is not statistically significant, there is a tendency for increased CPK enzyme activity after a certain period of therapy.[8] However, the low AUC value indicates that other factors play a greater role in determining the increase in CPK enzyme activity, such as the type of drug, dose, and the patient's clinical condition.[7]

This study also supports previous findings that increased CPK enzyme activity in schizophrenia patients can vary based on the type ofantipsychotics used. According to research by Hutagaol et al. (2023), the combination of typical and atypical antipsychotics often produces more significant side effects on CPK enzyme activity than monotherapy.[4] In addition, patients using first-generation antipsychotics are at greater risk of CPK elevations compared to second-generation ones due to their stronger extrapyramidal effects.[17] This is in line with research by Melkersson (2006), which showed that therapy with certain atypical antipsychotics such as clozapine and olanzapine tends to increase CPK enzyme activity more than conventional agents.[14] Other factors such as drug

https://doi.org/10.34011/juriskesbdg.v18i1.2863

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

dosage and the patient's clinical condition also play a role in increasing CPK enzyme activity. The strength of this study lies in the use of real-world clinical data from hospital medical records and CPK measurements based on standardized laboratory procedures and quality control, thereby increasing data reliability and providing an initial overview of the cut-off time point based on ROC analysis. However, this study was limited by its cross-sectional design and the use of secondary data, which restricted causal interpretation, as well as the relatively small sample from a single center. In addition, important confounding factors such as antipsychotic type and dose, cumulative exposure, additional therapy, physical activity, and acute clinical conditions were not fully controlled, which may explain the weak ROC predictive value. Therefore, therapy duration alone should not be used as the sole predictor of CPK elevation. CPK monitoring should instead be based on clinical risk factors, including the type and dose of antipsychotics and the patient's clinical condition. The 19–20 day cut-off may be considered a preliminary finding for clinical alert purposes and still requires validation through larger prospective studies.

Clinically, the finding that a significant proportion of patients exhibited elevated CPK enzyme activity indicates the need for vigilant monitoring of antipsychotic therapy side effects, particularly in patients with additional risk factors such as combination therapy, a history of extrapyramidal side effects, or underlying medical conditions. Although the duration of therapy was not shown to be a significant predictor, these results suggest that CPK monitoring should be based not solely on the duration of therapy but rather on a risk-based approach. Identification of a time point around days 19 and 20 may be considered an initial clinical alert period, although it is not yet robust enough to be considered a standard for routine testing. Therefore, a thorough clinical evaluation remains the primary basis for determining the need for CPK testing, particularly when symptoms such as rigidity, hyperthermia, or altered mental status suggestive of Neuroleptic Malignant Syndrome (NMS) occur.

CONCLUSION

No significant correlation was found between the duration of antipsychotic therapy and CPK enzyme activity in schizophrenia patients. This suggests that therapy duration alone cannot be used to predict increased CPK levels. Therefore, CPK monitoring should not rely solely on therapy duration, but also consider the patient's clinical condition, type and combination of antipsychotics, therapeutic dose, and neurological symptoms suggestive of side effects such as Neuroleptic Malignant Syndrome.

ACKNOWLEDGMENT

We would like to thank the West Java Provincial Mental Hospital for their permission and support in collecting the data for this study. We also extend our appreciation to the laboratory team at the RS Jiwa Provinsi Jawa Barat for their assistance in data collection and analysis. We also extend our gratitude to Poltekkes Kemenkes Bandung for the facilities and guidance provided during this research.

REFERENCES

1. Kementerian Kesehatan RI. Riskesdas 2018. *Lap Nas Riskesdas 2018*. 2018;44(8):181-222. http://www.yankes.kemkes.go.id/assets/downloads/PMK No. 57 Tahun 2013 tentang PTRM.pdf
2. Yudhantara DS, Istiqomah R. *Sinopsis Skizoprenia Untuk Mahasiswa Kedokteran*. UB Press; 2018.
3. Casarella J. First and Second Generation Antipschotic for Schizofrenia. Published 2024. https://www.webmd.com/schizophrenia/first-second-generation-antipsychotics
4. Hutagaol. Gambaran Pola Penggunaan Obat Antipsikotik Kombinasi Pada Pasien

https://doi.org/10.34011/juriskesbdg.v18i1.2863

Vol 18 No 1, Mei 2026
e-ISSN: 2579-8103
p-ISSN:1979-8253

Skizofrenia Paranoid Rwat Jalan di Rumah Sakit Jiwa Dr. Soeharto Heerdjan Periode Januari-Juni 2021. *J Kesehat Masa Depan*. 2023;2(2):113-137. https://jurnal.ruangide.org/JKMD

5. Huhn M, Nikolakopoulou A, Schneider-Thoma J, et al. Comparative efficacy and tolerability of 32 oral antipsychotics for the acute treatment of adults with multi-episode schizophrenia: a systematic review and network meta-analysis. *Lancet*. 2019;394(10202):939-951. doi:10.1016/S0140-6736(19)31135-3
6. Indera, Nuradyo D, Subagya. Neuroleptik Maligna Syndrome.Pdf Ugm. 2018;17(3).
7. Gründer P, Augustin M, Paulzen M, Gründer G. Influence of Kidney Function on Serum Risperidone Concentrations in Patients Treated With Risperidone. *J Clin Psychiatry*. 2019;80. doi:10.4088/JCP.19m12890
8. Bokern H, Jonker N, Cohen D. Creatine kinase elevation and discontinuation of clozapine: fear-driven clinical practice in a forensic case with treatment-resistant schizophrenia and persistent violent behaviour. *BJPsych Open*. 2021;7(1):1-4. doi:10.1192/bjo.2020.134
9. Shukmana DJ, Mentari IN, Anjelin DP. Study of Creatinin Levels of Patients Receiving Antipsycotic Treatment at Mutiara Sukma Psychiatric Hospital, Nusa Tenggara Barat. *Medicra (Journal Med Lab Sci*. 2021;4(2):78-82. doi:10.21070/medicra.v4i2.1613
10. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Psey LM. *Pharmacotherapy A Pathophysiologic Approach*.; 2023. doi:10.1016/B978-0-323-99992-2.00076-1
11. Bawean PL, Thristy I. Perbandingan Penggunaan Antipsikotik Atipikal Tunggal Dan Kombinasi Terhadap Kadar Glukosa Darah Pada Pasien Skizofrenia. *J Ilm Kohesi*. 2023;7(Vol 7 No 2):141-149.
12. Sheila L. Videbeck, PhD R. *Psychiatric-Mental Health Nursing Eighth Edition*.; 2020. https://dokumen.pub/psychiatric-mental-health-nursing-8th-edition-8thnbsped-9781975116378.html
13. Aujla RS, Zubair M, Patel R. Creatinine Phospokinase. In: *StatPearls*. StatPearls Publishing; 2024.
14. Melkersson K. Serum creatine kinase levels in chronic psychosis patients - a comparison between atypical and conventional antipsychotics. *Prog Neuro-Psychopharmacology Biol Psychiatry*. 2006;30(7):1277-1282. doi:10.1016/j.pnpbp.2006.04.025
15. Berndt AE. Sampling Methods. *J Hum Lact*. 2020;36(2):224-226. doi:10.1177/0890334420906850
16. Carbon M, Kane JM, Leucht S, Correll CU. Tardive dyskinesia risk with first- and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. *World Psychiatry*. 2018;17(3):330-340. doi:10.1002/wps.20579
17. Davis MC, Horan WP, Marder SR. Psychopharmacology of the negative symptoms: Current status and prospects for progress. *Eur Neuropsychopharmacol*. 2014;24(5):788-799. doi:10.1016/j.euroneuro.2013.10.010

https://doi.org/10.34011/juriskesbdg.v18i1.2863