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The Side Effect of Haloperidol in Schizophrenic Patients: Analysis of Red Blood Cell Distribution Width (RDW) and Mean Platelet Volume (MPV) Values

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Abstract

Introduction: Like the increase of pro-inflammatory cytokines and oxidative stress as schizophrenia pathophysiology, haloperidol also increases RDW and MPV values. Both of these values have been clinicians concern because they are a risk factor for the various type of vascular disease.

Objective: This study aims to determine the side effect of haloperidol on RDW and MPV values in schizophrenic patients.

Methods: This research method uses observational analytic design with a prospective cohort approach with pre and posts analysis conducted at the Regional Special Hospital of South Sulawesi Province during May - July 2018 in 30 schizophrenic subjects. The subjects were diagnosed as first episode schizophrenia based on ICD 10, blood samples were taken, for RDW and MPV values before and after haloperidol was given at the 4th and 8th weeks.

Results: The results showed that the mean RDW value at the 4th week was higher in 15 mg/day haloperidol group (15.8) compared to 7.5 mg/day haloperidol group (15.3) with $p<0.05$. Mean RDW value taken at 8th week was higher in 15 mg/day haloperidol group (16.4) compared to 7.5 mg/day haloperidol group (15.6) with $p<0.001$. Mean MPV value taken at 8th week was higher in 15 mg/day haloperidol group (13.3) compared to 7.5 mg/day haloperidol group (11.6) with $p<0.001$.

Conclusion: This study showed an increase in the RDW value in schizophrenia subjects prior to the haloperidol administration. RDW and MPV values were higher after haloperidol treatment compares to before haloperidol treatment. The increase of RDW and MPV values tend to be influenced by haloperidol dosage and administration duration.

Keywords: Haloperidol, RDW value, MPV value, schizophrenia

1. Introduction

Schizophrenia is the most common psychotic disorder, where symptoms usually appear in late adolescence or young adults between ages 15-45 years. The lifetime prevalence of schizophrenia is between 0.3% and 0.7% (Amir, 2010; Kaplan, 2015). Numerous studies reported that schizophrenic patients had a higher level of inflammatory cytokine concentrations in blood than controls. The high-level concentration of inflammatory cytokines is closely related to the mental status of the patient. When the concentration of inflammatory cytokines was high, it associated with recurrence of symptoms of schizophrenia. When patients are stable, there is no difference in the concentration of inflammatory cytokines with controls (Kirkpatrick & Miller, 2013; Meyer, Schwarz, & Muller, 2011).

Objective evidence of schizophrenia had been carried out by examining levels of cytokines and other pro-inflammatory agents, but these examinations required sophisticated equipment and also costly, another promising examination that can by measuring the RDW and the MPV values, which has become a routine procedure in most laboratories with lower cost compared to cytokines and other pro-inflammatory agents. Changes in the RDW and

MPV values had proved by several studies and related to inflammation, increased pro-inflammatory cytokines from schizophrenia, and as the effects of antipsychotic use (Asoglu et al., 2016; Semiz et al., 2013; Steiner et al., 2008; Suvisaari & Mantere, 2013).

The RDW is a mathematical description of erythrocyte size variations, which is a description of the variation in the size and shape of erythrocytes. RDW is a reflection of the coefficient of variation in the distribution of red blood cell volume obtained by the formula: (SD/ MCV) x 100%, the normal value of RDW ranges between 11.5-14.5%. The higher the RDW value, the greater the variation of cell size. The hematological analysis also gives the MPV value which is obtained by the formula: (PCT/ PLT) x 100 fL, with a normal range of 6.5-11.5 fL (Farah & Khamisy-Farah, 2015).

Examination of CBC became the focus of attention in this study, specifically the RDW and MPV values whereas several studies had found an association between changes in their value with the inflammatory process, subclinical side effects of antipsychotic use, especially haloperidol, and its role as a risk factor for various vascular diseases. In a study conducted by Asoglu et al. (2016), it found that an increase in cytokines as an inflammatory factor strongly associated with inhibition of erythrocyte maturation by erythropoietin as reflected by an increase in the RDW value. In vitro studies, showed platelet aggregation was higher in schizophrenic patients than in healthy individuals. The findings of this study support the previous literature, which showed that patients with schizophrenia showed an increased platelet activation associated with an increase of MPV values.

Previous research by Keser et al. (2016), found an association between RDW values and severity of coronary artery disorders and the left ventricular function. Another study conducted by Danese et al. (2015), suggested an increase in RDW value with an acute coronary syndrome. Sahin et al. (2014), illustrate the strong relationship between RDW values and the severity of coronary artery disease in patients with non-ST elevation myocardial infarction. Becker et al. (2009) also found that MPV is a predictor of cardiovascular risk (Chu et al., 2010; Danese, Lippi, & Montagnana, 2015; Keser et al., 2016; Sahin et al., 2015).

The use of haloperidol as one of the management of schizophrenia is an oxidative stress state, in which antioxidant enzymes and electron transport chain in mitochondria inhibited and as a result, oxidative cell damage occurs which in turn causing an imbalance between antioxidants and pro-oxidants, and increased the RDW and MPV values. Haloperidol affects the structure of blood platelets by increasing its volume. These findings explain the relationship between haloperidol and platelet activity. In the schizophrenia group, it is shown that the use of haloperidol is a free predictor of increased of the RDW and MPV values. Antipsychotics, haloperidol, for example, have an affinity for dopamine and serotonin receptors, which ultimately triggers the change in the activity of erythrocytes and platelets. Some studies have been carried out on the blood and brains of schizophrenic patients with haloperidol treatment showing a negative impact on the iron level that caused anemia which is one of the factors that can trigger of an increase in the RDW value (Wasti et al., 2013; Patel, 2015; Semiz et al., 2013).

Based on this review, the researchers are interested in conducting a study which aims to determine the side effect of haloperidol on RDW and MPV values in schizophrenic patients.

2. Methods and Materials

2.1 Subject

The study sample was schizophrenic patients based on ICD 10, both inpatients and outpatients at the Regional Special Hospital of South Sulawesi Province which met the inclusion criteria during May to July 2018.

2.2 Design and Procedures

This study used observational analytic design with a prospective cohort approach with pre and post analysis. Each subject who met the inclusion criteria and was willing to take part in the study was taken his identity including name, address, gender, age, latest education level, occupation, and history of physical illness. Written informed consent also obtained from all subjects.

Other measurements including blood pressure, pulse, respiration, temperature, height, weight, and physical examination, type of schizophrenia and dosage of medication were recorded. A blood sample was taken before and after haloperidol treatment in the 4th and eighth weeks. Then measurements of complete blood counts and data collection of RDW and MPV values were carried out.

2.3 Data Analysis Techniques

Statistical analysis was performed using Chi-Square, Independent-t, and Paired-t-tests.

3. Results

Observational analytic research with a prospective cohort approach with pre and post analysis was conducted to determine the side effect of haloperidol on RDW and MPV values in schizophrenic patients. The study was conducted at the Special Hospital of the South Sulawesi Province from May to July 2018.

During the study period, there were 36 subjects who met the inclusion criteria. 6 subjects were excluded because they could not be observed in the 4th and 8th weeks so that the total amount samples until the end of the study was 30 subjects. Most subjects were male (18 subjects or 60.0%), and 12 subjects were female (40%). Most subjects were 30-39 years old (56.7%), and subjects aged 20-29 years were 5 subjects (16.7%), and over 40 years were 8 subjects (26.7%). Most subject were entrepreneur (9 subjects or 30.0%), farmers (8 subjects or 26,7%), housewife (5 subjects or 16.7%), and 8 subjects (26.7%) were unemployed. The education level of subjects consisted of 2 subjects were an elementary school (6.7%), 14 subjects were a junior high school (46.7%), and 14 subjects were a senior high school (46.7%). 14 subjects were paranoid schizophrenia (46.7%), and 16 subjects were schizophrenia NOS (53.6%). Dosage of haloperidol consisted of 6 subjects (20.0%) were given 7.5 mg/day, and 24 subjects (80.0%) were given 15 mg/day (See Table 1).

Table 1. Characteristics of samples in the study (n = 30)

Characteristic		Frequency (n)	Percentage (%)
Sex	Male	18	60.0
	Female	12	40.0
*Age (Year)	20-29	5	16.7
	30-39	17	56.7
	≥ 40	8	26.7
Occupation	Farmer	8	26.7
	Housewife	5	16.7
	Entrepreneur	9	30.0
	Unemployed	8	26.7
Education	Elementary	2	6.7
	Junior high school	14	46.7
	Senior high school	14	46.7
Diagnosis	Paranoid schizophrenia	14	46.7
	Schizophrenia NOS	16	53.3
Haloperidol dosage	7.5 mg/day	6	20.0
	15 mg/day	24	80.0

*Age range: 25-45 years, source: primary data, 2018.

Independent t-test showed that the mean initial RDW value did not differ significantly between the two dosage group ($p>0.05$). However, a normal range of RDW is 11.5-14.5%, so both of dosage group had a high RDW. The mean RDW in the 4th week was significantly higher in 15 mg/day dosage group compared to 7.5 mg/day dosage group ($p<0.05$). The mean RDW value in the 8th week was significantly higher in 15 mg/day dosage group compared to 7.5 mg/day dosage group ($p<0.05$). Clinically, both dosage groups had a high RDW either in the 4th week or in the 8th week (See Table 2 and Figure 1).

Table 2. Comparison of RDW value based on haloperidol dosage

Variable	Haloperidol dosage	n	Mean ± SD	P
Initial RDW value	7.5 mg/day	6	15.0 ± 0.1	0.072
	15 mg/day	24	14.9 ± 0.3	
RDW value in the 4th week	7.5 mg/day	6	15.3 ± 0.3	0.012
	15 mg/day	24	15.8 ± 0.8	
RDW value in the 8th week	7.5 mg/day	6	15.6 ± 0.3	0.001
	15 mg/day	24	16.4 ± 0.7	

Independent t-test. n: samples amount, SD: Standard deviation, p: significance.

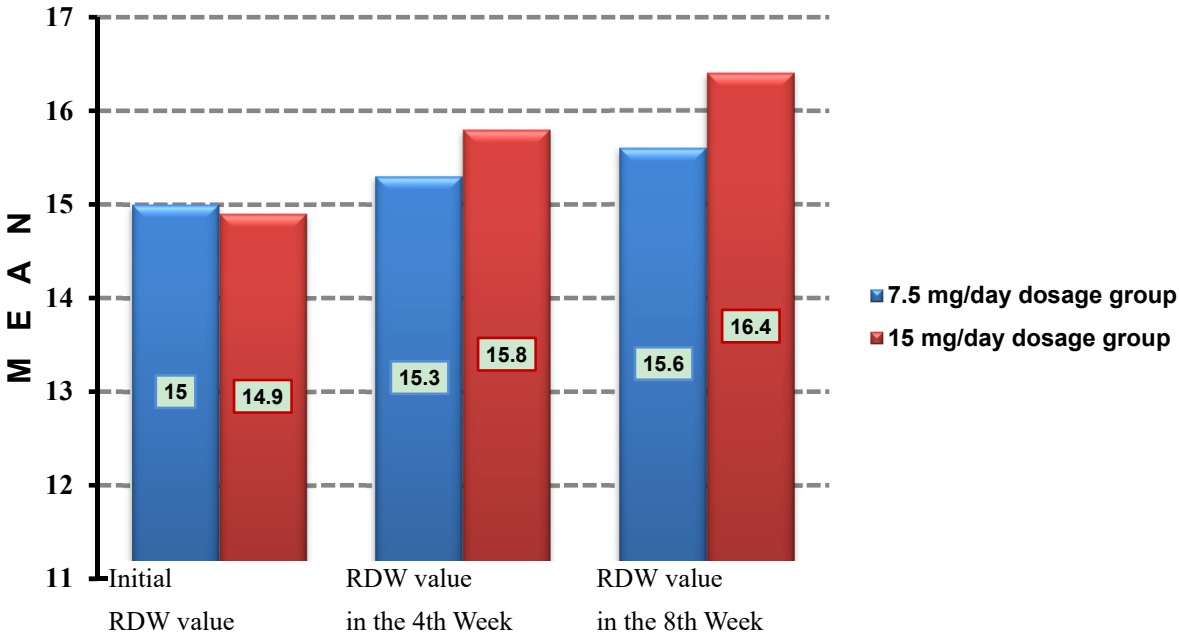

Figure 1. Comparison of RDW value based on haloperidol dosage

Paired-t-test showed that in 7.5 mg/day dosage group: the mean RDW value in the 4th week was not significantly different from the initial RDW value ($p>0.05$), the mean RDW value in the 8th week was significantly higher than the initial RDW value ($p<0.05$), the mean RDW value in the 8th week was significantly higher than in the 4th week ($p<0.05$). In 15 mg/day dosage group: the mean RDW value either in the 4th week or in the 8th week was significantly higher than the initial RDW value ($p<0.001$), the mean RDW value in the 8th week was significantly higher than RDW in the 4th week ($p<0.001$) (See Table 3).

Table 3. Comparison of RDW values according to a measurement time

Haloperidol dosage			n	Mean ± SD	P
7.5 mg/day	Pair 1	Initial RDW	6	15.0 ± 0.1	0.064
		RDW value in the 4th week	6	15.3 ± 0.3	
	Pair 2	Initial RDW	6	15.0 ± 0.1	0.006
		RDW value in the 8th week	6	15.6 ± 0.3	
	Pair 3	RDW value in the 4th week	6	15.3 ± 0.3	0.015
		RDW value in the 8th week	6	15.6 ± 0.3	
15 mg/day	Pair 1	Initial RDW	24	14.9 ± 0.3	0.000
		RDW value in the 4th week	24	15.8 ± 0.8	
	Pair 2	Initial RDW	24	14.9 ± 0.3	0.000
		RDW value in the 8th week	24	16.4 ± 0.7	
	Pair 3	RDW value in the 4th week	24	15.8 ± 0.8	0.000
		RDW value in the 8th week	24	16.4 ± 0.7	

Paired t-test. n: Samples amount, SD: Standard deviation, p: Significance.

Independent t-test showed that the mean MPV value did not differ significantly between the two groups ($p>0.05$) either in the initial week or in the 4th week. Laboratory finding showed that both had a normal MPV. The mean MPV value in the 8th week was significantly higher in the 15 mg/day dosage group compared to 7.5 mg/day dosage group ($p<0.001$). Laboratory finding showed that both groups had a high MPV (See table 4 and figure 2).

Table 4. Comparison of MPV values based on haloperidol dosage

Variable	Haloperidol dosage	n	Mean ± SD	p
Initial MPV value	7.5 mg/day	6	7.6 ± 0.5	0.975
	15 mg/day	24	7.6 ± 0.7	
MPV value in the 4th week	7.5 mg/day	6	8.8 ± 0.6	0.057
	15 mg/day	24	9.7 ± 1.8	
MPV value in the 8th week	7.5 mg/day	6	11.6 ± 0.8	0.000
	15 mg/day	24	13.3 ± 0.8	

Independent t-test. n: Samples amount, SD: Standard deviation, p: Significance.

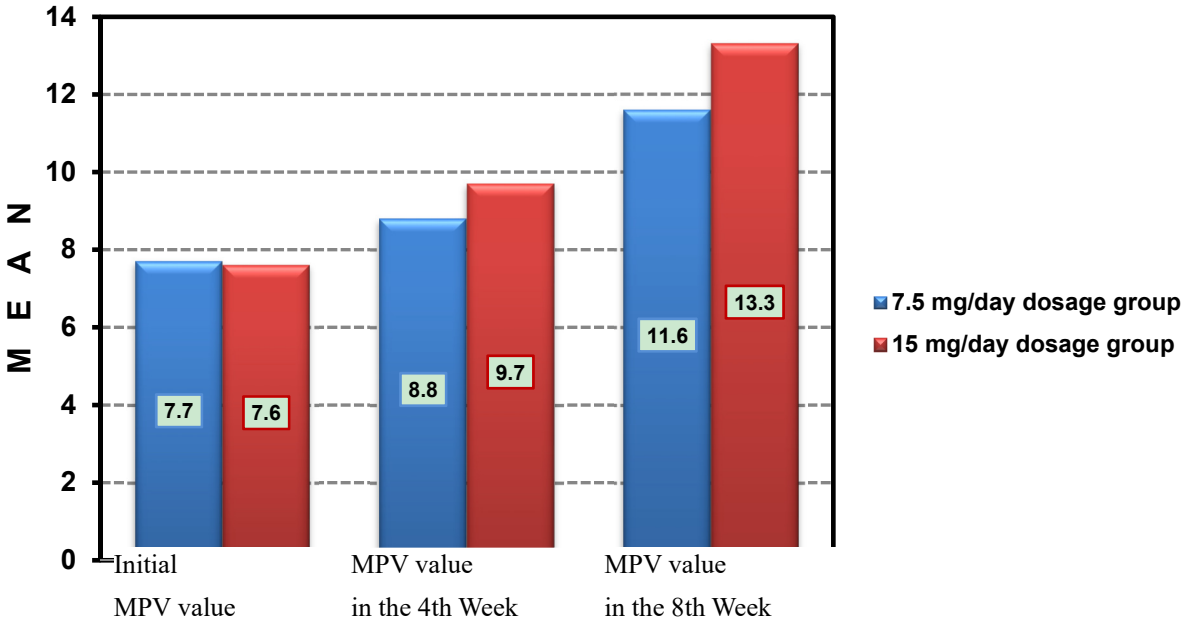

Figure 2. Comparison of MPV values based on haloperidol dosage

Paired-t-test showed that in 7.5 mg/day dosage group, the mean MPV value in the 4th week was significantly higher than the initial MPV value ($p<0.05$), the mean MPV value in the 8th week was significantly higher than the initial MPV value ($p<0.001$), the mean MPV value in the 8th week was significantly higher than in the 4th week ($p<0.001$). In 15 mg/day dosage group, the mean MPV value either in the 4th week or in the 8th week was significantly higher than the initial MPV value ($p<0.001$), the mean MPV value in the 8th week was significantly higher than in the 4th week ($p<0.001$) (See Table 5).

Table 5. Comparison of MPV values according to measurement time

Haloperidol dosage			n	Mean ± SD	p
7.5 mg/day	Pair 1	Initial MPV value	6	7.6 ± 0.5	0.026
		MPV value in the 4th week	6	8.8 ± 0.6	
	Pair 2	Initial MPV value	6	7.6 ± 0.5	0.000
		MPV value in the 8th week	6	11.6 ± 0.8	
	Pair 3	MPV value in the 4th week	6	8.8 ± 0.6	0.000
		MPV value in the 8th week	6	11.6 ± 0.8	
15 mg/day	Pair 1	Initial MPV value	24	7.6 ± 0.7	0.000
		MPV value in the 4th week	24	9.7 ± 1.8	
	Pair 2	Initial MPV value	24	7.6 ± 0.7	0.000
		MPV value in the 8th week	24	13.3 ± 0.8	
	Pair 3	MPV value in the 4th week	24	9.7 ± 1.8	0.000
		MPV value in the 8th week	24	13.3±0.8	

Paired t-test. n: Samples amount, SD: Standard deviation, p: Significance

4. Discussion

This study showed that the increase in RDW and MPV values in schizophrenic patients were influenced by the

dosage amount and duration of haloperidol administration. The longer haloperidol was administered and the greater the dosage of haloperidol given, the greater the increase of the RDW and MPV values.

The samples analyzed consisted of 30 subjects aged between 30-45 years (mean 35 years). Based on the characteristics of the sample data, most of the subjects were male. Although the prevalence was the same between men and women, there was a difference in the onset and course of the disease. Men had an earlier onset of schizophrenia than women. More than half of all hospitalized schizophrenic patients were male and only one-third of schizophrenic patients were female. Several studies had suggested that men are more likely to show early symptoms of schizophrenia in the form of negative symptoms as an onset, and a high prevalence of aggression. Women were more likely to have better social functioning than men. This is a major cause of men being hospitalized when suffering from schizophrenia than women (Kaplan, 2015).

Results of the Independent t-test from the ratio of RDW value to haloperidol 7.5 mg/day and haloperidol 15 mg/day, showed that the mean initial RDW value did not differ significantly between the two groups ($p>0.05$). Meanwhile, the mean RDW value in the 4th week was significantly higher in the group of 15 mg haloperidol per day compared to 7.5 mg per day, which was 15.8 to 15.3 ($p<0.05$). The mean RDW value in the 8th week was significantly higher in the group of 15 mg haloperidol per day compared to 7.5 mg per day, which was 16.4 to 15.6 ($p<0.001$). Noticeably that the group with 15 mg per day haloperidol gave a significant increase in the RDW value since the 4th week compared to the group with 7.5 mg haloperidol per day.

Based on the result of the analysis, it was concluded that the increase in the initial RDW value was probably not influenced by haloperidol dosing, but from other factors. This was consistent with the research conducted by Asoglu et al. (2016), who found that an increase in cytokines as an inflammatory factor was strongly associated with inhibition of erythrocyte maturation by erythropoietin, which was reflected by an increase in the RDW value. Another study conducted by Zhang et al. (2009); Boskovic and Vovk (2008); and Gonzalez et al. (2014), about RDW had shown a direct relationship between damage of blood cells in the circulation due to high oxidative stress and the increase of RDW values. Whereas Miller and Kirkpatrick (2013) found that pro-inflammatory cytokines, as well as oxidative stress, contribute to an increase in the RDW value in schizophrenia. The inflammatory response and oxidative stress from the pathogenesis of schizophrenia itself can increase the value of the RDW even before exposure to treatment. This discovery can be a diagnostic value for the development of schizophrenic pathophysiology.

Paired t-test of RDW values from 7.5 mg/day haloperidol group did not show a significant difference in the 4th week to initial study ($p>0.05$), and in the 8th week was significantly higher than in the initial study ($p<0.001$). The mean RDW value in the 8th week was significantly higher than RDW in the 4th week ($p<0.001$). Whereas in the 15 mg haloperidol group, the mean RDW value in the 4th week was significantly higher than the initial week, which was 15.8 to 14.9 ($p<0.001$). The mean RDW value in the 8th week was significantly higher than the initial week, which was 16.4 to 14.9 ($p<0.001$). In addition, the mean value of RDW in the 8th week was significantly higher than RDW in the 4th week, which was 16.4 to 15.8 ($p<0.001$).

Increased or larger dosages contribute to the increase of the RDW value. This result is consistent with the initial hypothesis that the administration of haloperidol had an effect on increasing the RDW value of schizophrenic patients. These results are consistent with research conducted by Wasti et al. (2013), which states that haloperidol contributes to an increase in RDW values and MPV values that can represent treatment side effects in schizophrenic patients and can be used to support monitoring strategies to reduce blood disorders from drug treatment antipsychotics. This finding could be a treatment value and prognostic value of antipsychotic drug treatment in schizophrenic patients.

Independent t-test results from the comparison of MPV values based on haloperidol 7.5 mg/day and 15 mg/day, found that the mean initial MPV value did not differ significantly between the two groups ($p>0.05$). Meanwhile, the mean MPV value in the 4th week did not differ significantly between the two groups ($p>0.05$). The mean MPV value in the 8th week was significantly higher in the 15 mg haloperidol group compared to 7.5 mg haloperidol group ($p<0.001$). Clinically, both had a high MPV value. Results of the paired t-test of MPV values based on the time of measurement of haloperidol 7.5 mg/day and 15 mg/day, showed that the administration of 7.5 mg/day haloperidol in the 4th week was significantly higher than the initial MPV value ($p<0.001$). While the mean MPV value at the 8th week was significantly higher than the initial MPV value ($p<0.001$). In addition, the mean of MPV value in the 8th week was significantly higher than in the 4th week ($p<0.001$).

In the group of 15 mg haloperidol, was found that the mean of MPV value in the 4th week was significantly higher than the initial MPV value ($p<0.001$). Whereas the mean of MPV value in the 8th week was significantly higher than the initial MPV value ($p<0.001$). In addition, the mean of MPV value in the 8th week was significantly higher

than in the 4th week ($p<0.001$). It could be concluded that the increase of the MPV value occurred at the 8th week of haloperidol administration, and both groups contributed to the increase in MPV value, whereas the administration of 15 mg was more significant to increase the MPV value compared with the administration of 7.5 mg.

The dosages amount greatly affected the rate of increased MPV values. These results were consistent with the initial hypothesis that the administration of haloperidol had an effect on increasing the MPV value of schizophrenic patients. These results were consistent with the research conducted by Semiz et al. (2013), stating that antipsychotics can affect the structure of blood platelets, which increases their volume. This finding contributes an explanation about the relationship between antipsychotics and platelet activity which was reflected in an increase in MPV values. Meanwhile, according to research conducted by Patel (2015), antipsychotics that have dopamine and serotonin receptor affinity can eventually trigger changes in platelet activity.

5. Conclusion

Researchers concluded that RDW and MPV values in schizophrenic patients were higher after haloperidol treatment than before haloperidol treatment. An increase in the RDW and MPV values in schizophrenic patients tend to be influenced by the duration of administration and the amount of haloperidol. The longer haloperidol was administered and the greater the dosage of haloperidol given, the greater the increase in the RDW and MPV values.

There was an increase in the RDW value before haloperidol administration. Researchers suggest that an initial screening check for RDW and MPV values for schizophrenic patients should be performed at the first admission to the hospital as a basis for consideration of selection and administration of antipsychotic. A study is needed compares the use of typical antipsychotics and atypical antipsychotics to see the side effect on RDW and MPV values of schizophrenic patients. Regular monitoring of RDW and MPV values is needed to support management strategies to reduce blood disorders from the treatment of antipsychotic drugs that can trigger various vascular diseases in schizophrenic patients.

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Competing Interests Statement

The authors declare that there are no competing or potential conflicts of interest.

References

Amir. (2010). *Schizophrenia* (2nd ed.). Jakarta: Faculty of Medicine, University of Indonesia.

Asoglu, M., Aslan, M., Canbolat, O., Imre, O., Savik, E., Kivrak, Y., ... & Altıparmak, A. A. (2016). Red cell distribution width, mean platelet volume, and vitamin B. *Int J Clin Exp Med*, *9*(8), 16629-16636. https://doi.org/10.1177/1076029612462761

Bitanihirwe, B. K., & Woo, T. U. W. (2011). Oxidative stress in schizophrenia: an integrated approach. *Neuroscience & Biobehavioral Reviews*, *35*(3), 878-893. https://doi.org/10.1016/j.neubiorev.2010.10.008

Boskovic, Vovk T. Oxidative Stress in Schizophrenia. Slovenia: University of Ljubljana; 2008.

Chu, S. G., Becker, R. C., Berger, P. B., Bhatt, D. L., Eikelboom, J. W., Konkle, B., ... & Berger, J. S. (2010). Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis*, *8*(1), 148-156. https://doi.org/10.1111/j.1538-7836.2009.03584.x

Danese, E., Lippi, G., & Montagnana, M. (2015). Red blood cell distribution width and cardiovascular diseases. *Journal of thoracic disease*, *7*(10), E402. https://doi.org/10.3978/j.issn.2072-1439.2015.10.04

Farah, R., & Khamisy-Farah, R. (2015). Significance of MPV, RDW with the presence and severity of metabolic syndrome. *Experimental and Clinical Endocrinology & Diabetes*, *123*(09), 567-570. https://doi.org/10.1055/s-0035-1564072

Gonzalez et al. (2014). Oxidative stress in schizophrenia: a case-control study on the effects on social cognition and neurocognition. *BMC Psychiatry, 14*(1). https://doi.org/10.1186/s12888-014-0268-x

Kaplan, S. (2015). Schizophrenia. In *Psychiatry Synopsis* (vol. 1). Jakarta: Bina Rupa Aksara; 2015.

Keser et al. (2016). The relationship between Red Blood Cell Distribution, Levels, and Severity of Coronary Artery Ectasia. *European Review for Medical and Pharmacological Sciences, 20*, 1571-1574. PMID:27160130.

Meyer et al. (2011). Inflammatory Process in Schizophrenia: A Promising Immunological Target. *J. Pharmacology and therapy, 132*, 96-110. https://doi.org/10.1016/j.pharmthera.2011.06.003

Miller, B., & Kirkpatrick, B. (2013). Inflammation and Schizophrenia. *Schizophrenia Bulletin, 39*(6), 1174-1179. https://doi.org/10.1093/schbul/sbt141

Patel. (2015). Associations between Venous Thromboembolism and Antipsychotic Use. *Graylands Hospital Drug Bulletin, 221*(3), 1323-1251.

Sahin, O., Akpek, M., Sarli, B., Baktir, A. O., Savas, G., Karadavut, S., ... & Arinc, H. (2015). Association of red blood cell distribution width levels with severity of coronary artery disease in patients with non-ST elevation myocardial infarction. *Medical Principles and Practice, 24*(2), 178-183. https://doi.org/10.1159/000369396

Semiz et al. Typical Antipsychotic Use Is an Independent Predictor for the Increased Mean Platelet Volume in Patients with Schizophrenia: A Preliminary Study. *J Res Med Sci., 18*, 560-65. PMID: 24516487

Steiner, J., Bielau, H., Brisch, R., Danos, P., Ullrich, O., Mawrin, C., ... & Bogerts, B. (2008). Immunological aspects in the neurobiology of suicide: elevated microglial density in schizophrenia and depression is associated with suicide. *Journal of psychiatric research, 42*(2), 151-157. https://doi.org/10.1016/j.jpsychires.2006.10.013

Wasti et al. (2013). Antipsychotic Drugs Induced Iron Deficiency Anemia In Schizophrenic Patients. *International Journal of Advanced Research, 1*(10), 111-118.