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Comparative Study of Treatment and Potential Drug Interactions with Mental Disorders Phase at Lampung Psychiatric Hospital

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ABSTRACT

Background: There are some phases in mental disorders, acute, stabilization, and maintenance phase. Each phase has a different treatment goal using several types of drugs. Hospitalized patients with mental disorders are typically prescribed 5-9 drugs. Using more than one drug increase the potential for drug interactions.

Objectives: This study aims to compare treatments and potential drug interactions with the mental disorders phase at Psychiatric Hospital Lampung Province.

Methods: This study was a retrospective with a cohort design. Data were secondary in medical records and inpatient prescription sheets from January to December 2019. Purposive sampling techniques were used. The inclusion criteria in this study were all male patients hospitalized at Psychiatric Hospital Lampung Province who received and completed treatment from January to December 2019.

Results: The results showed most of 134 patients were in aged 26-35 years (27.3%), had completed high school (34.3%), were married (61.2%), and were diagnosed with paranoid schizophrenia (93.3%). Average number of medicines was 4.12 in acute phase and 3.89 in stabilization-maintenance phase. Average length of stays were 3.89 days in acute phase and 18.36 days in stabilization-maintenance phase. The second-generation antipsychotics are the most common class of drugs. There was a statistical difference (p = 0.000) for drug classes in both phases. The potential drug interactions in both phases were not significantly different (p = 0.093). The greatest severity was moderate at 88.44% in the acute phase and 94.60% in the stabilization-maintenance phase.

Conclusion: There is a statistical difference in drug classes whereas the potential drug interactions were not.

Keywords: acute phase; drug interaction; maintenance phase; mental disorder phase; stabilization phase

INTRODUCTION

The burden of mental health disorders is increasing, which can have a significant impact on health, social life, human rights, and economy in around the world. Based on Indonesia Basic Health Research, the prevalence of mental disorders in 2018 increased compared to 2013. The prevalence of schizophrenia increased from 1.7% to 7%, mental-emotional disorders increased from 6% to 9.8%, and depression increased by 6.1%.[1] Depression, bipolar, and schizophrenia are mental disorders with the highest prevalence among the ten health problems that can cause disability.[2]

There are some phases in mental disorders, which are the acute phase, stabilization phase, and maintenance phase. Intervention in the acute phase aims to adjust the dose to achieve an effective dose. In the stabilization phase, treatment aims to achieve the highest cure rate with minimal side effects and maintain the achieved treatment effect. The maintenance phase aims to prevent recurrences of the mental disorders.[3] Study conducted by Rode, Ajagallay, and Salankar (2014) shows the average prescribed drug in one prescription sheet

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is 2.51±0.75.[4] As much as 83.4% of inpatients who are discharged get more than two medications, most of them get psychiatric drugs, and only 17.3% get supplements such as multivitamins, iron, and folic acid.[5]

A previous study by Alosaimi et al. (2016) showed that patients who were undergoing hospitalization get more medication than outpatients (2.1±0.8 vs. 1.8±0.7, p<0.001).[6] The incidence of polypharmacy is higher in patients ≥65 years old, men, and occurs as much as 100% in patients with a diagnosis of organic mental disorders. Polypharmacy and the large number of drugs in one prescription can increase the potential for drug interactions in patients.[7] A study by Kirilochev et al. (2019) showed the potential for drug-drug interactions in people with a mental health condition undergoing hospitalization shows that the average number of drugs prescribed is in the range of 5-9 drug items. As many as 77.2% of patients have the potential to experience drug interactions.

Using more than one drug in patients with mental disorders is reasonable to overcome comorbidities, reduce the side effects of the primary drug, and speed up recovery. The use of more than one drug in patients has the potential to cause drug-drug interactions. The high incidence of potential drug–drug interactions (pDDIs) in hospitalized psychiatric patients was found in other studies.[8,9] Drug-drug interaction occurs when the effects of one drug are changed due to the presence of another drug. The results can be hazardous if the interaction leads to increased drug toxicity. A decrease in efficacy due to drug-drug interaction can sometimes be just as dangerous as an increase. Many types of interactions in psychiatric drugs are pharmacokinetic interactions compared to pharmacodynamics, primarily related to CYP450 isoenzymes.[10]

This study aims to compare treatment and potential drug interactions with the mental disorders phase at Psychiatric Hospital Lampung Province. Psychiatric Hospital Lampung Province is the only psychiatric hospital in Lampung Province, so that it will be very accommodating for the sampling. There has been no previous research on the correlation of therapy to the treatment phase in patients with psychiatric disorders in the hospital where the researchers took the research data, so researchers are interested in conducting this study.

METHODS

Study design

The research was a retrospective cohort design study. Purposive sampling techniques were used in this research.

Population and samples

The population in this study was all male patients hospitalized at Psychiatric Hospital Lampung Province and received treatment from January to December 2019. Sample is male patients because the phase of hospitalization can be seen based on room changes. Acute phase and stabilization-maintenance rooms were different.

Inclusion criteria were all men hospitalized at Psychiatric Hospital Lampung Province who received and completed treatment from January to December 2019. The exclusion criteria were: Patients with incomplete medical record data; Patients who have not gone through the acute and maintenance-stabilization phases of treatment.

The proportion of men who experienced mental disorders was higher than that of women, so there are 134 samples in this study. Researchers carried out sample by grouping into two groups. The first group was for patients undergoing acute phase treatment who were hospitalized in the Psychiatric Intensive Care Unit and emergency department. Second group consisted of patients undergoing stabilization-maintenance phase therapy who were hospitalized in the Cendrawasih Ward and Kutilang Ward. Data was collected using the data collection sheet. Potential drug interaction data was obtained by accessing the database from Drugs.com®.

Study instruments

The instrument used in this study was a data collection sheet consisting of initial name, sex, education level, marital status, diagnosis, list of drugs used in every phase, and length of stay in phase.

Data collection

We collected demographic and clinical data of all patients hospitalized at Psychiatric Hospital Lampung Province, which are forms of medical records and inpatient prescription sheets in January-December 2019. Demographic and clinical data were recorded, including age, education level, marital status, psychiatric diagnoses, and prescription drugs.

Data Analysis

Demographic and clinical data were analyzed with univariate analysis to describe the characteristics of respondents in the form of frequency distribution tables and percentages for age, education level, marital status, and diagnoses. The average number of drugs was obtained by calculating the number of drugs each day divided by the total days in one phase. The average length of stay was obtained by calculating the length of stay each phase divided by the total patients.

The treatment phase in this study was divided into two phases: the acute phase and the stabilization-maintenance phase. The treatment comparison between the mental disorders phase and the drug-drug interaction comparison between the mental disorders phase were analyzed by bivariate analysis. The marginal Homogeneity Test was used for comparative tests of paired samples. If the value of significance $p< 0.05$, then there is a significant difference between the two variables tested.

RESULTS AND DISCUSSION

There are 134 samples in this study. The highest number of patients (37.3%) is in the 26-35 age group. Likewise in previous research, which shows that 61.7% of patients are in the age range of 25-40 years.[11] Similar findings show that schizophrenia patients hospitalized are in the age range of 24-49 years, most diagnosed with paranoid-type schizophrenia.[12]

All patients in this study were in Indonesia's productive age range of 15-64 years. Productive age is when a person can produce goods or services to fulfill needs for himself, his family, and the environment.[13] At this productive age, many pressures arise which, if not appropriately lived, can interfere with mental health. The number of patients is decreasing as the age increases, although still in the productive age range for the late adult age group (36-45 years), then the early elderly (46-55 years), and late elderly (56-65 years). This can be because this age group has formed mental maturity and wisdom in responding to the pressures and problems of life.[14]

About 61.9% of patients in this study were at a low education level (junior high school and below), and the rest (38.1%) were at a higher education level (above senior high school). This is in line with research at Ghrasia Hospital, with a percentage of 61% and 39%, and research at the Pati II health center, with a rate of 71% and 29%, that patients in lower education had higher percentages than higher education level.[11] Low education level related to the type of work in the informal sector with limited or low income. This will undoubtedly add pressure to personal and or family economic life.[15]

The most common admissions were paranoid schizophrenia (93.3%), followed by acute psychosis (3.7%) and organic mental disorders (3.0%). The same thing also happened in research at South Jakarta Psychiatric Hospital, showing 74.1% of patients who have paranoid schizophrenia.[16] The average number of drug items used in the acute phase was 4.12 items, while in the stabilization-maintenance phase, it was 3.89 items. Higher numbers in the acute phase can be due to this phase being the most unstable.

The average length of treatment in the acute phase is lower than in the stabilization-maintenance phase. This is in line with the Guidelines for Mental Health Services, which states that the duration of treatment in the stabilization condition is 8-10 weeks. The acute phase can last for 1-3 weeks. This can also be due to the capacity in the acute phase space, which is a maximum of 15 people.[17]

Clinical characteristics

The result from Table II obtained p value = 0.000. This indicates that there is a difference in therapy between the acute phase and the stabilization-maintenance phase. Psychopharmaceutical drugs are more widely used in both phases than non-psychopharmaceuticals.

The most widely used class of psychopharmaceutical drugs in this study are second-generation antipsychotics (22.82%), anticholinergics (19.7%), low-potency first-generation antipsychotics (17,08%), antianxiety (12.78%), high-potency first-generation antipsychotics (10.43%), SSRI antidepressants (2.22%), mood stabilizers (0.13%), and tricyclic antidepressants (0,13%). Acute phase of schizophrenia, agitation and aggressive attitudes generally occur. Agitation is characterized by increased impulsive and aggressive behavior. Appropriate intervention with rapid onset of work is necessary to prevent patients from harming themselves or others.[18]

The goals of therapy in the acute phase are to prevent the patient from harming himself or others, control destructive behavior, and reduce the severity of psychotic symptoms and other related symptoms, such as agitation, aggression, and restless rowdy.[18] Oral therapy is a better option, although the use of injection drugs to achieve a faster onset of action and immediate relief of symptoms needs to be considered.[17] In this study, based on dosage form, the most widely used injection drugs in the acute phase were diazepam (52.2%) and haloperidol

Table I. Socio-demographic characteristics

Demographic data	N	%
Age (years)		
17 – 25	39	29.1
26 – 35	50	37.3
36 – 45	32	23.9
46 – 55	7	5.2
56 – 65	6	4.5
Education level		
Not in school	3	2.2
Elementary school	37	27.6
Junior high school	43	32.1
High school	46	34.3
Diploma	4	3.0
Undergraduate	1	0.7
Marital status		
Unmarried	52	38.8
Married	82	61.2
Diagnosis		
Paranoid schizophrenia	125	93.3
Acute psychosis	4	3.0
Organic mental disorders	5	3.7
Average number of medicines (amounts)		
Acute phase	4.12	-
Stabilization-Maintenance phase	3.89	-
Average length of stay (days)		
Acute phase	3.89	-
Stabilization-Maintenance phase	18.36	-

Table II. Medication prescription data

Classification/ Medications	Acute phase (n=767)		Stabilization-maintenance phase (n=824)		Total (n=1591)	%
	N	%	N	%		
Second-generation antipsychotics	175	22.82	225	27.31	400	25.14
Risperidone	169	96.57	203	90.22	372	23.38
Aripiprazole	2	1.14	5	2.22	7	0.44
Clozapine	2	1.14	12	5.33	14	0.88
Olanzapine	2	1.14	5	2.22	7	0.44
Anticholinergics	147	19.7	168	20.39	315	19.80
Trihexyphenidyl	147	100	168	20.39	315	19.80
Low-potency first-generation antipsychotic	131	17.08	124	15.05	255	16.03
Chlorpromazine	131	17.08	124	15.05	255	16.03
Antianxiety	98	12.78	48	5.83	146	9.18
Diazepam	70	71.43	3	6.25	73	4.59
Lorazepam	28	28.57	43	93.75	73	4.59
Anticonvulsants	51	6.65	75	9.10	126	7.92
Valproic Acid	44	86.27	65	86.67	109	6.85
Phenytoin	6	11.96	7	9.33	13	0.82
Oxcarbazepine	1	1.96	2	2.67	3	0.19

Table II. (Continued)

Classification/ Medications	Acute phase (n=767)		Stabilization-maintenance phase (n=824)		Total (n=1591)	%
	N	%	N	%		
Carbamazepine	0	0.00	1	1.33	1	0.06
High-potency first-generation antipsychotic	**80**	**10.43**	**42**	**5.10**	**122**	**7.67**
Trifluoperazine	3	3.75	11	26.19	14	0.88
Haloperidol	77	96.25	31	73.81	108	6.79
Selective serotonin reuptake inhibitors (SSRIs)	**17**	**2.22**	**40**	**4.85**	**57**	**3.58**
Fluoxetine	11	64.71	25	62.50	36	2.26
Sertraline	6	35.29	15	37.50	21	1.32
Mood stabilizers	1	0.13	0	0.00	1	0.06
Lithium	1	100.00	0	0.00	1	0.06
Tricyclic antidepressants	**1**	**0.13**	**0**	**0.00**	**1**	**0.06**
Maprotiline	1	100.00	0	0.00	1	0.06
Antibiotic	25	3.26	28	3.40	53	3.33
Amoxicillin	4	16.00	6	21.43	10	0.63
Chloramphenicol	1	4.00	1	3.57	2	0.13
Ciprofloxacin	11	44.00	11	39.29	22	1.38
Cefadroxil	2	8.00	0	0.00	2	0.13
Thiamphenicol	6	24.00	8	28.57	14	0.88
Ofloxacin	1	4.00	0	0.00	1	0.06
Cefixime	0	0.00	1	3.57	1	0.06
Cefotaxime	0	0.00	1	3.57	1	0.06
Hepatoprotective agents	14	1.83	24	2.91	38	2.39
Vitamins/ Neurotropic/ Nootropics	**8**	**1.04**	**23**	**2.79**	**31**	**1.95**
Neurotropic B Vitamins (B1, B6, B12)	7	87.50	15	65.22	22	1.38
Ringer lactate	0	0.00	1	4.35	1	0.06
Folic acid	1	12.50	4	17.39	5	0.31
Pyridoxine	0	0.00	1	4.35	1	0.06
Potassium	0	0.00	1	4.35	1	0.06
Piracetam	0	0.00	1	4.35	1	0.06
Analgesics/anti -inflammatory	**9**	**1.17**	**8**	**0.97**	**17**	**1.07**
Acetaminophen	6	66.67	5	62.50	11	0.69
Mefenamic acid	2	2.22	2	25.00	4	0.25
Sodium diclofenac	0	0.00	1	12.50	1	0.06
Ketoprofen	1	11.11	0	0.00	1	0.06
Antihypertensive	**6**	**0.78**	**5**	**0.61**	**11**	**0.69**
Amlodipine	6	100.00	5	100.00	11	0.69
Antifungal	**1**	**0.13**	**5**	**0.61**	**6**	**0.38**
Ketoconazole	1	100.00	1	20.00	2	0.13
Miconazole ointment	0	0.00	1	20.00	1	0.06
Gentamicin ointment	0	0.00	1	20.00	1	0.06
Ketoconazole ointment	0	0.00	1	20.00	1	0.06
Anti-diarrhea	**0**	**0.00**	**5**	**0.61**	**5**	**0.31**
Attapulgite	0	0.00	5	100.00	5	0.31

Table II. (Continued)

Classification/ Medications	Acute phase (n=767)		Stabilization-maintenance phase (n=824)		Total (n=1591)	%
	N	%	N	%		
Antihistamine	**1**	**0.13**	**2**	**0.24**	**3**	**0.19**
Diphenhydramine	0	0.00	2	100.00	2	0.13
Chlorpheniramine maleate	1	100.00	0	0.00	1	0.06
Corticosteroid	**2**	**0.26**	**0**	**0.00**	**2**	**0.13**
Prednisone	1	50.00	0	0.00	1	0.06
Hydrocortisone topical	1	50.00	0	0.00	1	0.06
Antacids	**0**	**0.00**	**1**	**0.12**	**1**	**0.06**

(38.81%). The high use of these two drugs in the acute phase is because patients in the acute phase need medication with rapid onset. The same thing also happened in previous research, that as much as 74.69% of haloperidol was used in schizophrenia patients at Atma Husada Mahakam Samarinda Psychiatric Hospital.[19] Second-generation antipsychotics are the most widely used group in this study (25.14%). Second-generation antipsychotics are beneficial in overcoming negative symptoms and cognitive deterioration. Second-generation antipsychotics have less sedative effect than first-generation drugs, though they are more expensive and can cause metabolic syndrome.[20] Olanzapine, risperidone, quetiapine, ziprasidone, and aripiprazole are now the preferred therapies in schizophrenia. Currently, clozapine is the most effective antipsychotic, with the lowest affinity for D2 receptors. Weak bonding to D2 receptors results in a low-induced extra-pyramidal effect.[21] In this study, the most widely used second-generation antipsychotic is risperidone (23.38%). Similarly with this study's result, a previous study stated that risperidone was the most widely used atypical antipsychotic (41%) at Mutiara Sukma Psychiatric Hospital.[22] Risperidone is very quickly and well absorbed after oral administration, and less than 1% is excreted in the stool in unchanged form. The peak time of the plasma is also speedy, either in liquid or tablet form, and 90% bound to plasma proteins.[23]

The second most widely used drug class in both phases is anticholinergic, is trihexyphenidyl (19.8%). In another study, 96.8% of patients received trihexyphenidyl therapy without checking for extra-pyramidal effect symptoms, and 88.3% received trihexyphenidyl twice daily. Trihexyphenidyl is used as a prophylactic therapy in extra-pyramidal syndrome.[24]

Typical antipsychotics are still widely used in this study, with the most common type being chlorpromazine, though the number is still small when compared to atypical antipsychotics. First-generation antipsychotics remain the first line of antipsychotic therapy prescribed in Kenya, Uganda, and Utopia.[25] Research conducted at Jiwa Tampan Hospital in January-June 2015 and Madani Sulawesi Province Psychiatric Hospital in January–April 2014 showed that the use of atypical antipsychotics is more dominant than atypical antipsychotics at 78% and 56.8%, respectively.[26] The unsuccessful treatment of schizophrenia with a single typical therapy leads to the emergence of a combination of treatments.[16]

The number of patients taking chlorpromazine in this study in the acute and stabilization-maintenance phase groups was 17.08% and 15.05%, respectively. A study comparing chlorpromazine and haloperidol showed that both had similar effects. In another study, haloperidol injection showed better effects than chlorpromazine in overcoming agitation.[27] Promethazine had the fastest sedative effect compared to other medications in this study. Chlorpromazine has superior effects to other antipsychotics, but the side effects are also significant. Patients who use chlorpromazine instead of haloperidol are at risk of severe side effects.[27]

The antianxiety used in this study are benzodiazepine, lorazepam, and diazepam. Benzodiazepines are used to overcome catatonia, anxiety, and agitation until the effect of antipsychotic therapy is achieved. Benzodiazepines are often used alongside typical antipsychotics. Its use is also limited due to frequent side effects. For example, benzodiazepines can cause respiratory depression, excessive sedation, or disinhibition behavior, which can make things worse.[28] However, benzodiazepines are still used in the acute phase of anxiety because the therapeutic benefits of SSRIs still need to be proven.[29] The use of atypical antipsychotics, in particular, has a relatively moderate effect in overcoming negative symptoms.

The doctor often prescribes SSRIs for both inpatients and outpatients.[30] Fluoxetine was the most widely used antidepressant in this study, with a total usage of 2.26%. The results of the systematic review showed that 50% of double-blind studies provided fluoxetine results beneficial in overcoming the negative symptoms of

schizophrenia patients, while the other 50% indicated the opposite. In the same systematic review, sertraline did not address this symptom.[31]

The therapies used in the non-psychopharmaceuticals group are anticonvulsants, antibiotics, hepatoprotective medicine, vitamins, analgetics, antihypertensives, antifungals, antidiarrheals, antihistamines, corticosteroids, and anti-ulcers. Case reports and studies conducted on psychiatric inpatients show that psychosis gets worse due to certain infections. The potential for urinary tract infections (UTIs) is nine times higher in psychiatric patients. Anticholinergic drugs can also increase the risk of oral diseases and UTIs, as well as antipsychotic drugs that cause dysphagia dystonia. Extra-pyramidal syndrome, as a side effect of anticholinergic drugs, can cause aspiration pneumonia.[32]

In a study conducted by Rattanaumpawan et al. (2017) on inpatients in mental hospitals in Slovenia who received antibiotics, the most common types of infections were UTIs and respiratory tract infections. In the same study, 10% of patients received antibiotics during hospitalization in mental hospitals, with the most commonly used types of antibiotics being co-amoxiclav (36.5%), cotrimoxazole (25.7%), ciprofloxacin (12.2%), and nitrofurantoin (6.80%).[33]

This study also used Hepatoprotective agents in both the acute and stabilization-maintenance phases. Alcohol use was three times higher in schizophrenia patients.[34] Alcohol increases the risk of liver damage. Chronic liver disease and schizophrenia are closely related due to the high prevalence of alcohol use and smoking in schizophrenic patients. In addition, an increase in liver enzymes or injury to the liver is closely related to the prescription of antipsychotics.[35] Central nervous system drugs, including antipsychotics, anticonvulsants, and antidepressants, ranked second as drugs that induce liver damage after antibiotics.[36] Ten percent of patients who use antipsychotics routinely suffer liver function abnormalities and statistically significantly different parameters of alkaline phosphatase, albumin, and serum bilirubin.[37]

Potential Drug-Drug Interactions

Potential drug interactions are obtained by using drug interaction checkers from Drugs.com®. The results obtained showed that all patients have the potential to experience interactions between drugs used. The drug-drug interaction type was more prevalent in the maintenance-stabilization phase than in the acute phase. The difference was not statistically significant, p-value was 0.093.

Based on Table III, risperidone had the highest number of interactions, with 21 types of interactions. Trihexyphenidyl is the medicine that interacts with risperidone the most in both phases, with percentages of 85.82% and 88.06%, respectively. Drug-drug interactions are common due to the use of drug combinations.

The impact can be clinically significant, so monitoring needs to be done. Another study conducted on hospitalized patients showed that 77% of patients experienced drug-drug interactions, with 1352 cases occurring from 353 interacting drug combinations.[9] In this study, there were 1012 cases in the acute phase of 66 interacting drug pairs and 797 cases in the stabilization phase of 95 interacting drug pairs. Risperidone, as a psychopharmaceutical, has the most types of interactions with other drugs (21 types).

Although risperidone and trihexyphenidyl are widely used in clinical use, there is an increased possibility of side effects, such as central nervous system depression and tardive dyskinesia. In addition, the anticholinergic effect may increase toxicity, causing constipation, dry mouth, mydriasis, blurred vision, and urinary retention.[38] In this study, drug interaction potential with moderate severity occurred the most. Potential drug interaction with moderate severity is 88.44% in the acute phase and 94.60% in the stabilization-maintenance phase. The prevalence of potential drug interactions with major severity was 10.47% in the acute phase and 4.26% in the stabilization phase. The combination of haloperidol-risperidone (50.9%) and haloperidol-chlorpromazine (42.4%) gets the highest number of occurrences in major severity.

Haloperidol may cause a dose-related QT interval extension. Theoretically, co-administration with other agents that can extend the QT interval could lead to additive effects and an increased risk of ventricular arrhythmias, including torsade de pointes and sudden death.[39] In general, the risk of an individual agent or combination of agents causing ventricular arrhythmias concerning the prolongation of the QT interval is largely unpredictable. Still, it can be increased by certain underlying risk factors such as congenital long QT syndrome, heart disease, and electrolyte disturbances (e.g., hypokalemia, hypomagnesemia). The rate of drug-induced QT prolongation depends on the specific drug involved and the dose of the drug. In addition, particular agents with anticholinergic properties (e.g., antihistamines, antispasmodics, neuroleptics, muscle relaxants, tricyclic antidepressants) may have parasympatholytic additive and central nervous system depressant effects when used in combination with haloperidol.[40]

Table III. Potential Interaction between Psychopharmaceuticals

Types of psychopharmaceutical active substances	Number of interactions with other medications
Risperidone	21
Trihexyphenidyl	18
Chlorpromazine	17
Lorazepam	14
Haloperidol	13
Fluoxetine	13
Olanzapine	11
Diazepam	10
Sertraline	8
Phenytoin	8
Trifluoperazine	8
Clozapine	7
Aripiprazole	5
Carbamazepine	4
Maprotiline	3
Oxcarbazepine	3
Lithium	2

CONCLUSION

Majority of 134 patients were 26-35 years old (27.3%), high school (34.3%), married (61.2%), paranoid schizophrenia (93.3%). Average number of medicines were 4.12 in acute phase and 3.89 in stabilization-maintenance phase. Average length of stay were 3.89 days in acute phase and 18.36 days in stabilization-maintenance phase. The second-generation antipsychotics are the most common class of drugs in hospitalized patients with risperidone as active substances in both phases. There was a statistical difference (p = 0.000) in drug classes between the acute and stabilization-maintenance phases. The potential drug interactions in the acute and maintenance-stabilization phases were not significantly different (p = 0.093), with the most common type being risperidone, and the greatest severity were moderate at 88.44% in the acute phase and 94.60% in the stabilization-maintenance phase.

CONFLICT OF INTEREST

None to declare

STATEMENT OF ETHICS

The Health Polytechnic of Tanjung Karang Ethics Commission determined this research's ethical clearance with number 15/Perb/KEPK-TJK/VI/2020.

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