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ORIGINAL ARTICLE

Overview of The Incidence of Hyperprolacinemia Side Effects in Schizophrenia Patients with Antipsychotic Therapy

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Abstract: Antipsychotic-induced hyperprolactinemia disorder affects the morbidity and quality of life of the patient, and can lower the patient's adherence to taking antipsychotics, thereby lowering the therapeutic success rate. This study aims to figure out the incidence of hyperprolactinemia side effects in schizophrenia patients receiving antipsychotic therapy. This descriptive research was conducted at HB Saanin Psychiatric Hospital Padang in January-June 2018. The population in this study is all schizophrenia patients in the HB. Saanin Psychiatric Hospital Padang Year 2018 and involved participants as many as 100 people recruited in consecutive sampling. Data were analyzed using a descriptive statistical method. The results showed that more than half of the patients were 59 people (59.0%) hyperprolactinemia. Patients with gynecomastia amounted to 16 people (16%). Patients with galactorrhea amounted to 3 people (3%). Patients with sexual dysfunction amounted to 19 people (19%). Male patients amounted to 60 people, 21 people (35%) The sexual dysfunction of female patients amounted to 40 people, 26 people (65%) Menstrual cycle changes. More than half of the Schizophrenia patients receiving antipsychotic therapy in this study suffer symptoms of hyperprolactinemia in the manifestation of galactorrhea, gynecomastia, menstrual disorders, and sexual dysfunction.

Keywords: Antipsychotic, Hyperprolactinemia, Schizophrenia.

INTRODUCTION

Schizophrenia is a serious psychiatric disorder characterized by loss of contact with reality (psychosis), hallucinations, delusions (false beliefs), abnormal thoughts and disturbing work, and social functions. Schizophrenia is characterized by positive and negative symptoms, positive symptoms such as chaotic speech, hallucinations, cognitive disorders (attention disorders, memory, and functions related to psychosocial) and perception of negative symptoms such as avolition (decreased interest and encouragement), reduced desire to talk and poor content of the conversation.[1]

Schizophrenia is ranked 4th of the top 10 diseases that burden worldwide. It is estimated that 1-2% of the total population suffers from schizophrenia. If the total population of Indonesia reaches 200 million, then there are around two million people suffering from schizophrenia.[2] World Health

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Organization (WHO) said that there are around 24 million people worldwide suffering from schizophrenia.[3] Based on 2018 Basic Health Research data, around 0.7% of Indonesia's population suffers from schizophrenia. The highest prevalence of schizophrenia was found in Bali (1.1%), Yogya (1%), NTB (1%) Aceh and West Sumatra by 0.9%.[4] Previous studies reported that there were 23,870 outpatients who were treated at the Prof. HB. Sa'anin Padang Psychiatric Hospital in 2011, and 9,483 (39.73%) of whom were schizophrenic patients and of the 1,573 inpatients, 812 (51.62%) of them were schizophrenic patients.[5]

Schizophrenic patients are treated with a typical antipsychotic drug also called first-generation antipsychotics and atypical antipsychotics called second-generation antipsychotics. Typical antipsychotic drugs work to inhibit dopamine receptors, especially D2 and also inhibit muscarinic, adrenergic acetylcholine, and serotonin 5-HT2A receptors. Both atypical antipsychotics work by blocking the receptors serotonin 5-HT2a and dopamine, although inhibition of the 5-HT2A receptor is more potent than the dopamine receptor.[6]

Dopamine D2 receptors are found in the mesolimbic, tuberoinfundibular, and nigrostriatal systems. Inhibition of these receptors in the mesolimbic region will lead to clinical improvement of the patient, on the other hand, inhibition in the tuberoinfundibular and nigrostriatal areas will cause side effects from antipsychotic drugs.[7] Dopamine along the tuberoinfundibular pathway has the role of inhibiting the secretion of anterior pituitary gland prolactin by binding to the D2 receptor. This inhibition will cause an increase in prolactin levels in the blood with symptoms of gynecomastia, galactorrhea, menstrual disorders, and sexual dysfunction.[8,9]

According to Carvalho MM, et al. Published in 2011 reported complaints of hyperprolactinemia in 42% of men and 75% of women receiving antipsychotics.[10] Another study conducted in Serbia reported 14.8% of patients taking clozapine had complaints of sexual dysfunction which is one of the symptoms of hyperprolactinemia.[11] These side effects will certainly affect the morbidity and quality of life of patients and can reduce patient compliance in taking antipsychotics thereby reducing the success rate of therapy. This has attracted the attention of researchers to identify the side effects of hyperprolactinemia in schizophrenia patients in the HB Saanin Hospital Padang.

METHODS

This research is a categorical descriptive study to look for a picture of hyperprolactinemia in schizophrenia patients receiving antipsychotic therapy. This study was approved by the Ethics Committee of the Faculty of Medicine at Baiturrahmah University and was carried out in January - June 2018, which covered the preparation and reporting stages.

The population in this study were all schizophrenic patients in the psychiatric hospital. HB. Saanin Padang in 2018. The samples in this study were selected based on consecutive sampling techniques that fit the inclusion and exclusion criteria. Subjects were included if diagnosed with schizophrenia based on DSM IV by a psychiatrist, taking either typical or atypical antipsychotics for at least 3 months, were cooperative, and were undergoing outpatient therapy. Patients were included if they had

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Diabetes Mellitus, were pregnant, breastfeeding, and used contraception.

Data collection using the Glasgow Antipsychotic Side-Effect Scale (GASS) questionnaire and the data obtained were then processed and analyzed using a computer using descriptive statistical methods, in order to obtain a picture of suspected sexual dysfunction in schizophrenic patients receiving antipsychotic therapy.

RESULTS

In this study, there were 100 research subjects who participated, filled out informed consent, and participated in interviews based on the GAAS questionnaire. The study subjects consisted of 60 men and 40 women, with the most age in early adulthood (26-35 years). More than half of the subjects did not work, most were single, and the majority received combination antipsychotic therapy at 83%. (see table 1).

In this research, it is known that hyperprolactinemia complaints that are often reported are changes in the menstrual cycle by 65% of all female subjects, erectile difficulties in male subjects by 32%. (see table 2). Other complaints were sexual dysfunction by 19%, gynecomastia was found in 16% of subjects, and galactorrhea by 4%. Of all subjects found symptoms of hyperprolactinemia by 59%.

Table 1. Subject Characteristics

Characteristics		n	%
Age			
	Late teens (17 – 25)	17	17.0
	Early adulthood(26 – 35)	35	35.0
	Late adulthood (36 - 45)	25	25.0
	Early Elderly (46 – 55)	15	15.0
	Late Elderly (56-65)	4	4.0
	Older Adults (>65)	4	4.0
Gender			
	Male	60	60.0
	Female	40	40.0
Occupation		n	%
	Employed	46	46.0
	Unemployed	54	54.0
Marital status			
	Not married	54	54.0
	Divorced	6	6.0
	Married	40	40.0
Antipsychotic drugs:			
	Atypical	5	5.0
	Typical	12	12.0
	Combined	83	83.0

Table 1. Side Effects of Hyperprolactinemia

No	Side effects	Never	Once	Sometimes	Everyday	Total
		n (%)	n (%)	n (%)	n (%)	n (%)
1	Gynecomastia	84 (84,0)	4(4,0)	9 (9,0)	3 (3,0)	16 (16,0)
2	Galactorrhea	97 (97,0)	1 (1,0)	2(2,0)	1 (1,0)	4 (4,0)
3	Sexual dysfunction (difficulty enjoying sex)	81 (81,0)	11 (11,0)	8 (8,0)	0(0,0)	19 (19,0)
4	For Men: Having Erectile Difficulties	39(65,0)	18(30,0)	3(5,0)	0(0,0)	21 (32,0)
	Side effects	**No**		**Yes**		**Total**
		n (%)		n (%)		n (%)
5	Especially for Women: Changes in Menstrual Cycles	14 (35,0)		26 (65,0)		26 (65,0)
6	Symptoms of hyperprolactinemia	41 (41,0)		59 (59,0)		41(41,0)

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DISCUSSION

Hyperprolactinemia is a condition where Prolactin increases abnormally (normal levels of Prolactin is 10-28 mg / L). About 0.4 - 10% of hyperprolactinemia occurs in normal people, 9-15% cause secondary oligomenorrhea and amenorrhoea, 25% galactorrhea, and about 43-70% have amenorrhoea and galactorrhoea.[12] The main function of Prolactin is to trigger breast development during pregnancy and to stimulate and maintain the lactation process.[9] Prolactin indirectly regulates the secretion of pituitary hormones that play a role in gonadal function, including luteinizing hormone (LH) and follicle-stimulating hormone (FSH). This is because Prolactin can bind to specific receptors in the gonads apart from lymphoid and liver cells..[13]

The effect of Prolactin on gonads is probably caused by abnormal pulsatility disorders of gonadotrophin-releasing hormone (GnRH) and changes in the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). This will result in anovulation with symptoms of amenorrhoea or oligomenorrhea.[14]

Increased levels of Prolactin in the male body affect the formation of testosterone. The result is decreased libido and erectile dysfunction. Increased levels of prolactin, in the long run, can cause clinical manifestations of gynecomastia and galactorrhea.[15] This can occur because prolactin can decrease androgen receptors and increase estrogen and progesterone receptors that play a role in breast formation. In addition, prolactin also stimulates milk production in breast tissue which has been triggered by estrogen and progesterone.[13]

Hyperprolactinemia is one of the side effects of antipsychotic treatment. This can occur in typical antipsychotics such as Haloperidol and Chlorpromazine, and some atypical antipsychotics such as risperidone and amisulpride, but rarely in some other atypical antipsychotics such as aripiprazole, clozapine, olanzapine, ziprasidone). Antipsychotic drugs work by inhibiting dopamine D2 receptors, inhibition of D2 receptors in the mesolimbic and mesocortical areas will have a clinical effect on the patient but inhibition of D2 receptors in lactotroph cells in the tuberoinfundibular pathway can cause hyperprolactinemia because dopamine plays a role in inhibiting prolactin secretion.[9,15] In another study, there was a reported increase in prolactin levels 10 times before during the antipsychotic treatment period. Increased levels of prolactin can cause symptoms as a direct effect of prolactin on the target tissue and due to hypogonadism that occurs due to prolactin disrupts the normal functioning of the hypothalamic-pituitary-gonadal axis.[12,16]

In this study the results obtained were more than half of the patients, 59 people (59.0%) had hyperprolactinemia. The results of this study are in line with studies conducted by Carvalho MM, et al. Published in 2011, reported that the prevalence of hyperprolactinemia due to antipsychotic use was 42% in men and 75% in women.[10]

Gynecomastia patients amounted to 16 people (16%) including 4 people (4%) had gynecomastia once, 9 people (9%) had gynecomastia several times, and 3 people (3%) had gynecomastia every day. Galactorrhea patients amounted to 3 people (3%) including 1 person (1%) experienced galactorrhea once and 2 people (2%) galactorrhea several times. Patients with sexual dysfunction amounted to 19 people (19%) including 11 people (11%) once had dysfunction sexually, and 8 people (8%) had

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sexual dysfunction several times. Male patients numbered 60 people, 21 people (35%) of whom experienced sexual dysfunction, namely, 18 people (30%) had erectile disorders once, 3 people (5%) had erection problems several times. Female patients numbered 40 people, 26 people (65%) of whom experienced changes in the menstrual cycle.

Hyperprolactinemia can cause gynecomastia in men and galactorrhea in men and women. Galactorrhea is more common in women than in men. Gynecomastia is less common and can occur unilateral or bilateral. It is estimated that galactorrhea affects about 10% -50% of women who receive antipsychotic therapy. One study reported 21 out of 150 women (14%) had galactorrhea within 75 days of atypical antipsychotic treatment.[15]

This study is in line with studies in Serbia which reported that 14.8% of research subjects complained of sexual dysfunction during clozapine antipsychotic treatment.[11] Another study in India reported that sexual dysfunction occurred in 84% of patients receiving risperidone, 48.3% of patients receiving olanzapine, and 31% of patients receiving clozapine.[17] This occurs due to an increase in prolactin and hypogonadism due to the use of antipsychotics. This can cause decreased libido. In a study conducted by Lundberg and Hulter, it was reported that women with hyperprolactinemia decreased libido by 84% compared with normal prolactin levels, the incidence was 32.6%.[15,18]

This study is also in line with previous studies which reported 48% of the subjects experienced menstrual cycle disorders after receiving risperidone therapy. Another study reported that 17% of subjects experienced menstrual cycle disorders after receiving typical antipsychotics and 33% in subjects receiving atypical antipsychotics. Menstrual irregularities can occur due to the use of antipsychotics that increase prolactin levels in the blood and cause hypothalamus-pituitary-ovarian dysfunction.[15,16]

In this study, it was found several complaints of hyperprolactinemia in patients at Prof. Psychiatric Hospital Dr. HB Saanin are menstrual disorders, galactorrhea, gynecomastia, and sexual dysfunction in female subjects. Males experience galactorrhea, gynecomastia, erectile disorders, and sexual dysfunction while undergoing antipsychotic drug treatment at HB Saa'nin Hospital in Padang. This condition can be input for clinicians and consider harm and benefit in the administration of antipsychotic therapy.

CONCLUSION

Based on the results of research on the side effects of antipsychotics in schizophrenic patients in the form of hyperprolactinemia in patients in HB Saanin Psychiatric Hospital Padang, January-June 2018 period, it can be concluded that more than fifty percent of patients receiving antipsychotic therapy experience hyperprolactinemia.

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