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Gender Difference and PANSS Score of Paranoid Schizophrenia Using Risperidone

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Abstract

Recently many focus study of schizophrenia on gender are about onset and reducing the severity of illness. Males typically experience a much earlier age of onset, make up a larger proportion of clinical cases, and are more likely to have primary negative symptoms that are associated with chronic course and poor outcome. These study used the standard mental state examination of Psychiatry Department of University of North Sumatera, and SCID (Structured Clinical Interview for DSM-IV) that had been translated in Indonesian. The psychotic symptoms were rated by PANSS, using the total PANSS score. All subjects was examined until 8 weeks for each week. From the 80 total subjects, the mean age of the study for males and females was 29,42±5,53 for males and 30,80±5,64, respectively. The onset was 25,60±6,86 and 26,98±7,44. There was significant difference between gender and PANSS total scores in week 1 until 6 ($p<0,05$) where males was higher than females, but no differences in other weeks. The decrease of total PANSS per week showed significant difference ($p<0,05$) in week 1,2, 7 and 8, but not significant in other week. No significant difference ($p\geq0,05$) of total PANSS score between gender, before and after using risperidone. The difference respons percentage between male and female was not significant ($p\geq0,05$). In these study, the mean dosis of risperidone for male and female respectively was 4,008±0,141 and 4,083±0,215. There was some significant difference between gender from the psychopathology perspective in schizophrenia using risperidone.

Keywords: gender, PANSS score, risperidone

1. Introduction

Recently many focus study of schizophrenia on gender are about onset and reducing the severity of illness. According to Goldstein and Lewine, males with schizophrenia generally have an earlier onset of illness and a more severe form of the disease as reflected in greater cognitive or social impairment, while female patients are more likely to suffer from anxiety and affective symptoms (Choi, Chon, Kang, Jung and Kwon, 2009).

Males typically experience a much earlier age of onset, make up a larger proportion of clinical cases, and are more likely to have primary negative symptoms that are associated with chronic course and poor outcome (Thaker, 2009). In the Netherlands study, younger age, living in an urban environment, low income, less education, unemployment, female gender, and being single were all associated with increased rates of hallucinations (Lewis, Escalone and Keith, 2009).

The risk of developing schizophrenia is similar in males and females; however, the sex of the patient plays an important role in the clinical manifestation of the disorder. Cross-sectional studies generally find that the symptoms of schizophrenia fall into three independent clusters: positive psychotic symptoms (or reality distortion), disorganization in thought and behavior, and negative symptoms. These symptom clusters wax and wane over the course of the illness, are independent of one another, and often respond differentially to treatment with antipsychotic agents. Symptoms of reality distortion are most amenable to antipsychotic drug treatment, followed by disorganized thinking and behavior (Thaker, 2009).

Positive and negative symptoms were facilitated by the creation of reliable and valid rating scales such as the Positive and Negative Syndrome Scale (PANSS), the Scale for the Assessment of Negative Symptoms, and the Scale for the Assessment of Positive Symptoms (SAPS) (Lewis, Escalone and Keith, 2009). As in the CATIE trial, CUtLASS 1 (*Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study*) found no advantage for SGAs (second- generation antipsychotics) in terms of PANSS total and positive subscale scores (Miyamoto, Merill, Lieberman, Fleischacker and Marder, 2008). However, these study tried to learn about gender difference on PANSS total score using SGA, risperidone.

The preferential use of SGAs over FGAs is now common in the treatment of first-episode patients because of their generally lower EPS burden and possible superiority in relapse prevention. It has also been hypothesized that the glutamatergic effects of some SGAs may provide a neuroprotective function, potentially

resulting in better long-term outcomes (Miyamoto, Merill, Lieberman, Fleischacker and Marder, 2008). Also the impact on overweight, elevated serum cholesterol and elevate prolactin levels, which can result in galactorrhea and irregular menses (Newcomer, Fahnestock and Haupt, 2009; Kane, Stroup and Marder, 2009). Mortality was significantly higher in men than in women, and the difference was primarily due to an excess of male suicides and accidents (Jablensky, 2009).

Risperidone has substantially higher affinity for 5-HT 2A and D 2 receptors than does clozapine. A PET study found that risperidone occupies 75–80% of striatal D 2 receptors and 78–88% of cortical 5-HT 2 receptors when administered to schizophrenic patients at a dose of 6 mg/day. Despite high levels of D 2 receptor occupancy, moderate-dose risperidone treatment (4–6 mg/day) poses a somewhat lower EPS risk than treatment with some FGAs. This may be due to the 5-HT 2A antagonistic properties of the drug (Miyamoto, Merill, Lieberman, Fleischacker and Marder, 2008). Risperidone also the first antipsychotic that given monotherapy as 24.5%, followed by olanzapine (20.3%), sulpiride (14.6%), quetiapine (12.5%) or haloperidol (9.4%). As the antipsychotics that showed the highest rates of use in polytherapy were olanzapine (37.1%), oral risperidone (36.4%), quetiapine (29.3%), haloperidol (27.9%), levomepromazine (26.5%) and clotiapine (21.9%) (Bernardo, Coma, Ibanez, Zara, Bari and Serrano-Blanco, 2012).

Women are generally more emotionally involved with their friends and families than are men, and effective treatment must take interpersonal stressors into greater account (Seeman, 2008). Atalayu in 2006 reported that women with schizophrenia have better social functioning than men (Atalay and Atalay, 2006). But Carpiniello et.al in 2011 with define clinical remission (scores less than or equal to 3 for all PANSS items), said no difference was found between genders (Carpiniello, Pinna, Tusconi, Zaccheddu and Fatteri, 2012). According to most of the studies revised, one possible explanation of this better adjustment could be that women presented a higher age of onset than men, which allows them to adjust better to the requirements of the community (Ochoa, Usall, Cobo, Labad and Kulkarni, 2012).

Mental Hospital of Province of North Sumatera had 70% paranoid schizophrenia patients as first and recurrent was 46,7% and 53,3%, by Hutagalung, 2009 (Hutagalung, 2009). We study first episode paranoid patients using risperidone as first line antipsychotic in that hospital. We compared the total PANSS between male and female.

2. Subject and Methods

This study was approved by the Research Ethics Committee of Medical Faculty University of Sumatera Utara. This study was performed in Mental Hospital of Province of North Sumatera, on the regulation of Medical Faculty of University of North Sumatera, from April-November 2013. Subject from the outpatient care, with first episode paranoid schizophrenia using risperidone. These study was two group pretest-posttest design, open trial,with consecutive sampling. The criteria inclusion was 15-55 years old, ideal body mass index and cooperative. We exclude the organic mental disorder, hypersensitivity with risperidone, pregnancy, using contrasepsi and heavy smoke (more than 5 ciggarettes for more than 2 years) (Waked, Khayat and Salameh, 2012).

2.1 Assessment and Rating

These study used the standard mental state examination of Psychiatry Department of University of North Sumatera, and SCID (Structured Clinical Interview for DSM-IV) that had been translated in Indonesian. The psychotic symptoms was rated by PANSS, using the total PANSS score. All subjects was examined until 8 weeks for each week.

Treatment would be given if there was any side effects, such as extrapyramidal symptoms. If the subjects was stop or never come back into these study, the last week of total PANSS score were used (LOCF-*Last Observation Carried Forward*).

2.2 Statistical Analysis

Univariat analysis was performed to describe each variable and was described by frequency table. The statistical analysis were assessed by T-test for the independent sample, using SPSS 15.5. A significant level was considered as 5%.

3. Result

Demographic characteristics of participants are illustrated in Table 1.

Table 1. Demographic characteristics

No	Variabel	Males	Females	*p*
1	Age (means±SD) years	29,42 ± 5,53	30,80 ± 5,64	0,27
	< 20	0	1 (2,5%)	
	20-29	22 (55%)	12 (30%)	
	30-39	16 (40%)	18 (45%)	
	40-49	1 (2,5%)	9 (22,5%)	
	>50	1 (2,5%)	0	
2	onset (means±SD) years	25,60 ± 6,86	26,98 ± 7,44	0,39
3	BMI (rerata±SD)	22,07 ± 0,97	22,32 ± 1,19	0,31

From the 80 total subjects, the mean age of the study for males and females was 29,42±5,53 for males and 30,80±5,64, respectively. The onset was 25,60±6,86 and 26,98±7,44. The body mass index was 22,07±0,97 and 22,32±1,19. From tabel 1, the difference of age, onset and BMI was not significant.

Table 2. Difference between gender and PANSS total score

	Total PANSS		
Weeks	Males	Females	P
0 (before)	84,78 ± 3,00	84,08 ± 3,94	0,37
1	76,63 ± 5,83	72,35 ± 6,65	**0,001***
2	70,45 ± 8,36	64,22 ± 8,66	**0,001***
3	64,00 ± 9,62	57,08 ± 10,30	**0,001***
4	58,55 ± 10,71	51,35 ± 11,49	**0,001***
5	52,52 ± 11,22	46,33 ± 9,59	**0,01***
6	48,33 ± 10,71	42,85 ± 8,11	**0,01***
7	45,55 ± 10,41	41,88 ± 8,02	0,08
8	43,92 ± 9,70	41,35 ± 7,91	0,20

* *t-test*

From tabel 2, there was significant difference between gender and PANSS total scores in week 1 until 6 (p<0,05) where males was higher than females, but no differences in other weeks.

Table 3. Decrease of total PANSS score

	Total PANSS decrease		
Week	Male	Female	P
1	-8,15 ± 4,95	-11,73 ± 6,32	**0,01***
2	-6,17 ± 3,93	-8,13 ± 4,2	**0,03***
3	-6,45 ± 3,77	-7,15 ± 4,63	0,46
4	-5,45 ± 4,08	-5,72 ± 4,03	0,76
5	-6,03 ± 4,62	-5,03 ± 4,64	0,34
6	-4,20 ± 4,04	-3,48 ± 3,78	0,41
7	-2,77 ± 3,47	-0,98 ± 1,70	**0,001***
8	-1,63 ± 3,17	-0,53 ± 1,13	**0,04***

* *t-test*

The decrease of total PANSS per week in table 3, showed significant difference (p<0,05) in week 1,2, 7 and 8, but no significant in other week.

Table 4. Total PANSS score between gender with risperidone

Total PANSS decrease	Male	Female
Before (week 0)	84,78±3,00	84,08 ± 3,94
After (week 8)	43,92 ± 9,69	41,35 ± 7,91
Decrease (before-after)	-40,85 + 8,98	-42,75 +9,11

* *t-test*, p=0,357

From table 4. There is no significant difference (p≥0,05) of total PANSS score between gender, before and after using risperidone.

Table 5. Respons using risperidone

Respons Percentage	Male(%)	Female(%)
Week 1	5	17,5
Week 8	97,5	100

* *Chi square*, p= 0,300

The difference respons percetage between male and female was not significant (p≥0,05). In these study, the mean dosis of risperidone for male and female respectively was 4,008±0,141 and 4,083±0,215.

Tabel 6. *Inter-rater*

	Spearman *)	*p* **)
Week 0 (before)	0,672-1,000	0,01
Week 1	0,806-1,000	0,01
Week 8	0,768-1,000	0,01

*) Spearman correlation test

**) 2 *tailed*

From table 6 showed significant correlation (p<0,05) between rater and the inter-rater.

4. Discussion

The present study provided a two group pretest-posttest design, open trial with consecutive sampling. From the first week, risperidone have had a significant difference between gender for the total PANSS score and the decrease of the total PANSS. For the first week males where significant higher than females (76,63 ± 5,83 vs 72,35 ± 6,65, p<-0,05) with the decrease of PANSS score also females significant higher than males (-8,15 ± 4,95 vs -11,73 ± 6,32, p<0,05). This study was different with Nawka et. al, 2013 using BPRS where females was higher significant than males (58,9±14,5 vs 54,6±14,0). These difference may because the Nawka study subjects consisted difference diagnosis where mainly patients with paranoid schizophrenia (with slight prevalence of men) and residual schizophrenia (with slight prevalence of women) (Nawka, Kalisova, Raboch, Giacco, Cihal, et al, 2013). These result also may be explained by neurodevelopment theory of gender. Lenroot et. al, 2007 said that the male brain is larger than the female brain across all the stages of development, and certain structures within the brain differ in size in males and females (Kleinhaus, Harlap, Perrin, Manor, Weiser, et al, 2011).

Labelle et.al, 2001 found there was no significant difference total PANSS score over 8 weeks study, where the mean decease of PANSS for males and females was -23,1 and 21,6 (p>0.05). The difference with the present study that Labelle used chronis and subchronis schizophrenia as for DSM-III-R. But these two study also found no significant difference between gender for the response with risperidone over 8 weeks. Also they found no significant difference in the mean final dosage of risperidone, where the mean final dosage was 6,1 mg in male and 6,2 mg in female participants (Labelle, Light and Dunbar, 2001).

These significant difference between males and females in these study may be because the estrogen hormon with the antidopaminergic effects, give women the better response to antipsychotic (Kulkarni, 2009). Estrogens modulate the neurotransmitters responsible for cognitive and emotional processes. For example, estrogens reduce dopamine receptor sensitivity and increase D2 receptor density in the striatum of ovariectomised rats, while also significantly enhancing serotonergic neurotransmission. Its effects on mental state are thought to occur via an influence on the availability of these mood-relevant neurotransmitters in the synapse (Kulkarni, Gavrilidis, Worsley, Rheenen and Hayes, 2013). In Kulkarni et.al, 2010 trial in 53 men with schizophrenia was conducted to evaluate the efficacy of 2 mg oral estradiol valerate as an adjunct to atypical antipsychotic treatment, had demonstrated for estradiol participants a more rapid reduction in general psychopathology that occurred in the context of greater increases in serum estrogen levels and reductions in FSH and testosterone levels (Kulkarni, Castella, Headey, Marston, Sinclair, et al, 2011).

For the difference between gender, Wilhite et.al, 2008 found that Male and female participants did not vary significantly in any relevant demographic variables, including age. The absence of an age difference in our clinical population could be explained by a variety of reasons. Female may have a longer prodromal period than males (*i.e.* males may experience a faster deterioration once subthreshold psychotic symptoms arise).

Additionally, some recent studies have suggested that the age of onset differences may only exist in certain kinds of psychosis, namely among those patients who develop paranoid schizophrenia (Wilhite, Niendam, Bearden, Zinberg, O'Brien and Cannon, 2008).

Also Jaaskelainen et.al, 2013 said that there were no statistically significant differences when the estimates were stratified according to sex, midpoint of intake period, strictness of the diagnostic criteria, duration of follow-up, or other design features. They suggested major changes in treatment option, because the proportion of recovered cases has not increased (Jaaskelainen, Juola, Hirvonen, McGrath, Saha, Isohanni et. Al, 2013).

Genetic study about gender by Feng et.al, 2009 found that functional analyses of ectopically expressed copies of the variant miRNA precursors demonstrate loss of function, gain of function or altered expression levels. They study suggests that microRNA mutations can contribute to schizophrenia (Feng, Sun, Yan, Noltner, Li et. al)

5. Conclusion and Limitation

There was some significant difference between gender from the psychophatology perspective in schizophrenia using risperidon. The significant difference of PANSS score was on week 1 and 6, where males was greater than females. The decrease of PANSS score also had significant difference where on week 1 and 2, feremales had higher decrease than females, but in week 7 and 8. The difference before and after 8 weeks using risperidone has no significant difference. Also the response treatment between males and females had no significant difference.

The limitation of these study was smoking behavior that just get from the interview (i.e. <5 cigarette, 2 years). The adherence also been considered. As Julius et.al said that there's three factore of adherence: medication-related risk factors, psychological risk factors, and social/environmental risk factors. Then Maguro, et.al 2011 said Identifying predictors of medication adherence among patients with dual psychiatric and substance misuse problems is important because poor adherence is associated with relapse and re-hospitalization (Magura, Rosenblum and Fong, 2011).

The suggestion was on demographic factors and smoking behavior of the schizophrenia study. Also more study on the pre-psychotic, recurrent schizophrenia and each phase of treatment. The comparasion of neuroimaging of schizophrenia have been interested, as well as the neurodevelopmental study, estrogen hormon and genetic.

References

Atalay F, Atalay H. (2006), "Gender differences in patients with schizophrenia in terms of sociodemographic and clinical characteristics", German J Psychiatry **9**, 41-47

Bernardo M, Coma A, Ibanez C, Zara C, Bari JM, Serrano-Blanco A. (2012), "Antipsychotic polypharmacy in a regional health service: a population-based study", BMC Psychiatry **12**, 42

Carpiniello B, Pinna F, Tusconi M, Zaccheddu E, Fatteri F. (2012), "Gender Differences in Remission and Recovery of Schizophrenic and Schizoaffective Patients: Preliminary Results of a Prospective Cohort Study", Schizophrenia Research and Treatment, 1-7

Choi JS, Chon MW, Kang DH, Jung MH, Kwon JS. (2009), "Gender Difference in the Prodromal Symptoms of First-episode Schizophrenia", J Korean Med Sci **24**,1083-8

Feng J, Sun G, Yan J, Noltner K, Li W, et.al. "Evidence for X-Chromosomal schizophrenia associated with microRNA alterations", PLoS ONE **4**(7), e6121

Hutagalung RE. (2009), "Pengobatan risperidon pada pasien skizofrenik", Psychiatry Dept. FK-USU, 1-34

Jablensky A. (2009), "Worldwide burden of schizophrenia", In Sadock BJ, Sadock VA, Ruiz P (Editors), Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 9th ed. New York: Lippincott Williams & Wilkins, 1413

Jääskeläinen E, Juola P, Hirvonen N, McGrath JJ, Saha S, Isohanni M, Veijola J, Miettunen J. (2013), "A systematic review and meta-analysis of recovery in schizophrenia", Schizophr Bulletin **39**(6), 1296-306

Kane JM, Stroup S, Marder SR. (2009), "Schizophrenia: Pharmacology treatment", In Sadock BJ, Sadock VA, Ruiz P (Editors), Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 9th ed. New York: Lippincott Williams & Wilkins, 1548-56

Kleinhaus K, Harlap S, Perrin M, Manor O, Weiser M, et al. (2011), "Age, sex and first treatment of schizophrenia in a population cohort", J Psychiatr Res **45**(1), 136–141

Kulkarni J, Castella A, Headey B, Marston N, Sinclair K, et al. (2011), "Estrogens and men with schizophrenia: Is there a case for adjunctive therapy?", Schizophrenia Research **125**, 278–283

Kulkarni J, Gavrilidis E, Worsley R, Rheenen TV, Hayes E. (2013) "The role of estrogen in the treatment of men with schizophrenia", Int J Endocrinol Metab **11**(3), 129-136

Labelle A, Light M, Dunbar F. (2001), "Risperidone treatment of outpatients with schizophrenia: no evidence of sex difference in treatment response", Can J Psychiatry **46**, 534–541

Lewis S, Escalone R, Keith SJ. (2009), "Phenomenology of schizophrenia", In Sadock BJ, Sadock VA, Ruiz P (Editors) Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 9th ed. New York: Lippincott Williams & Wilkins, 1440

Magura S, Rosenblum A, Fong C. (2011), "Factors associated with medication adherence among psychiatric outpatients at substance abuse risk", The Open Addiction Journal **4**, 58-64

Miyamoto S, Merrill DB, Lieberman JA, Fleischacker WW, Marder SR. (2008), "Antipsychotics drugs", In Tasman A, Kay J, Lieberman JA, First MB, Maj M (Editors) Psychiatry 3rd ed. Chichester: John Wiley & Sons, 2161-243

Nawka A, Kalisova L, Raboch J, Giacco D, Cihal L, et.al. (2013), "Gender differences in coerced patients wih schizophrenia", BMC Psychiatry **13**, 257

Newcomer JW, Fahnestock PA, Haupt DW. (2009), "Medical health in schizophrenia", In Sadock BJ, Sadock VA, Ruiz P (Editors) Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 9th ed. New York: Lippincott Williams & Wilkins, 1573-82

Ochoa S, Usall J, Cobo J, Labad X, Kulkarni J. (2012) "Gender difference in schizophrenia and first-episode psychosis: a comprehensive literature review", Schizophrenia Research and Treatment, 1- 9

Seeman MV. (2008), "Gender", In Mueser KT, Jeste CV (Editors) Clinical handbook of schizophrenia. New York: The Guildford Press, 575-80

Thaker GK. (2009), "Schizophrenia: phenotypic manifestations", In Sadock BJ, Sadock VA, Ruiz P (Editors) Kaplan & Sadock's Comprehensive Textbook of Psychiatry, 9th ed, New York: Lippincott Williams & Wilkins, 1542-7

Waked M, Khayat G, Salameh P. (2012), "Cigarette smokers' profile in lebanese adults", JRHS **12**(2), 75-80

Kulkarni J. (2009), "Oestrogen-a new treatment approach for schizophrenia?", Med J Aust **190**(4), S37-8

Willhite RK, Niendam TA, Bearden CE, Zinberg J, O'Brien MP, Cannon TD. (2008), "Gender differences in symptoms, functioning and social support in patients at ultra-high risk for developing a psychotic disorder", Schizophr Res **104**(1-3), 237–245

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