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Medication Compliance in Outpatients with Schizophrenia in One Veterans Hospital in Taiwan

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ABSTRACT

Medication compliance is an important determinant in schizophrenia treatment outcomes. This study aimed to investigate medication compliance in cases of patients receiving a single antipsychotic medication among adult outpatients with schizophrenia, and examine whether their antipsychotic therapy and other factors may affect the medication compliance. Subjects with schizophrenia who had received any single outpatient first- or second-generation antipsychotic therapy from the Yuli Veterans Hospital, Taiwan, during August and November 2006 were identified from medical chart reviews. The selected subjects were surveyed for information including their medication compliance, sociodemographics, treatment-related side effects, social support, and perceived treatment-related benefits. Their physicians were also surveyed on their medication compliance, Clinical Global Impression (CGI) scores, and comorbid mental illness(es). Good medication compliance was defined as consumption of more than 75% of prescribed antipsychotics in the previous month. Subjects were categorized into this group when both their self-reported consumption and their physicians' estimation were higher than 75%. A logistic regression model was adopted to evaluate the association of each factor with medication compliance. Of the 76 subjects surveyed, 39 (51%) received second-generation antipsychotics (amisulpride, risperidone, or olanzapine), while 37 (49%) received first-generation antipsychotics (haloperidol or sulpiride). Thirty-eight (50%) consumed more than 75% of prescribed medications in the previous month. The average age was 41, and 62% of the sample was male. Education level and employment type were significantly different between individuals with good and poor medication compliance. The regression result indicated that education of above nine years was significantly associated with an increased likelihood of good medication compliance. Employment and perceived treatment benefits were marginally significantly correlated with good medication compliance. Second-generation antipsychotics, however, had no correlation with good medication compliance.

Key words: schizophrenia, medication compliance, antipsychotics

INTRODUCTION

Antipsychotics play a crucial role in treating individuals with schizophrenia, both in acute therapy to control symptoms and in maintenance therapy to prevent relapses. Even though medication compliance is an important determinant in schizophrenia treatment outcomes, individuals suffering from schizophrenia were found to be poorly compliant with antipsychotic medication regimens, with noncompliance rates ranging from 24% to 90%[(1-5)]. Partial or poor medication compliance, however, was associated with higher relapse rates[(6)], increased use and costs of hospitals and emergency rooms[(3,7,8)], adverse long-term functional outcomes such as poorer mental functioning and poorer life satisfaction[(9)], suicide[(10,11)], and therefore a higher societal burden[(12)].

Many factors have been found to be associated with medication compliance. Patient-related factors included religious beliefs and insight[(1,5,13-15)]. Illness factors such as severity, cognition impairment, and substance abuse were correlated with medication compliance[(1,5,13,16-18)]. Medication-related factors, including adverse drug reactions, route of administration, complexity of regimen, and effectiveness, affected medication compliance[(1,5,14,17,20)]. Environmental factors, such as social support and therapeutic alliance also played a role in medication compliance[(1,5,14,20,21)].

Second-generation antipsychotics differ from first-generation ones in terms of their efficacy and side-effect profiles. They are comparably efficacious against positive

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symptoms, more efficacious against negative symptoms, and less likely to induce neurotoxic symptoms, such as extrapyramidal symptoms, than their conventional counterparts. However, they increase the risks of weight gain, hyperlipidemia, and type II diabetes mellitus. While neurotoxic symptoms, such as extrapyramidal symptoms, affect compliance, so do adverse effects such as weight gain, hyperlipidemia, and diabetes mellitus. The extent to which the treatment benefits and side-effect profiles of antipsychotics of different generations contribute to compliance is inconclusive. Even though some studies found that second-generation antipsychotics, compared to first-generation ones, were correlated with marginally better medication compliance[22-26], others did not find such pattern[3,27-31].

In Taiwan, previous research has addressed the association between medication compliance and insight into illness[32]. As we knew, there was no study so far to examine the impact of different antipsychotic therapy on medication compliance in Taiwanese with schizophrenia. Therefore, the objectives of this study were to assess the antipsychotic medication compliance of individuals receiving any single outpatient antipsychotic medication from the Yuli Veterans Hospital, and to examine whether their antipsychotic regimen, of first-generation or second-generation antipsychotics, and other factors may affect their medication compliance.

MATERIALS AND METHODS

Subjects with schizophrenia who had received any single outpatient antipsychotic therapy (amisulpride, risperidone, olanzapine, quetiapine, ziprasidone, haloperidol, or sulpiride) from the Yuli Veterans Hospital, Taiwan, during August and November 2006 were identified from medical chart reviews. The selected subjects were interviewed with a questionnaire containing five categories of questions: (1) medication compliance of the antipsychotic therapy: the percentage of the medications they had taken in the previous month; (2) sociodemographics: age, gender, marital status, religion, education level, and employment; (3) treatment-related side effects; (4) social support from family, relatives, friends, or partners; (5) perceived treatment-related benefits. Their physicians were surveyed on their patients' medication compliance, age of onset, the Clinical Global Impression (CGI) scores, and comorbid mental illness(es). The CGI scores ranged from 1-7, with 1 indicating "normal, not at all ill" and 7 indicating "among the most extremely ill patients." This study was approved by the institutional review board, and each subject signed an informed consent form.

In this study, subjects were categorized as having good medication compliance only when both their self-reported consumption of their prescribed antipsychotics in the previous month and their physicians' estimation were higher than 75%. The rest of the subjects were classified as poor medication compliance. A chi-square test or t test was used to test the difference of categorical or continuous variables between the two groups. A multivariate logistic regression model was adopted to evaluate associations of different factors with good medication compliance. The model consisted of a continuous variable of age, and dichotomous variables indicating other patient sociodemographic characteristics including gender, education level (more than nine years or not), marital status, religion, and employment. This model also contained dichotomous variables related to clinical characteristics – the CGI (> 3, ≤ 3 as reference), comorbid mental illness – and variables indicating social support, treatment-related side effects (≥ 2, < 2 symptoms as reference), and perceived treatment-related benefits (> 4, ≤ 4 as reference).

RESULTS

Seventy-six subjects were selected in the study. Of the 39 subjects who received second-generation antipsychotics, 20 received risperidone, 13 olanzapine, and 6 amisulpride. Twenty-eight subjects received sulpiride, and nine received haloperidol. Of the 76 subjects selected in this study, 38 (50%) had taken more than 75% of their prescribed antipsychotics which was confirmed by their physicians (Table 1). The average age was 41, and 62% of the sample was male. Education levels and employment were significantly different between individuals with good and poor medication compliance.

Table 2 shows the regression results of this study. The overall model was significant (chi-square = 25.01, p = 0.01). Education of above nine years was significantly associated with an increased likelihood of good medication compliance, and the odds ratio was 3.92 (95% CI: 1.15 - 13.34, p = 0.0289). Employment and perceived treatment benefits were marginally significantly correlated with good compliance, and the odds ratios were 4.74 (95% CI: 0.79 - 28.35, p = 0.0880) and 4.42 (95% CI: 0.88 - 22.32, p = 0.0717), respectively. Second-generation antipsychotics, compared to first-generation ones, were not found to be significantly associated with good medication compliance.

DISCUSSION

This study examined the potential associations of medication compliance with antipsychotics of different generations and other factors. Second-generation antipsychotics were found not correlated with good medication compliance, which was consistent with previous studies[3,27-31]. However, of 37 subjects who had received first-generation antipsychotics in this study, 28 had received sulpiride, which is pharmacologically similar to amisulpiride. They are both benzamides and, at low dose, dopamine partial agonists, one of the pharmaceutical properties of second-generation antipsychotics [33].

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Table 1. Characteristics of the Sample

		Total		Good Compliance		Poor Compliance		Chi-sq or t test
		N	%	N	%	N	%	
Subject no		76		38		38		
Age		41		42		40		
Gender	Male	47	62	24	63	23	61	
	Female	29	38	14	37	15	39	
Education	> 9 years	42	55	28	74	14	37	**
	≤ 9 years	34	45	10	26	24	63	
Married	Yes	14	18	4	11	10	26	
	No	62	82	34	89	28	74	
Religion	Yes	59	78	29	76	30	79	
	No	17	22	9	24	8	21	
Employment	Yes	61	80	36	95	25	66	**
	No	15	20	2	5	13	34	
CGI[a]	>3	38	50	18	47	20	53	
	≤ 3	38	50	20	53	18	47	
Comorbid mental illness	Yes	9	12	2	5	7	18	
	No	67	88	36	95	31	82	
Social support	Yes	64	84	33	87	31	82	
	No	12	16	5	13	7	18	
Side effect event	More	37	49	18	47	19	50	
	Less	39	51	20	53	19	50	
Treatment benefit	More	61	80	33	87	28	74	
	Less	15	20	5	13	10	26	
Antipsychotic	2nd-generation	39	51	18	47	21	55	
	1st-generation	37	49	20	53	17	45	

*P < 0.5; **P < 0.01

[a] Clinical Global Impression

The similarities might reduce the disparities between subjects receiving antipsychotics of different generations, and therefore partially account for the finding that there was no significant association between good medication compliance and second-generation antipsychotics.

In addition, even though benefits and risks of a treatment affect medication compliance, these are not the only factors, and other determinants have been shown to play important roles in compliance behavior. In this study, subjects were selected if they had received single first- or second-generation antipsychotic medication. Their simple antipsychotic regimens, to some extent, reflected their relatively stable illness and better symptom controls in comparison to those who needed to change their treatment regimens (switch or augmentation) or were treated by complex regimens. In addition, as their average duration of schizophrenia was 17.50 years (eight subjects without age of onset), they had been under antipsychotic therapy for a long period of time. Therefore, they were probably more likely to comply with the treatment, regardless of receiving first- or second-generation antipsychotics.

The findings of this study indicated that a higher education level was associated with good medication compliance, which was consistent with previous

Table 2. Regression Results – Good versus Poor Compliance

	β	SE	Odds Ratio	95% CI
Intercept	-3.77	2.33		
Age	0.03	0.04	1.03	0.96 – 1.11
Male	0.09	0.64	1.09	0.31 – 3.80
Higher education	1.37*	0.63	3.92	1.15 – 13.34
Married	-1.42	0.89	0.24	0.04 – 1.37
Religion	-0.61	0.73	0.54	0.13 – 2.26
Employment	1.56#	0.91	4.74	0.79 – 28.35
Higher CGI	-0.98	0.63	0.37	0.11 – 1.29
Comorbid illness	-0.71	1.13	0.49	0.05 – 4.49
No social support	-0.36	0.80	0.70	0.15 – 3.34
More side effect events	0.93	0.66	2.55	0.70 – 9.26
More treatment benefits	1.49#	0.83	4.42	0.88 – 22.32
2nd-generation antipsychotic	0.26	0.61	1.30	0.40 – 4.28
Chi-sq	25.01*			
C	0.80			
R^2	0.28			

*P < 0.5; **P < 0.01

#P < 0.1

research[34,36]. A higher education level could imply higher premorbid cognitive functions and better insight into illness, which were correlated with better medication compliance[1,5,13-15]. However, patient-related factors such as age, gender, education, and religious beliefs were not found to be consistent predictors of good medication compliance[5].

Employment was found to be significantly different between subjects with good and poor medication compliance, and marginally associated with good medication compliance in the regression analysis (odds ratio = 4.74, 95% CI: 0.79 - 28.35, p = 0.0880). In this study, 61 out of 76 subjects had a job. Compared to the UK (12.9%), France (11.5%), Germany (30.3%), and the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study in the US (27.1%)[34,35], the employment rate of subjects in this study was high (80%). This relatively high rate was mostly due to supported employment, which was a key element of rehabilitation therapy in the Yu-Li Veterans Hospital, where work opportunities and appropriate work training were well provided. In addition, as these subjects were relatively stable in their illness and had better symptom control in comparison with those receiving complex antipsychotic regimens, they were more likely able to work. Previous research, however, did not reveal significant association between employment and good medication compliance[32,34]. In addition to the impact of supported employment, subjects with employment more likely have less cognitive impairment and better psychosocial functioning, and therefore better medication compliance. However, as this was a cross-sectional study, no causation of employment and medication compliance could be inferred from the findings. Further studies will be necessary to tell how these two variables affect each other.

In this study, comorbid mental illness was not significantly correlated with medication compliance. However, among the nine subjects reported with comorbid mental illness, four of them with alcohol abuse or dependence were all classified as poor medication compliant. This was consistent with previous findings that substance and alcohol abuse was an important predictor of poor medication compliance[1,5,13,16-18]. Even though depressive state was found to be associated with poor compliance[37], there was only one of two subjects with this condition poorly compliant to the therapy. One of two subjects with manic state was categorized as poorly medication compliant. A subject with obsessive-compulsive disorder was poorly compliant to the therapy.

The findings of this study indicated that perceived

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treatment benefits were marginally significantly associated with good compliance (odds ratio = 4.42, 95% CI: 0.88 - 22.32, p = 0.0717), which was consistent with previous studies[1,5,13,19]. Factors such as social support and treatment side-effects, however, were not found to be significantly correlated with good medication compliance.

This study had some limitations. First, this study did not select subjects from all individuals with schizophrenia receiving antipsychotic therapy but only those who had received single antipsychotic medications of interest. This was in accordance with our study objectives. However, as single antipsychotic therapy might imply less severe and more stable illness, the results could not be generalized to individuals with more severe schizophrenia or any groups with a different case mix.

Second, as this study collected data from a single hospital, characteristics of the hospital and the community could affect the generalizability of the findings. The Yuli Veterans Hospital is an integrated psychiatric teaching hospital, providing comprehensive services that include supported employment. In addition, the community not only accepts individuals receiving treatments from the hospital, but also is willing to provide jobs to them.

Third, self-reported data might be biased, especially from individuals with severe mental illnesses whose answers might be affected by memory deficits, levels of psychosis, substance abuse, or lack of insight into illness[38]. To avoid overestimation of the medication compliance, both the subjects' self-reported compliance and physicians' assessed compliance were collected, and the subject was classified as having good compliance only when both were higher than 75%. So far, there is no perfect method to measure medication compliance as each has its own advantages and disadvantages. Some studies adopted other methods such as pill counts and plasma drug levels to verity self-reported compliance, which are also subject to bias due to pill dumping and variations in metabolism[1].

Fourth, this study was subject to type II error due to limited sample size. Therefore, a larger sample size will be needed to examine which factors might also be significantly associated with medication compliance.

CONCLUSIONS

In this study, second-generation antipsychotics were not found to be associated with good medication compliance in subjects received single antipsychotic medication. Higher education level, employment, and perceived treatment benefits were associated with better medication compliance. As this was a cross-sectional study, future research with a larger sample size and longer follow-up would be of importance to identify determinants of medication compliance, and examine outcomes and economic costs associated with medication compliance.

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