

Study of factors affecting drug compliance in schizophrenia- cross sectional survey

Gopalan M.R¹, Vidhu Kumar K²

¹Dr Mohan Roy Gopalan, Assistant Professor, Department of Psychiatry, ²Karunakaran Vidhukumar, Additional Professor, Department of Psychiatry, Government Medical College, Trivandrum Kerala, India.

Address for Correspondence: Dr Mohan Roy Gopalan, Email: drmohanroy@gmail.com

Abstract

Introduction: Schizophrenia is a condition characterized by delusions, hallucinations, disorganized behavior, disorganized thought, and negative symptoms. There is overwhelming evidence that antipsychotics can be effective in treating the symptoms of schizophrenia. Approximately 75% of individuals relapse without drugs compared to 25% with drug. Patients who receive long-acting depot have lower relapse rates than patients who receive oral medications. The factors affecting drug compliance include side effects, psychopathology, social support, and insight. Indian studies are comparatively few in this area; knowledge of these factors can help in formulating strategies for enhancing drug compliance and outcome. **Methods:** This study was conducted at the Department of Psychiatry T D Medical College, Alleppey, a tertiary care teaching hospital. Patients who attended the Outpatient department were assessed with following instruments, Positive and negative symptom scale, Udvalg Klinske Undersogelser Side Effect Rating Scale, Multidimensional scale of perceived social support, Scale to assess Unawareness of Mental Disorder (SUMD), Compliance was assessed by using the criteria of fully compliant defined as those miss less than 20% of medication, partially compliant those who misses 20% to 80% of medication and noncompliant those who miss more than 80% of medicines. Data was analysed using Chi square test and regression analysis. **Result:** Sex, Education status, marital status, Occupation, and drugs administered had significant relationships with Compliance. **Conclusion:**, it is advisable to use minimum number of drugs for ensuring compliance.

Key words: Drug compliance, Schizophrenia, Delusions, Insight.

Introduction

Schizophrenia is a condition characterized by delusions, hallucinations, disorganized behavior, disorganized thought, and negative symptoms [1]. There is overwhelming evidence that antipsychotics can be effective in treating the symptoms of schizophrenia [2]. Approximately 75% of individuals relapse without drugs compared to 25% with drug. Patients who receive long-acting depot have lower relapse rates than patients who receive oral medications [3].

The factors affecting drug compliance include side effects, psychopathology, social support, and insight. Indian studies are comparatively few in this area; knowledge of these factors can help in formulating

strategies for enhancing drug compliance and outcome.

Awareness of having an illness is associated with better medication compliance and better outcome [4]. Patient who live alone have low compliance rates than who live in supportive environment [5]. Side effects that occur early in treatment lead to a substantial reduction in compliance later [6].

It is suggested that it may be possible to identify patients most likely to benefit from adherence intervention [7]. Knowledge of factors affecting drug compliance in schizophrenia is very vital in Indian scenario. But unfortunately studies in this area are less from this part of the world. This study aims to bridge this gap and tries to assess the drug compliance of patients taking antipsychotics. It also plans to assess the

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variables of recruited patients using appropriate rating instruments for Insight, severity of psychopathology, social support and side effects of medications and aims to study the interrelationship between these factors and drug compliance

Compliance is defined in many ways one of them is “compliance can be expressed as the ratio between an observed treatment behavior and given treatment standards” [8]. Definitions of compliance differ among different groups of workers, but it can be considered to be the degree to which a patient’s behavior is consistent with medical advice [3].

The term *adherence* has been proposed as an alternative to compliance as it emphasizes the role of the patient as a collaborator in decisions regarding treatment. Study by Cramer and Rosenheck [9] reviewed studies of medication compliance for both psychiatric and medical illnesses.

The mean levels of compliance were 58% for antipsychotics, 65% for antidepressants and 76% for nonpsychiatric condition. Studies in arthritis and seizure disorders reviewed by Fenton and coworkers [10] have found higher rates of noncompliance.

Materials and Methods

Sample- This study was conducted at the Department of Psychiatry T D Medical College, Alleppey a tertiary care teaching hospital. Patients who attended the Outpatient department were the subjects for the study

Table 1 represents relationship between sociodemographic factors and compliance it shows that females has significant compliance rates than males, compliance increasing with number of years of education, unmarried persons, Hindus and unemployed have more compliance rates.

Table 2 represents relationship between various illness factors and compliance. It shows that persons who has to spent between Rs. 51 and 100 has maximum compliance rates, analysing religious/alternate treatments and compliance rates it was found that people who doesn’t go for alternate treatment has maximum compliance rates, analysing depot preparations and compliance rates it was found that people who take depot has less compliance compared to people who are not on depot, analysing the relationship between number of drugs administered and compliance it was found that persons with less number of medicines has more drug compliance then persons with more drugs.

Table 3 shows the relationship between symptom related factors and compliance. The relationship between positive symptoms and compliance showed that persons with average positive symptoms were more compliant compared to people with low positive symptom score, comparison of negative symptoms with compliance showed that people with average negative symptoms have more compliance rates compared to people with low negative symptom scores, comparing illness insight and compliance it was found that persons with low insight are more complaint compared to persons with high insight

The study was a cross sectional survey and following were the inclusion and exclusion criteria

Inclusion criteria

- Age 18 to 65
- Diagnosis of schizophrenia (D S M IV based)
- Patients living with at least one key relative who is available for interview

Exclusion criteria

- Patients who currently meet criteria for substance withdrawal
- Mental retardation
- Patients with Co morbid axis I disorder

Tools

- Compliance was defined at three levels in the following way
- Compliant-misses < 20% of medication
- Partially compliant- misses 20% to 80 of medication
- Noncompliant-misses > 80% of medication
- Positive and negative symptom scale¹¹
- Udvalg Kliniske Undersogelser Side Effect Rating Scale¹²
- Multidimensional scale of perceived social support¹³
- Scale to assess Unawareness of Mental Disorder (SUMD)¹⁴

Results

Table-1: Sociodemographic Factors

		Compliance (Score)			Total
		Non Compliant	Partially Compliant	Fully Compliant	
Age (years)	< 50	5	4	18	27
		18.51	44.40%	58.10%	54.00%
	≥ 50	5	5	13	23
		50.00%	55.60%	41.90%	46.00%
<i>Chi square: 0.601; p >0.05</i>					
Gender	Male	-	5	9	14
			35.71%	64.28%	100.00%
	Female	10	4	22	36
		27.77%	11.10%	61.10%	100.00%
<i>Chi square: 7.295; p <0.05</i>					
Education	SSLC	5	-	23	28
		50.00%		74.20%	56.00%
	5th Std	-	4	4	8
			44.40%	12.90%	16.00%
	3rd Std	5	-	-	5
		50.00%			10.00%
	2nd Std	-	5	-	5
			55.60%		10.00%
	Nil	-	-	4	4
				12.90%	8.00%
<i>Chi square : 58.503; p <0.001</i>					
Marital Status	Married	10	5	5	20
		100%	55.60%	16.10%	40.00%
	Unmarried	-	4	22	26
			44.40%	71.00%	52.00%
	Widow/Widower	-	-	4	4
				12.90%	8.00%
<i>Chi square : 23.856; p <0.001</i>					
Religion	Hindu	5	4	17	26
		50.00%	44.40%	54.80%	52.00%
	Christian	5	-	9	14
		50.00%		29.00%	28.00%
	Muslim	-	5	5	10
			55.60%	16.10%	20.00%
<i>Chi square : 12.336; p <0.05</i>					
Occupation	Unemployed	5	9	26	40
		50.00%	100%	83.90%	80.00%
	Housewife	5	-	5	10
		50.00%		16.10%	20.00%
<i>Chi square : 8.165; p <0.05</i>					

Table 2: Illness Related Factors.

		Compliance (Score)			Total
		Non Compliant	Partially Compliant	Fully Compliant	
Duration of Illness	≤ 10	-	-	13	13
				41.90%	26.00%
	11 - 20	10	-	13	23
		100%		41.90%	46.00%
	> 20	-	9	5	14
			100%	16.10%	28.00%
<i>Chi square : 39.581; p <0.001</i>					
Duration of Treatment	≤ 10	-	-	13	13
				41.90%	26.00%
	11 - 20	10	5	13	28
		100%	55.60%	41.90%	56.00%
	> 20	-	4	5	9
			44.40%	16.10%	18.00%
<i>Chi square : 17.877; p <0.01</i>					
Money Expenditure (Rs.)	≤ 50	10	9	9	28
		100%	100%	29.00%	56.00%
	51 - 100	-	-	18	18
				58.10%	36.00%
	≥ 101	-	-	4	4
				12.90%	8.00%
<i>Chi square : 24.078; p <0.001</i>					
Other Treatments	Religious	-	5	5	10
			55.60%	16.10%	20.00%
	Alternative	-	-	5	5
				16.10%	10.00%
	Nil	10	4	21	35
		100%	44.40%	67.70%	70.00%
<i>Chi square : 13.134; p <0.05</i>					
Depot Preparations	Yes	5	9	13	27
		50.00%	100%	41.90%	54.00%
	No	5	-	18	23
		50.00%		58.10%	46.00%
<i>Chi square : 9.548; p <0.01</i>					
Drugs administered	Clozapine	5	-	4	9
		50.00%		12.90%	18.00%
	Olanzapine	-	-	5	5
				16.10%	10.00%
	Risperidone + Depot	-	-	13	13
				41.90%	26.00%
	Depot + Olanzapine	-	-	4	4
				12.90%	8.00%
	Risperidone + Clozapine + Trihexyphenedyl	-	-	5	5
				16.10%	10.00%
Risperidone + Depot + Trihexyphenedyl	-	5	-	5	
		55.60%		10.00%	
Risperidone + Soium Valproate + Nitrazepam	5	-	-	5	
	50.00%			10.00%	
Clozapine + Trihexyphenedyl + Haloperidol	-	4	-	4	
		44.40%		8.00%	
<i>Chi square : 85.305; p <0.001</i>					

Table-3: Symptom Related Factors.

		Compliance (Score)			Total
		Non Compliant	Partially Compliant	Fully Compliant	
Positive Symptoms	Low	10	-	13	23
		100%		41.90%	46.00%
	Average	-	9	18	27
			100%	58.10%	54.00%
<i>Chi square : 19.612; p <0.001</i>					
Negative Symptoms	Low	5	5	5	15
		50.00%	55.60%	16.10%	30.00%
	Average	5	4	26	35
		50.00%	44.40%	83.90%	70.00%
<i>Chi square : 7.544; p <0.05</i>					
Insight	Low (< 30%)	-	-	14	14
				45.20%	28.00%
	High (≥ 60%)	10	9	17	36
		100%	100%	54.80%	72.00%
<i>Chi square : 11.918; p <0.01</i>					

Table-4: Insight Related Factors.

		Compliance (Score)			Total
		Non Compliant	Partially Compliant	Fully Compliant	
Insight: Hallucination	Low (< 30%)	10	4	22	36
		100%	44.40%	71.00%	72.00%
	Medium (30-60%)	-	5	4	9
			55.60%	12.90%	18.00%
	High (≥ 60%)	-	-	5	5
				16.10%	10.00%
<i>Chi square : 14.407; p <0.01</i>					
Insight: Delusion	Low (< 30%)	10	-	22	32
		100%		71.00%	64.00%
	Medium (30-60%)	-	9	9	18
			100%	29.00%	36.00%
<i>Chi square : 22.278; p <0.001</i>					
Insight: Blunt Effect	Low (< 30%)	10	-	13	23
		100%		41.90%	46.00%
	Medium (30-60%)	-	9	18	27
			100%	58.10%	54.00%
<i>Chi square : 19.612; p <0.001</i>					
Insight: Asociality	Low (< 30%)	5	5	13	23
		50.00%	55.60%	41.90%	46.00%
	Medium (30-60%)	5	4	14	23
		50.00%	44.40%	45.20%	46.00%
	High (≥ 60%)	-	-	4	4
				12.90%	8.00%
<i>Chi square : 2.821; p >0.05</i>					
Total Insight	Low (< 30%)	10	-	18	28
		100%		58.10%	56.00%
	Medium (30-60%)	-	9	13	22
			100%	41.90%	44.00%
<i>Chi square : 19.365; p <0.001</i>					

Table 4 shows the relationship between insight and compliance. Comparing insight to hallucinations and compliance it was found that people with high insight are likely to be more compliant than persons with low insight, comparing insight to delusions and compliance it was found that people with high insight are likely to be more compliant than persons with low insight, comparing insight to blunt affect and compliance it was found that people with medium insight scores to blunted affect are likely to be more compliant than persons with high insight.

Table-5: Social Support Related Factors.

		Non Compliant	Partially Compliant	Fully Compliant	Total
Significant Other	Low (< 30%)	10	9	23	42
		100%	100%	74.20%	84.00%
	Medium (30-60%)	-	-	8	8
				25.80%	16.00%
<i>Chi square : 5.837; p >0.05</i>					
Family	Medium (30-60%)	10	-	-	10
		100%			20.00%
	High (≥ 60%)	-	9	31	40
			100%	100%	80.00%
<i>Chi square : 50.00; p <0.001</i>					
Friends	Low (< 30%)	10	9	23	42
		100%	100%	74.20%	84.00%
	Medium (30-60%)	-	-	4	4
				12.90%	8.00%
High (≥ 60%)	-	-	4	4	
			12.90%	8.00%	
<i>Chi square : 5.837; p >0.05</i>					
Total Score	Low (< 30%)	5	-	-	5
		50.00%			10.00%
	Medium (30-60%)	5	9	27	41
		50.00%	100%	87.10%	82.00%
High (≥ 60%)	-	-	4	4	
			12.90%	8.00%	
<i>Chi square : 24.154; p <0.001</i>					

Table 5 shows the relationship between social support and compliance. Analysis of compliance with a social support from significant other showed no statistically significant relationships, analysis of compliance with a social support from family showed that persons with high social support from family were more compliant than persons with low social support (P<0.001), analysis of compliance with a social support from friends showed no statistically significant relationships, analysis of compliance with total social support showed that persons with higher social supports were likely to be more compliant than persons with low social support (P <0.001).

Table-6: Side effects.

Psychic	Low (< 30%)	5	9	18	32
		50.00%	100%	58.10%	64.00%
	Medium (30-60%)	5	-	13	18
		50.00%		41.90%	36.00%
<i>Chi square : 6.387; p <0.05</i>					

Table 6 shows the relationship between side effects and compliance. Analysis of psychic side effects scores showed that persons with low side effects are likely to be more compliant than persons with medium side effects scores

Table-7: Regression analysis with compliance.

Parameters	B	Beta	t
Sex	0.502	0.281	-5.089**
Education	0.213	0.982	11.802**
Marital Status	1.279	0.98	15.824**
Religion	0.211	0.207	0.924
Occupation	0.355	0.354	-2.259*
Duration of Illness	0.922	0.844	-1.744
Duration of Treatment	0.783	0.643	1.194
Depot Preparations	0.002	0.001	-0.007
Drugs Administered	0.004	0.361	-2.38*
Other Treatments	0.205	0.169	1.239
* P < 0.05; ** P < 0.01			

Regression analysis showed that Sex, Education status, marital status, Occupational status (being unemployed), and drugs administered (less number of drugs) had significant relationships with Compliance

Discussions

Comparing between age and compliance (Table 1) it was found that there was no significant relationship between age and compliance. Studies have shown that patients at the extreme ends of the age distribution have more problems adhering to treatment recommendations. Young, especially male, patients have been found to be poor compliers [15]. Elderly persons with memory deficits have reduced compliance [16].

Present study sample consisted of 14 (28%) males and 36 (72%) females analyzing the relationship between gender and compliance (Table 1) it was found that females has statistically significant compliance rates than males ($P < 0.05$). Studies have shown that women tend to be more compliant than men, and younger women have been found to show better compliance than older women [17]. Findings from our study is consistent with these studies

Comparing educational status and compliance (Table 1) it was found that 28 (56%) had studied up to SSLC i.e. has more than 10 years of education. We could see that compliance rates increases with number of years of education and difference was statistically highly significant ($P < 0.001$) it may be explained by the fact that persons with high educational status are more

aware of the benefits of medicines and that's why they take medicines.

Comparing marital status with compliance (Table 1) it was found that the group had more unmarried persons (52%) and they had high compliance rates ($P < 0.001$) the relationship was highly significant the reason could be that married persons may be living in nuclear families and the spouse going for work cannot ensure the drug compliance but unmarried usually live in extended families where someone will be there to take care of them on further analysis it was observed that unmarried has more social support compared to married ($P < 0.001$).

Comparing religious status (Table 1) the group consisted mostly of Hindus (52%) and they were found to have more compliance rates ($P < 0.05$) on further analysis it was found that Hindus opt for less alternative treatments compared to Muslims and that could be a reason for their poor drug compliance.

Analysing duration of illness and compliance (Table 2) it was found that only 5 persons (16.1%) were fully compliant in the more than 20 year illness duration category ($P < 0.05$) literature reviews show that

compliance decreases with increasing duration of illness [18] analysis of the treatment duration also showed similar results

Analyzing the relationship between expenditure of treatment and compliance (Table 2) it was found that persons who has to spent between Rs.51 and 100 has maximum compliance rates and relationship was highly significant ($P < 0.001$) but on further analysis it was found that they have maximum social support and that could be the reason for increased compliance.

Analysing religious/alternate treatments and compliance (Table 2) rates it was found that people who doesn't go for alternate treatment has maximum compliance rates ($P < 0.05$) it is may be concluded that alternate treatment can lead to treatment subversion.

Analysing depot preparations and compliance (Table 2) rates it was found that people who take depot has less compliance compared to people who are not on depot ($P < 0.01$). There is some evidence that managing patients with depot antipsychotics leads to higher rates of medication adherence. Young and coworkers [19] reviewed 26 studies and found a mean default rate of 25% for depot medications and 41% for oral antipsychotics. A study of patients from urban and rural environments found compliance rates exceeding 90% for both settings. [20] Reason could be that being on depot preparations itself is a sign of poor drug compliance and these people continue the same pattern even when they are on depot preparations.

Analysing the relationship between number of drugs administered and compliance (Table 2) it was found that persons with less number of medicines has more drug compliance then persons with more drugs ($P < 0.001$) in western studies also it was found that complexity of prescription plays a role in compliance. [21] Patients who have complicated treatment regimens- who must take drugs at different times in the day or take two or more different medications - have less compliance.

Psychopathology and compliance- Patients who feel persecuted or are afraid to be poisoned will be reluctant to take medication. On the other hand, it is difficult to convince patients suffering from grandiose delusions or manic symptoms to comply with treatment recommendations [22]. The influence of negative symptoms in schizophrenia patients is controversial:

negative symptoms have been shown to be predictors of both good [23] and bad compliance [24]. Apart from the primary illness, co morbid alcohol or substance abuse is a strong predictor of noncompliance [25-27].

Van Putten [28] identified disease features in schizophrenia that were related to poor treatment adherence and reported that patients who had pleasant delusions, particularly grandiose delusions, were more likely to refuse their medications. Severity of psychopathology can influence treatment adherence. In a study in New York, the severity of psychotic symptoms was the strongest predictor of medication noncompliance [29]. This association is supported by a study by Marder and coworkers, [30] that focused on the related issue of medication refusal. The role of impaired cognition appears to be particularly important

The relationship between positive symptoms and compliance (Table 3) showed that persons with average positive symptoms were more compliant ($P < 0.001$) compared to people with low positive symptom score.

It is possible that people with more positive symptoms may take drugs to get a relief from symptoms compared to persons with low positive symptom scores.

Comparison of negative symptoms with compliance (Table 3) showed that people with average negative symptoms have more compliance rates compared to people with low negative symptom scores ($P < 0.05$) negative symptoms were found to have good and bad relationship with compliance social support further analysis showed that people with average negative symptoms had more social support compared to persons with low negative symptom scores ($P < .001$).

Insight and compliance- Comparing illness insight and compliance (Table 3) it was found that persons with low insight are more complaint compared to persons with high insight ($P < 0.05$) on further analysis it was shown that persons with low insight has more social support than persons with high insight which will explain increase compliance in this group.

Pyne et al [31] found that patients who did not believe they were ill (Who had lack of insight) were more likely to be nonadherent. Adams and Scott [32] found that patients who were noncompliant differed from compliant patients in their understanding of the severity of their illness.

Comparing insight to hallucinations and compliance (Table 3) it was found that people with high insight are likely to be more compliant than persons with low insight ($P < 0.05$) it is possible that persons with high insight take medicines because of their awareness.

Comparing insight to delusions and compliance (Table 3) it was found that people with high insight are likely to be more compliant than persons with low insight ($P < 0.001$) it is possible that persons with high insight take medicines because of their awareness to the delusions.

Comparing insight to blunt affect and compliance (Table 3) it was found that people with medium insight scores to blunted affect i.e. low insight are likely to be more compliant than persons with high insight ($P < 0.001$) persons with a high score in a component like blunted affect (a negative symptom) are less likely to have even the motivation to take drugs.

Comparing total insight scores and compliance (Table 3) it was found that people with high insight are likely to be more compliant than persons with low insight ($P < 0.001$) it is possible that persons with high insight are aware about all components of illness including disturbing hallucinations and delusions and take medicines because of their increased distress with these symptoms.

Social support and compliance- Patients who live alone generally have lower compliance rates, while patients who live in supportive environments where they have people caring for them are more likely to be compliant.^[33] An overly emotional, demanding family or significant others who do not share the patient's positive attitudes toward treatment are common examples of this problem [34].

Analysis of compliance with a social support from significant other (Table 5) showed no statistically significant relationships this finding is very significant because in west there can be a person other than a friend or family member who will be there to help the patient. But in our study such a person was not at all influential in the life of the patient highlighting the importance of family in our socio cultural background. Analysis of compliance with a social support from family (Table 5) showed that persons with high social support from family were more compliant than persons with low social support ($P < 0.001$). Analysis of compliance with

a social support from friends (Table 5) showed no statistically significant relationships. Analysis of compliance with total social support showed that persons with higher social supports were likely to be more compliant than persons with low social support ($P < 0.001$).

Side effects- Van Putten et al [35] were the first to show that side effects that occur early in treatment lead to a substantial impairment of compliance later. An additional problem with treating schizophrenia is that most drugs have a delayed onset of action, so patients do not experience immediate positive effects. To the contrary, patients sometimes experience side effects before intended effects [35]. But other reports have failed to find significant correlations between the advent of side effects and poor compliance [8, 36].

Patients who experience side effects are less likely to take their medications as prescribed [37] Van Putten et al [38] and colleagues found that mild side effects, such as mild subjective akathisia, could result in poor compliance. Grunebaum et al [39] evaluated medication adherence in residential facilities. A negative view of medication—one that is likely to have been derived from side effects—was significantly related to noncompliance

Analysis of psychic side effects scores (Table 6) showed that persons with low side effects are likely to be more compliant than persons with medium side effects scores ($P < 0.05$).

The overall compliance in the study was 62%. Regression analysis (Table 7) showed that Age, sex, Education status, marital status, Occupation, and drugs administered had significant relationships with Compliance

Limitations

1. Cross sectional survey
2. No follow up studies were done
3. Low sample size

Conclusion

It is advisable to use minimum number of drugs for ensuring compliance.

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