A study to assess factors affecting drug-compliance in patients with schizophrenia and bipolar disorder

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Abstract

Introduction: Non – compliance to medication in psychiatric disorders costs enormously to patients and health care system. In order to improve the drug compliance it is important to know the crucial factors responsible for poor drug compliance so that proper management strategies may be planned to improve the compliance.

Aim: To study and compare factors affecting compliance among patients with schizophrenia and bipolar disorder in remission and to study and compare severity of medication induced side effects with compliance.

Materials and Methods: A cross sectional study was done on patients who were attending psychiatry review outpatient department of a tertiary care hospital in an urban city for a duration of six months. Subjects were entered on a semi-structure intake pro-forma, compliance was assessed using Hogan's drug attitude inventory. Severity of side-effects were assessed using LUNSER's scale.

Results: The percentage of compliance was found to be 36% among patients with schizophrenia and 82% among bipolar patients. In schizophrenia patients compliance was significantly associated with marital status (66.6%) (p= 0.0086), urban domicile (65%) (p= 0.011), diagnosis, fear of relapse of illness (71.43%) (p= 0.035224), presence of stigma (57.5%) (p= 0.017), insight (81.81%) (p= 0.000699), family history of mental illness (80%) (p= 0.0307), comorbid chronic medical conditions (93.33%) (p= 0.004) and presence of substance abuse (83.33%) (p= 0.00001).

Among bipolar patients compliance was significantly associated with illness related factors like fear of relapse (97%) (p= 0.000), insight (70.73%) (p= 0.0342), duration of illness less than 5 years (72.41%) (p= 0.005) and in above 45 years age group patients. (45%) (p= 0.01977)

Conclusion: The factors affecting compliance in schizophrenia and bipolar disorder were determined. The study emphasizes need for psycho education about nature of illness and duration of treatment and improvement of community services to the patient.

Keywords: Schizophrenia, Bipolar disorder, Pharmacotherapy, Compliance.

Introduction

Schizophrenia is a severe form of mental illness affecting about 7/1000 adults globally.[1] Although the incidence is low, the prevalence of schizophrenia is high as it is a long term chronic illness. In the past 60 years there has been tremendous improvement in pharmacological treatment of schizophrenia. Antipsychotic medications play an important role in treatment of schizophrenia. Long term treatment is needed to keep symptoms under control and to prevent relapse.[2] The course of schizophrenia, number of relapses, social functioning and final outcome depends on compliance to treatment.[3] In this progressive disease around 60% of patients stop treatment after 2-3 months without consulting the treating physician and after 2 years 80% of patients discontinue treatment.[4] Noncompliance may be the most challenging aspect in treatment of schizophrenia disorder.[5] Data from CATIE trial showed that 74% of patients discontinued medication within 18 months of initiation, due to side effects and insufficient efficacy.[6]

Medication treatment compliance among bipolar disorder patients is also quite widespread. Montoya et al reported 40% of bipolar patients are partially or completely non adherent.[7] Other studies have indicated that 20-70% of bipolar patients are poorly adherent.[8,9] Noncompliance is the frequent cause for relapse in bipolar patients. Ganzalez, pinto et al observes rates of suicide as 5.2 times greater in nonadherent patients than in patients on lithium.[10] Compliance can be defined as the extent to which a person's behavior coincides with medical or health advice.[11] Compliance suggests a passive approach where the patient faithfully follows the advice and directions of health care provider. It denotes a paternalistic point of view of practitioner patient relationship. Adherence is a collaboration between patient and health care provider. Adherence is alternative to compliance which reduces the attribution of greater power to the doctor in doctor patient relationship. It helps in fostering ownership and continuation of treatment decisions by patient.[12] However both terms can be used interchangeably.

Studies have shown that illness related factors like poor insight, side-effects of medicines, poor remission of symptoms, poor therapeutic alliance, stigma associated with illness are associated with non-compliance.[13-17] In Indian studies patient related factors like poor family support, diagnosis of patient, economic factors, distance to hospital, ignorance of patient's family members about illness, comorbid substance abuse were observed as reasons for non-compliance.[18,19]

In an Indian study overall prevalence of non-adherence among patients with mental illnesses was found to be 38%. Of these schizophrenia was 50%, bipolar disorder 33.33% and depression 16%. Younger patients with good social support had good adherence where as those with severe illnesses and who had sedation as side effect of medication were non adherent.[20]

The overall incidence of medication non adherence in patients with mental illness was found to be 43% in one Indian study. There was a significant association between non adherence and education, number of drugs and family income. Patient related factors account for 33.5%, drug related factors contribute for 32% and disease related factors contributed for 31% of non-compliance.[21]

Non adherence is strongly related to relapse, re-hospitalization, self-harming behavior in schizophrenia and bipolar affective disorder. It also results in poor quality of life and financial burden with 40% of total costs of illness being attributed to hospitalization.[22-24]

Hence current study was planned to assess and compare factors affecting compliance to medication among patients with schizophrenia and bipolar disorder and its association with side effects of antipsychotic medications.

Aims

1. To Study and compare the prevalence of compliance to medication in patients with schizophrenia and bipolar affective disorder.
2. To study and compare the factors (patient related and illness related) associated with compliance among study subjects.
3. To study the severity of side-effects of antipsychotic medication in study sample.
4. To study the association between compliance and severity of side-effects of antipsychotic medication.

Material and Methods

A cross sectional and comparative study was conducted in a review op of tertiary care hospital in Hyderabad for 6 months during September 2017- march 2018. By using Convenient sampling method 50 patients of schizophrenia and 50 patients of bipolar disorders were taken for the study. Patients with age above 18 years and below 60 years, having a primary diagnosis of schizophrenia and bipolar affective disorder of both genders, currently under remission as per CGI scale and who are on regular treatment for the past 6 months, with reliable informant were taken as study sample. Patients below 18yrs and above 60 years and those with diagnoses other than two psychotic disorders selected for study, who are suffering from neurotic disorders and who needed urgent medical attention for physical problems are excluded from study. Patients who are mentally retarded (intellectually disabled) or intoxicated, having cognitive impairment and who are without a reliable informant were also excluded from the study.

After taking written informed consent, patients were interviewed along with informant. Study subjects were provided with information regarding nature and purpose of study. Confidentiality was assured and voluntary nature of the study was explained. Those who met inclusion criteria were entered on semi structured intake pro-forma, compliance was assessed using Hogan's drug attitude inventory. Severity of side-effects were assessed using LUNSER's scale. (The Liverpool University side effect rating scale). Modified Kuppuswamy scale was used to assess socioeconomic status.

For the purpose of our studyremission was defined as those patients who were on regular medication for 6 months and scored 2 or less on objective version of CGI-S.

Scales used:

1. **Hogan's Drug attitude inventory:**[25] this 30 item scale is a self-report inventory, rating the patient's attitude to drugs taken. The inventory has been previously used in many studies. It has good reliability and discriminative validity. This instrument includes questions with 15 true and 15 false options in a fully compliant response. A positive total score means a compliance response, a negative total score means a noncompliant response.
2. **Liverpool University Neuroleptic side-effect rating scale:**[26] is a self-rating scale for measuring neuroleptic side effects. It has got good test retest reliability. It is an efficient, valid and reliable method of assessing neuroleptic side effects. The scores are ranging from 0-40 – low, 41-80 - moderate and 81-100 - high.
3. **Clinical global index of severity CGI- S:**[27] scale was used to assess severity of illness. It is a clinician rated scale and rated on how ill patient was at the time of interview on a 7- point scale. 1- normal; 2- borderline mentally ill; 3- mildly ill; 4- moderately ill; 5- markedly ill; 6- severely ill; 7- extremely ill. This rating is based on observed and reported symptoms, behavior and function in the past 7 days.
4. **Modified Kuppuswamy scale:** is commonly used to measure socioeconomic status. It is measured by composite score of education, occupation of head of the family and monthly income of family, yields a score of 3-29. Updated in 2017 by Singh T.[28]

The system adopted by Kaplan and Sadock in their comprehensive text book of psychiatry was used to grade the patient's level of insight. Patient's level of insight out of 6 was graded as follows: absent if less than 3, present if 3 and above 3.[29]

5. **Semi-structured intake pro-forma:** Patient related factors- socio-demographic factors like age, gender, education, marital status, socioeconomic status were taken.

   Illness related factors- duration of illness, treatment, insight, stigma, family history of mental illness, comorbid medical illnesses, substance abuse, fear of relapse were taken.

Statistical analysis

Data was analyzed using statistical package for social sciences (SPSS), for windows, version 19. Chi square analysis was done for variables of interest. P value was set at 0.05.

Results

A total of 100 patients (34% males, 66% females), mean age 27 were enrolled and their demographic characteristics were compared. Equal number of patients with schizophrenia and bipolar disorders were taken for study. Non-compliance rate among patients with schizophrenia was found to be 64% and in bipolar it is 18%. (p value= 0.0001) [Table 1]

Table 1: Showing prevalence of non compliance in schizophrenia and BPAD

Disorder	Compliant (n-59)	Non compliant (n-41)	Chi square	P value
Schizophrenia(N-50)	18 (36%)	32(64%)	21.8685	0.0001 (sig)
BPAD(n-50)	41 (82%)	9(18%)		

Socio-demographic factors of patient related, illness related, medication induced side effects were studied in compliant and noncompliant groups of patients with schizophrenia and bipolar disorder.

Schizophrenia group: Among socio-demographic factors, non-compliance was found significantly in patients who are from rural background (73.68%), (p value= 0.0111) unmarried (71.43%), (p value= 0.0086) divorced and single (46.87%, 37.5%). [Table 2]

Table 2: Socio demographic factors affecting compliance in schizophrenia

Domicile	Compliant (n-18)	Non- Compliant (n-32)	Chi Square	P value
Rural(n-38)	10(26.31%)	28(73.69%)	6.4449	0.0111 (sig)
Urban(n-12)	8(66.66%)	4(33.33%)		
Marital status Married(n-15)	10(66.66%)	5(33.33%)	9.4907	0.0086 (sig)
Unmarried(n-21)	6(28.57%)	15(71.43%)		
Divorced/ (n-14)seperated	2(14.28%)	12(85.17%)		

Among illness related factors- Patients having family history of mental illness (68.89%), (p value= 0.03) fear of relapse (71.43%) (p value= 0.035) and insight into illness (81.81%) (p value= 0.000699) were significantly compliant. Patients who are having multiple physical illnesses (93.33%), (p value= 0.00467) comorbid substance abuse (83.33%), (p value= 0.00001) stigma perceived by patient towards mental illness (87.5%), (p value= 0.017) were associated with non-compliance. [Table 3]

Table 3: Illness related factors affecting compliance in schizophrenia

Family H/O	Compliant (n-18)	Non compliant (n-32)	Chi sqaure	P value
YES(n-5)	4(80%)	1(20%)	4.6682	0.03 (sig)
NO(45)	14(31.11%)	31(68.89%)		
Substance abuse Yes(n-36)	6(16.66%)	30(83.34%)	24.5614	0.00001(sig)
NO(n-14)	12(85.71%)	2(14.29%)		
Any other medical illness YES(n-15)	1(6.67%)	14(93.33%)	8.0026	0.00467 (sig)
NO(n-35)	17(48.57%)	18(51.43%)		
Medication induced side effects Low(n-18)	17(36.17%)	30(63.82%)	0.0099	0.920941
Medium(n-32)	1(33.33%)	2(66.66%)		
Stigma Yes(n-16)	2(17.5%)	14(87.5%)	5.6398	0.017 (SIG)
NO(n-34)	16(47.05%)	18(52.94%)		
Fear of relapse Yes(n-7)	5(71.42%)	2(28.58%)	4.4343	0.035224 (SIG)
NO(n-43)	13(30.23%)	30(69.76%)		
Insight Present(n-11)	9(81.81%)	2(18.19%)	11.4929	0.000699(sig)
Absent(n-39)	10(25.64%)	29(74.36%)		

In subjects with bipolar disorder, the compliance was significantly associated with age more than 45 years (p value= 0.01977) [table 4] and among illness related factors, fear of relapse (97.36%) (p value= 0.000) duration of illness <5 years (72.41%) (p value= 0.005) and insight. (70.73%) (p value= 0.034) [Table 5]

Table 4: Socio demographic factors affecting compliance in BPAD

Age	Compliance	Non compliance	Chi- square	P value
18- 30	9(22.5%)	1(10%)	7.8464	0.01977 (SIG)
31-44	12(30%)	8(80%)		
>45	19 (45%)	1(10%)		

Table 5: Showing Illness Related Factors Affecting Compliance In BPAD

Insight Present(n-41)	29(70.73%)	12(29.26%)	4.48	0.034293(sig)
Absent(n-9)	3(38.33%)	6(66.66%)		
Duration of illnes< 5yrs(n-29)	21(72.41%)	8(38.09%)	10.6966	0.005(sig)
5-10yrs(n-12)	7(24.13%)	5(23.80%)		
>10yrs(n-9)	1(3.44%)	8(38.09%)		
Fear of relapse Yes(n-38)	37(97.36%)	1(2.64%)	25.3864	0.000 (SIG)
No(n-12)	4(33.33%)	8(66.66%)		

Medication compliance was found to be significantly associated with diagnosis of bipolar disorder. (82%) (p= 0.00001).

Table 6: Medication induced side effects affecting compliance in BPAD

Medication side effects Low(n-43)	35(81.39%)	8(18.61%)	1.311	0.1600 (non sig)
Medium(n-7)	6(85.71%)	1(14.29%)		

Among bipolar group patients, the association between compliance to medication and severity of medication induced side effects was not statistically significant.

Discussion

Our study has found higher percentage of non-compliance in schizophrenic group (64%) compared to bipolar group (18%). The association between clinical diagnosis and non-compliance was statistically significant. Non-compliance rates of schizophrenic group reported in previous published studies were 40-50% which is slightly less than our study.[30,12] In bipolar group it was similar to our study10-60%.[31]

In schizophrenia group, patient related socio demographic factors associated with compliance were marital status and domicile. Married study subjects were more compliant to treatment than unmarried, divorced, separated patients. The reason may be because of support and care they get from spouses which is lacking in unmarried, divorced and single patients. This is in agreement with a study by Srinivas Murthy and Rabinovitch.[32,33] Patients from urban areas were more compliant than from rural areas. The reason for this may be better availability and accessibility to medical facilities in urban areas.

Other socio demographic factors associated with compliance were male gender, age more than 40 years, educated up to tenth standard, high socioeconomic status, though not statistically significant. This is in consonance with Buchnan study in which socio demographic factors did not influence compliance.[34] Our study is in contrast to other Indian studies in which age above 40 years, illiteracy, female gender, low socioeconomic status were found to be associated with non-compliance.[14,18]

Illness related factors associated with non-compliance in schizophrenia patients were family history of mental illness, fear of relapse, comorbid multiple substance abuse, stigma perceived by patient towards illness. Compliance was better in patients having family history of mental illness (80%) than those who don't. This may be because those who had family history were aware of nature and consequences of mental illness, about need to continue treatment, possibility of relapse in the event of cessation of treatment. This is in contrast to study by Rao KN, family history of mental illness didn't affect compliance.[14] Noncompliance was associated with stigma of patient towards mental illness (57.5%), this is in consonance with previous studies.[35]

Having high physical comorbidity was associated with poor compliance. Patients tend to neglect mental illness when they have comorbid physical illness (93.33%) leading to poor complianceThis is in agreement with Rao KN study.[14] Compliance was better in those who had fear of relapse and thus take medication regularly. (71.43%)

Medication induced side-effects were also found to be barrier for compliance in previous studies. Our study

also found that mild severity of side-effects were predominantly seen in compliant group (94%), moderate severity in noncompliant group but the was not statistically significant in both groups. (Table 3&6) This is in contrast with studies by Sultan, Roy and Moritz who found side effects of medication was associated with noncompliance.[18,19,35]

Presence of stigma in patients towards mental illness was found to be associated with noncompliance. Stigma has been reported to play a major role in compliance by studies done in past by Moritz, Lang.[16] Noncompliance was associated significantly with presence of substance abuse, (83.33%)the reason may be patientsmissing their appointments and hence non-compliant. This is in line with Spar study.[17]

Bipolar disorder

Age was the only patient related socio demographic factor associated significantly with compliance in bipolar group. Age above 45years group was found to be associated with compliance. The reason for this may be younger patients (18-45 years) may have negative perception of medication, think medications are harmful and feel that they can manage themselves without medication. This is in line with study by Berk who stated that young age affects compliance negatively in patients with bipolar.[36] In contrast to our study, age did not affect compliance in a study by Dolder.[37] While study by Mann reported better compliance in younger age group of patients.[38]

Among illness related factors, fear of relapse was associated with compliance in bipolar group. Compliance was statistically significantly associated with fear of relapse. The reason for this may be patients comply with treatment if they are aware of nature of illness, duration of treatment and possibility of relapse in the event of cessation of treatment. This is in line with studies by Moritz and Lang.[35] But our study is in contrast to Nagaraj Rao study, who found a less role of fear of relapse in compliance.[14]

Presence of insight was significantly associated with compliance to medication. This is in line with Fenton and Roy study.[13,19] Duration of illness less than 5 years was associated with good compliance.

Among schizophrenia group patient's good compliance was associated statistically significantly with marital status, urban background, presence of insight, fear of relapse of illness and family history of mental illness. Non-compliance was associated with presence of stigma, other chronic medical illness and presence of substance abuse. Factors associated with medication compliance in bipolar group were age more than 45 years, insight, fear of relapse and duration of illness.

Strengths of our study: Side effects of medication and compliance were assessed using standardized rating scales. Results must be interpreted in view of draw backs and limitations of our study, they are:

1. Size of sample was small so inferences cannot be made
2. Study was done in tertiary care hospital where refractory cases are present,
3. Study design was cross sectional,
4. Stigma was not assessed by using standardized scales,
5. Compliance was assessed using patient's version, which is subjected to recall bias.

Conclusion

Studies involving larger sample size with longitudinal study design and done at one or two centers could throw more insight into factors associated with compliance to treatment.

Poor compliance is related to illness related factors like insight which has to be addressed to reduce noncompliance. The fact that those with positive family history and fear of relapse are associated with good compliance to treatment, this emphasizes need to address ignorance of patients about illness. There is comorbid physical illness and comorbid substance abuse among study subjects which is hindering compliance. There is every need to detect and adequately manage both the issues. This study emphasizes the need for taking steps like psycho-education to patients and caregivers about nature of illness and need to continue treatment.

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