

Research Article

Factors affecting adherence in patients with schizophrenia

Mohd A. Siddiqui^{1*}, Amrit Patojoshi², Christoday R.J. Khess³

¹Department of Psychiatry, Era's Lucknow Medical College & Hospital, Lucknow, UP, India

²Department of Psychiatry, Hi tech Medical College, Pandara, Bhubhaneshwar, Orissa, India

³Department of Psychiatry, Central Institute of Psychiatry, Ranchi, Jharkhand, India

Received: 02 December 2015

Revised: 05 December 2015

Accepted: 09 December 2015

*Correspondence:

Dr. Mohd Aleem Siddiqui,

E-mail: docaleem@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Nonadherence with medication regimens is among the most common causes of psychotic relapse and the need for rehospitalisation. This study was designed to look into the factors affecting attitude towards medication adherence in Schizophrenia and its relationship with severity of illness, side effects of medication.

Methods: Adult males and females in the age range of 18-55 years fulfilling criteria for schizophrenia according to ICD – 10, DCR, and reporting at outpatient department were taken up for this study. Severity of illness was assessed by Brief Psychiatric Rating Scale (BPRS), Side effects to medication were assessed by Udvalg for Kliniske Undersogelser (UKU) side effect scale, and Adherence was assessed by Medication adherence rating scale (MARS).

Results: Adherence negatively correlated with severity of illness, and side effects in the form of increased sleep duration, asthenia, increased fatigability, lassitude and diminished sexual desire. Regression analysis with MARS as dependent variable showed side effects of medication in the form of increased sleep duration in followed by asthenia, lassitude, and increased fatigability to be predictors of poor adherence in the sample.

Conclusions: Poor adherence is associated with severity of schizophrenia, sedation and asthenia like side effects due to medication. Sedation and asthenia like side effects caused a decline in adherence.

Keywords: Adherence, Medication side-effects, Schizophrenia

INTRODUCTION

Schizophrenic illnesses are typically long term illnesses. Nonadherence to medication can lead to relapse, which can mean more visits to the emergency room, rehospitalizations and increased need for clinician intervention – all of which lead to increased costs to healthcare systems.¹

Rates of non-compliance in psychotic disorders have been reported to vary from 11 to 80% and in most of the cases it would result in relapse.^{2,3} Nonadherent patients have an average risk of relapse that is 3.7 times greater than that of adherent patients.⁴ As per World Health Organization (WHO) estimates the median treatment gap

for schizophrenia, including other non-affective psychosis, was 32.2 % and so the poor adherence results in wastage and under utilization of already limited treatment resources and compounds the challenges of improving health in poor populations.⁵ Weiden and Olfson found that nonadherence in schizophrenia accounted for about 40% of the annual costs of rehospitalization.⁶ Johnson et al, reported that patients with schizophrenia who experienced a relapse did not return to their pre relapse level of social adjustment 1 year after recovery, implying that the cost of relapse is much greater than just the cost of rehospitalization.⁷ The cost of relapse may be particularly severe for patients with jobs and family responsibilities since they have the most to lose. Knowledge of how to improve adherence

could contribute as much to treatment as introduction of neuroleptics itself did.⁸

The term 'adherence' has been defined as the extent to which a person's behavior coincides with medical or health advice.⁹ It is conceptualized as a continuum and recognizes that self-care behaviors are essentially decisions made by the individual based upon the information provided by the health care professionals. Adherence must involve multiple indicators of self-care, not judged solely upon one specific or problematic behavior.

World Health Organization in 2003 has adopted the following definitions of adherence to long-term therapy "the extent to which a person's behavior – taking medication, following a diet and / or executing life style changes corresponds with agreed recommendation from a health care provider".¹⁰

Five dimensions of adherence have been discussed below.¹⁰

- Socio economic factors
- Therapy related factors
- Patient related factors
- Illness related factors
- Health care team and system related factors

METHODS

In this study, we tried to see the factors affecting medication adherence in Schizophrenia and whether there was any relationship between severity of illness, side effects of medication and medication adherence in Schizophrenia.

This study was conducted at the Central Institute of Psychiatry (CIP), Ranchi, India. CIP is a postgraduate teaching hospital and imparts training in psychiatry, clinical psychology, psychiatric social work and psychiatric nursing. It has bed strength of 643 and a wide catchment area. The study was approved by the institutional ethics committee.

It was a cross sectional study with the sampling being purposive, where subjects were assessed for attitude towards adherence. 60 Adult patients in the age range of 18-55 years and fulfilling criteria for schizophrenia according to ICD – 10, DCR reporting for follow up at CIP OPD were taken up for the study. Those with comorbid mental retardation, personality disorder and general medical illnesses (requiring additional treatment) were excluded.

Informed consent was taken from them. Socio demographic profiles of all patients were carefully noted in a specially designed data sheet which also includes treatment history, cost & availability of medication.

Severity of illness was assessed by Brief Psychiatric Rating Scale (BPRS). It is an observer rated scale developed by Overall & Gorham.¹¹ The manual consists of an interview module, symptoms definitions and specific anchor points for rating symptoms, 24 item scale would be used where items 11-18, 23-24 are based on patient's behavior during the interview period & the time frame for rest of the items is past two weeks. Each item is rated on 7 point severity scale rating from "not present" to "extremely severe".

Side effects to medication were judged by Udvalg For Kliniske Undersogelser (UKU) side effect scale. According to Lingjaarde et al it is an observer rated scale which has three parts, single symptoms rating scale, scale for global assessment, and for stating consequences of side effect. For statistical analysis patients with a score of one or more on any item of UKU side effect rating scale is considered.¹²

Attitude towards Adherence was judged by Medication adherence rating scale (MARS) by Thomson.¹³ This scale is based on two already existing self-report measures of compliance. The first is the Drug Attitude Inventory (DAI) and the second is the Medication Adherence Questionnaire (MAQ).^{14,15} These compliance measures have been combined to produce a compliance scale. The MARS consists of 10 items which require yes/no responses. A total score will then reflect a greater degree of compliance if it is high, and non-compliance if it is low.

RESULTS

The mean age of the participants was 31.58 (SD ± 7.75) years. Male participants were about four times i.e. 49 (81.7%) as compared to the 11 females. 24 (40%) were living without a partner and 36 (60%) were with a partner. Most of them were unemployed (n=27, 45.1%), while 20 (33.3%) were doing skilled/semiskilled jobs, 9 (15%) were house wives, 2 (3.3%) were professionals and 2 (3.3%) were students.

Mean age of onset of illness was 23.2 (SD ± 7.09) years. Mean duration of illness was 8.31 (SD ± 5.9) years. Maximum 35 (58.3%) were diagnosed as having Paranoid schizophrenia, while 23(38.3%) were suffering from Undifferentiated schizophrenia and 1 (1.7%) each had Catatonic and Hebephrenic schizophrenia. 22 (36.7%) had a family history of psychiatric illness and 1 (1.7%) had family history of medical disorders. Substance abuse was present in 6 (10.0%) of the sample.

With regards to medication 22 participants (36.7%) were on atypical antipsychotics along with additional medication (defined as any medication except typical and atypical antipsychotic which also included anticholinergics), 16 (26.7%) were on atypical along with typical antipsychotics and additional medication, 12 (20%) were on only atypical antipsychotics, 6 (10.0%)

were on typical antipsychotic along with additional medications. 2 (3.3%) were on only typical antipsychotics and 2 (3.35) were on no medication. Medications were given under supervision in 43 (71.7%) while they were unsupervised in 17 (28.3%). Mean duration of treatment was 5.04 (SD \pm 5.02) years.

Attitude towards Medication adherence was rated by using Medication Adherence Rating Scale (MARS) which had a mean score of 7.63 (SD \pm 1.90) out of a possible score of 0-10. Median score was 8.00 which was taken as cut off for good adherence with those scoring 7 or below were considered as having poor adherence.

Table 1: Correlation of medication adherence with severity of illness and side effects of medication.

		BPRS Total score	UKU Psychic Side Effects Total Score	UKU Neurologic Side Effect Total Scores	UKU Autonomic Side Effects Total Score	UKU Other Side Effects Total Score	UKU Side Effects Total Score
MARS	Pearson Correlation	-.277(*)	-.591(**)	-.040	.067	-.271(*)	-.438(**)
	Significance (2-tailed)	.032	.000	.761	.611	.036	.000
	N	60	60	60	60	60	60

* significance at less than 0.5 p value; It was found that adherence *negatively correlated* with BPRS total score, and Psychic Side Effect Subscale and Other Side Effects Subscale of the UKU Side Effect Rating Scale and the Total score of UKU.

Table 2: Frequency distribution of psychic side effect subscale of the uku side effect rating scale.

	Score	Frequency	Percent	Cumulative Percent
UKU1.1	.00	58	96.7	96.7
	1.00	2	3.3	100.0
	Total	60	100.0	
(UKU 1.2)* Asthenia, Increased Fatigability, Lassitude	.00	48	80.0	80.0
	1.00	11	18.3	98.3
	2.00	1	1.7	100.0
	Total	60	100.0	
UKU1.3	.00	58	96.7	96.7
	1.00	1	1.7	98.3
	2.00	1	1.7	100.0
	Total	60	100.0	
UKU1.4	.00	56	93.3	93.3
	1.00	4	6.7	100.0
	Total	60	100.0	
UKU1.5	.00	58	96.7	96.7
	1.00	2	3.3	100.0
	Total	60	100.0	
UKU1.6	.00	58	96.7	96.7
	1.00	2	3.3	100.0
	Total	60	100.0	
UKU1.7* Increased Sleep Duration	.00	47	78.3	78.3
	1.00	12	20.0	98.3
	3.00	1	1.7	100.0
	Total	60	100.0	
UKU1.8	.00	60	100.0	100.0
UKU1.9	.00	60	100.0	100.0
UKU1.10	.00	59	98.3	98.3
	1.00	1	1.7	100.0
	Total	60	100.0	

Table 2 shows the frequency distribution of Psychic Side Effect Subscale of the UKU Side Effect Rating Scale and it revealed maximum occurrence of Increased Sleep Duration (UKU 1.7) in 13 (21.7%) of the participants followed by Asthenia, Increased Fatigability, Lassitude (UKU 1.2) in 12 (20%) of the participants.

Table 3: Frequency distribution of other side effects subscale of the UKU side effect rating scale (UKU 4.1–UKU 4.19).

	Score	Frequency	Percent	Cumulative Percent
UKU4.1	.00	60	100.0	100.0
UKU4.2	.00	60	100.0	100.0
UKU4.3	.00	58	96.7	96.7
	1.00	2	3.3	100.0
	Total	60	100.0	
UKU4.4	.00	59	98.3	98.3
	1.00	1	1.7	100.0
	Total	60	100.0	
UKU4.5	.00	55	91.7	91.7
	1.00	5	8.3	100.0
	Total	60	100.0	
UKU4.6	.00	60	100.0	100.0
UKU4.7	.00	60	100.0	100.0
UKU4.8	.00	60	100.0	100.0
UKU4.9	.00	60	100.0	100.0
UKU4.10	.00	60	100.0	100.0
UKU4.11	.00	60	100.0	100.0
UKU4.12* Diminished Sexual Desire	.00	51	85.0	85.0
	1.00	8	13.3	98.3
	2.00	1	1.7	100.0
	Total	60	100.0	
UKU4.13	.00	54	90.0	90.0
	1.00	3	5.0	95.0
	2.00	1	1.7	96.7
	3.00	2	3.3	100.0
	Total	60	100.0	
UKU4.14	.00	58	96.7	96.7
	1.00	1	1.7	98.3
	2.00	1	1.7	100.0
	Total	60	100.0	
UKU4.15	.00	59	98.3	98.3
	1.00	1	1.7	100.0
	Total	60	100.0	
UKU4.16	.00	60	100.0	100.0
UKU4.17	.00	59	98.3	98.3
	1.00	1	1.7	100.0
	Total	60	100.0	
UKU4.18	.00	60	100.0	100.0
UKU4.19	.00	60	100.0	100.0

Table 3 shows frequency distribution of Other Side Effect Subscale of the UKU Side Effect Rating Scale and it revealed that the most frequently reported item was Diminished Sexual Desire (UKU 4.12) in 9 (15%) of the participants.

Chi square test was applied to the socio demographic variables and it showed no significant association of adherence to marital status, religion, educational level or occupation, however a trend was seen as females having poorer adherence as compared to males but this also did not amount to being statistically significant, family income, background of patients and type of family, type of schizophrenia, past history, family history, substance abuse, type of medication or its route of administration, cost of medication, its availability, and whether they

were given under supervision or not and regularity of previous follow ups.

Correlation of Medication Adherence (assessed by MARS) was tested with Severity of Illness (assessed by total score of brief psychiatric rating scale (BPRS) and Side effects of medication (UKU side effect rating scale).

It was found that adherence negatively correlated with BPRS total score, and psychic side effect subscale and

Other Side Effects Subscale of the UKU Side Effect Rating Scale and the Total score of UKU, while it was not correlated with Neurological and Autonomic Side Effect Subscale of UKU scale as shown in Table 1.

As shown in Table 2, the frequency distribution of Psychic Side Effect Subscale of the UKU Side Effect Rating Scale revealed maximum occurrence of Increased Sleep Duration (UKU 1.7) in 13 (21.7%) of the participants followed by Asthenia, Increased Fatigability, Lassitude (UKU 1.2) in 12 (20%) of the participants.

Table 3 shows frequency distribution of Other Side Effect Subscale of the UKU Side Effect Rating Scale and it

revealed that the most frequently reported item was Diminished Sexual Desire (UKU 4.12) in 9 (15%) of the participants.

Table 4 shows Regression analysis with MARS taken as dependent variable and its relation to severity of psychopathology and side effects of medication, which showed UKU Psychic Side Effect Subscale as the predictor variable (Beta = - .591, Significance = 0.000), thus showing side effects of medication in the form of Increased Sleep Duration in 13 (21.7%) followed by Asthenia/ Lassitude/ Increased Fatigability in 12 (20%) of the participants to be a predictor of poor adherence in the sample.

Table 4: Regression analysis to see the relationship of medication adherence with clinical variables, severity of illness and side effects of medication.

	Beta	t	Sig.
Age	-.017(a)	-.156	.877
Age at onset of illness	-.172(a)	-1.649	.105
Duration of illness	.192(a)	1.810	.076
Treatment duration	.185(a)	1.736	.088
BPRS total	-.167(a)	-1.563	.124
UKU Psychic Side Effect total	-.591	-5.579	.000*
UKU Neurologic side effect total	.091(a)	.839	.405
UKU Autonomic side effect total	.071(a)	.668	.507
UKU Other side effect total	-.148(a)	-1.373	.175
UKU Total	-.055(a)	-.374	.710

a = Predictors in the Model: (Constant), UKU Psychic SE total; b =Dependent Variable: MARS;*significant at less than 0.5 p value. Table 4 shows Regression analysis with MARS taken as dependent variable and its relation to severity of psychopathology and side effects of medication, which showed UKU Psychic Side Effect Subscale as the predictor variable (Beta = - .591, Significance = 0.000). This can be elaborated (as in Table 2) the side effects of medication in the form of Increased Sleep Duration in 13 (21.7%) followed by Asthenia/ Lassitude/ Increased Fatigability in 12 (20%) of the participants to be a predictor of poor adherence in the sample.

DISCUSSION

As mentioned earlier, the rates of non-compliance in psychotic disorders have been reported to vary between 11% to 80%^{2,3} and in our study it was 36.7%. This study revealed no significant association of adherence to sociodemographic variables. In literature also it is opined that socio-demographic factors are the least rewarding of the predictors of compliance.^{16,17} Diagnosis of substance abuse did not correlate significantly with nonadherence in our sample. In some studies it has been considered one of the most important reasons for nonadherence (substance abuse seems to be a strong predictor of non-compliance in psychosis¹⁸ while in others it did not play a major role but any definitive conclusion should not be drawn as in our study incidence of substance abuse was 10%, while in others where it has been found significant, the incidence was more than 30%.¹⁹

It was found that adherence correlated negatively with BPRS total score. There is past evidence that severity of

psychopathology can influence treatment adherence. Disorganization and cognitive disturbances are additional symptoms of schizophrenia that interfere with regular intake of medication.^{20,21} In a study of consecutive admissions to a day care program in New York, the severity of psychotic symptoms was the strongest predictor of medication noncompliance.²² This association is also supported by a study by Marder and coworkers that focused on the related issue of medication refusal.²³

No significant difference was observed between use of typical and atypical antipsychotic on adherence. Study by Shepherd who analyzed prescription refill records for patients taking older antipsychotics and atypical antipsychotics noted that patients who received older drugs were without medications for an average of 7 days per month compared with 4 days per month among those receiving newer drugs, suggesting a small advantage for the new drugs.²⁴ Another study failed to find a significant difference favoring atypical antipsychotics, although there was a nonsignificant advantage for the newer

agents.²⁵ Dolder et al also did not find significant differences in antipsychotic adherence among patients prescribed typical versus atypical agents.²⁶ So far the evidence regarding atypical antipsychotics and better compliance in schizophrenia has been inconclusive.^{27,28}

No significant difference was seen between oral and depot injectables on adherence, however from previous studies there is some evidence that managing patients with depot antipsychotics leads to higher rates of medication adherence. Young and coworkers found a mean default rate of 25% for depot medications compared with 41% for oral antipsychotics.²⁹ Weiden and colleagues found that inpatients with a history of noncompliance that were switched to a depot agent had higher rates of medication compliance at 1 month than patients who remained on treatment with oral medication.⁶ However, this difference was not statistically significant by 6 and 12 months, that is the benefit of depot medication, did not hold over time. And in our sample mean duration of illness was 8.31 (SD \pm 5.9) years which could have accounted for this result.

It was found that adherence correlated negatively with Psychic Side Effect Subscale and Other Side Effects Subscale of the UKU Side Effect Rating Scale. Frequency distribution revealed maximum occurrence of Increased Sleep Duration in 13 (21.7%) of the participants followed by Asthenia, Increased Fatigability, Lassitude in 12 (20%) of the participants. Among Other Side Effect Subscale of the UKU rating scale the most frequently reported item was Diminished Sexual Desire in 9 (15%) of the participants. From previous studies atypical antipsychotic agents have shown superiority over conventional antipsychotic drugs by producing less extra-pyramidal side-effects and enhancing cognitive functioning.³⁰⁻³² Patients that experience side effects are less likely to take their medications as prescribed.³³ This is particularly true for side effects that are uncomfortable to the patient and result in dysphoric responses. Van Putten and colleagues also found that mild side effects, such as mild subjective akathisia, could result in poor compliance when patients experience discomfort every waking hour.³³ There is a general notion that unwanted side effects have a negative influence on compliance.^{34,35} Also there are reports that some patients discontinue prescribed neuroleptic medicines because of side effects such as sexual dysfunction, sedation, or extra pyramidal symptoms.³⁶ More earlier studies have emphasized on extra pyramidal side effects and later studies on sedation and sexual side effects. In our study 39 patients (65%) were on anticholinergic medications in addition to antipsychotics, and most were on olanzapine or clozapine which may have led to lesser frequency of extra pyramidal side effects, therefore sedation and lassitude became more important in our patient sub group. Negative attitudes towards antipsychotic medication predict non-compliance and diminished sexual desire after taking medication can lead to formation of negative attitude to it thus affecting adherence.^{37,38,4}

Regularity of follow ups did not have a bearing on adherence in our sample; while it has been noted that having regular visits to a psychiatrist was correlated with good adherence. A possible inference from that result is that regular visits to a psychiatrist serve as a protective factor against nonadherence. Not visiting a psychiatrist might be viewed as just another aspect of nonadherence which may have been excluded, making this a limitation of our study.⁷

CONCLUSION

We found out attitude towards adherence correlated negatively to severity of illness and side effects in the form of increased sleep duration, asthenia, increased fatigability, lassitude and diminished sexual desire. Increased sleep duration followed by asthenia, lassitude, increased fatigability came out as predictors of poor adherence in our patient sub population

The limitations of present study were that the sample size was relatively small. Not visiting a psychiatrist might be viewed as just another aspect of nonadherence which may not have been highlighted in our single contact hospital based study as these patients would not have been included in this study. Any measure of self-reported compliance such as Medication adherence rating scale which was used in our study overestimates compliance by approximately 30%.

Future studies should consider a larger sample size. Patients not reporting to hospital can be included by conducting a study in the community which could be more informative than only hospital based study. Self-reported measures of compliance can be improved by combining it with other measures as biochemical and physiological measures, pill counts and electronic medication monitoring. Assessment of therapist related parameters will add to the fund of information.

ACKNOWLEDGEMENTS

The authors would like to thank all the participants who took part in the study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

- Haddad PM, Brain C, Scott J. Nonadherence with antipsychotic medication in schizophrenia: challenges and management strategies. *Patient Related Outcome Measures.* 2014;5:43–62.
- Kane JM. Compliance issues in outpatient treatment. *J Clin Psychopharmacol.* 1985;5(Suppl 3):S22-7.

3. Ayuso-Gutierrez JL, del Rio Vega JM. Factors influencing relapse in the long-term course of schizophrenia. *Schizophr Res.* 1997;28:199-206.
4. Fenton WS, Blyler CR, Heinssen RK. Determinants of medication compliance in schizophrenia: empirical and clinical findings. *Schizophr Bull.* 1997;23:637-51.
5. Kohn R, Saxena S, Levav I, Saraceno B. World Health Organisation: The treatment gap in mental health care. 2004;82(11):858-66. Accessed 12 October 2015.
6. Weiden PJ, Olfson M. Cost of relapse in schizophrenia. *Schizophr Bull.* 1995;21:419-29.
7. Johnson DAW, Pasterski JM, Ludlow JM, Street K, Taylor RD. The discontinuance of maintenance neuroleptic therapy in chronic schizophrenic patients: drug and social consequences. *Acta Psychiatr Scand.* 1983;67:339-52.
8. Kissling W. Compliance, quality assurance and standards for relapse prevention in schizophrenia. *Acta Psychiatrica Scandinavica.* 1994;89(Suppl):16-24.
9. McNabb WL. Adherence in diabetes: Can we define it and can we measure it? *Diabetes Care.* 1997;20, 215-8.
10. World Health Organization: Adherence to long-term therapies: Evidence for action. Geneva, Switzerland http://www.who.int/chp/knowledge/publications/adherence_introduction.pdf. Accessed on 25 October, 2015.
11. Overall JE, Gorham DP. The brief psychiatric Rating Scale (BPRS) recent development in ascertainment and scaling. *Psychopharmacology Bulletin.* 1988;24(1):97-117.
12. Lingjaerde O, Ahlofors UG, Bech P, Dencker SJ, Elgen K. The UKU Side Effect Rating Scale. A New Comprehensive Rating Scale for Psychotropic Drugs and a Cross-Sectional Study of Side Effects in Neuroleptic Treated Patients". *Acta Psychiatr Scand Suppl.* 1987;334:1-100.
13. Thompson K, Kulkarni J, Sergejew AA. Reliability and validity of a new medication adherence rating scale (MARS) for the psychoses. *Schizophrenia Research.* 2000;42(8):241-7.
14. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug. *Psychol Med.* 1983;13(1):177-83.
15. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care.* 1986;24(1): 67-74.
16. Blackwell B. Commentary –the drug defaulter. *Clinical Pharmacology and Therapeutics.* 1972; 13:841-50.
17. Conelly CE, Devenport YB. Adherence to treatment in lithium carbonate clinic. *Arch Gen Psychiatry.* 1982;39:585-8.
18. Miner CR, Rosenthal RN, Hellerstein DJ, Muenz LR. Prediction of compliance with outpatient referral in patients with schizophrenia and psychoactive substance use disorders. *Arch Gen Psychiatry.* 1997;54:706-12.
19. Robinson DG, Woerner MG, Alvir JM, Bilder RM, Hinrichsen GA, Lieberman JA. Predictors of medication discontinuation by patients with first-episode schizophrenia and schizoaffective disorder. *Schizophrenia Research.* 2002;57:209-19.
20. Babiker IE. Noncompliance in schizophrenia. *Psychiatric Developments.* 1986;186:329-37.
21. Bebbington PE. The content and context of compliance. *International Clinical Psychopharmacology.* 1995;9(suppl 5):41-50.
22. Corriss DJ, Smith TE, Hull JW, Lim RW, Pratt SI, Romanelli S. Interactive risk factors for treatment adherence in a chronic psychotic disorders population. *Psychiatry Res.* 1999;89:269-74.
23. Marder SR, Mebane A, Chien CP, Winslade WJ, Swann E, Van Putten TA. Comparison of patients who refuse and consent to neuroleptic treatment. *American Journal of Psychiatry.* 1983;140:470-2.
24. Shepherd J. Tomorrow's world: atherosclerosis in the year 2000. *Neth J Med.* 1997;50:221-7.
25. Olfson M, Mechanic D, Hansell S, Boyer CA, Walkup J, Weiden PJ. Predicting medication noncompliance after hospital discharge among patients with schizophrenia. *Psychiatr Serv.* 2000; 51:216-22.
26. Dolder CR, Lacro JP, Dunn LB, Jeste DV. Antipsychotic medication adherence: is there a difference between typical and atypical agents? *American Journal of Psychiatry.* 2002;159:103-8.
27. Allison DH, Casey DE. Antipsychotic-induced weight gain: a review of the literature. *J Clin Psychiatry.* 2001;62(Suppl 7):22-31.
28. Chakos M, Lieberman L, Hoffman E, Bradford D, Sheitman B. Effectiveness of second-generation antipsychotics in patients with treatment-resistant schizophrenia: a review and meta-analysis of randomized trials. *Am J Psychiatry.* 2001;158:518-26.
29. Young JL, Zonana HV, Shepler L. Medication noncompliance in schizophrenia: codification and update. *Bull Am Acad Psychiatry Law.* 1986;14:105-22.
30. Leucht S, Pitschel-Walz G, Abraham D, Kissling W. Efficacy and extrapyramidal side-effects of the new antipsychotics olanzapine, quetiapine, risperidone, and sertindole compared to conventional antipsychotics and placebo. A meta-analysis of randomized controlled trials. *Schizophr Res.* 1999;35:51-68.
31. Geddes J, Freemantle N, Harrison P, Bebbington P. Atypical antipsychotics in the treatment of schizophrenia: systematic overview and meta-regression analysis. *Br Med J.* 2000;321:1371-6.
32. Meyer PS, Bond GR, Tunis SL, McCoy ML. Comparison between the effects of atypical and traditional antipsychotics on work status for clients in a psychiatric rehabilitation program. *J Clin Psychiatry.* 2002;63:108-16.

33. Van-Putten T. Why do schizophrenic patients refuse to take their drugs? *Arch Gen Psychiatry*.1974;31:67–72.
34. Van-Putten T, May PRA, Marder SR. Response to antipsychotic medication: The doctors and the consumer's view. *American Journal of Psychiatry*. 1984;141:16-9.
35. Marder SR, May PRA. The benefits and limitations of neuroleptics and other forms of treatment in schizophrenia. *American Journal of Psychotherapy*. 1986;40:357-69.
36. DelCampo EJ, Carr CF,Correa E. Rehospitalized schizophrenics: What they report about illness, treatment and compliance. *Journal of Psychosocial Nursing and Mental Health Services*.1983;21(6):29-33.
37. Falloon LR. Developing and maintaining adherence to long-term drug-taking regimens. *Schizophr Bull*. 1984;10:412-7.
38. Ludwig W, Huber D, Schmidt S, Bender W, Greil W. Assessment of compliance related attitudes in psychiatry. A comparison of two questionnaires based on the Health Belief Model. *Soc Psychiatry Psychiatr Epidemiol*. 1990; 25:298-303.

Cite this article as: Siddiqui MA, Patojoshi A, Khess CRJ. Factors affecting adherence in patients with schizophrenia. *Int J Adv Med* 2016;3:25-32.