PARTIAL ADHERENCE WITH ANTIPSYCHOTIC MEDICATIONS AND FACTORS RELATED TO MEDICATION RELAPSE IN JORDANIAN PATIENTS WITH SCHIZOPHRENIA

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Abstract

Objectives and aim: Partial adherence with antipsychotic medications increases the relapse rate in patients with schizophrenia. The aim of the present study is to assess the frequency of and factors contributing to partial adherence.

Method: During May 2012, psychiatrists working in a psychiatric hospital in Amman- Jordan were asked to participate in a compliance study. They were requested to evaluate the compliance of patients with schizophrenia using a questionnaire consisting of 11 questions. The frequency of unintentional and intentional partial adherence as well as patient-related factors contributing to relapse was assessed. Demographic data of participants were collected and the responses of patients were analyzed using descriptive statistics.

Results: The psychiatrists regarded 74%of the evaluated patients as unintentionally partially adherent, 40% of the patients were intentionally partially adherent with medication throughout the study period. The most frequently assessed patient-related factors contributing to partial adherence were denial of illness (80%),lack of or insufficient information about their disease and medication(74.9%/73.7%),needing someone to remind them to take their medication(74.3%), side-effects related causes (64.8%), the cost of medication (63.1%), and long duration and complexity of regimen(60.9%).

Keywords: Schizophrenia, adherence, antipsychotic, partial compliance

Backgrounds and literature

Schizophrenia is a severe psychiatric (Garzya, et al., 2007) chronic and disabling illness (Kazadi et al., 2003) that has around 1% lifetime risk and affects young age group. Half of those individuals, their illness will be lifelong, probably requiring long-term medication (Lean et al., 2003) and has a life time prevalence of 4.0/1000 individuals worldwide (Stip et al., 2010) and 0.7% in the united state with serious physical, social and economic consequences (Csernansky et al., 2002) which is often accompanied by relapse even while on treatment (Kazadi et al., 2003). Prevention of relapse is a major goal of maintenance treatment in patients with psychotic disorders (Csernansky et al., 2002). Certain criteria are used to define relapse that includes aggravation of positive or negative symptoms, hospital admission in past months, and intensive case management and/or change in medication (Kazadi et al., 2003). Relapse may result in hospitalization, treatment resistance, cognitive impairment, and personal distress, extra costs by health providers, incarceration and inference with rehabilitation efforts (Kazadi et al., 2003). Diagnostic features of schizophrenia include positive symptoms (hallucinations(Garzya et al.,2007), delusions, disorganized thoughts (stip et al.,2010;Garzya et al.,2007;Caepenter,2010) and behavior (stip et al.,2010;Caepenter,2010)), negative symptoms (loss of motivation(stip et al.,2010;Garzya et al.,2007), social withdrawal(Garzya et al.,2007), affective flattening, restricted emotional experience and expression, poverty of speech, reduced hedonic capacity(Stip et al., 2010)) and cognitive dysfunction symptomatic of the illness having persistent negative impact on patient ability to maintain relationships and engage in productive work in addition to disorganized thinking and memory impairments(Garzya et al.,2007). Any of those elements of the illness in theory reduces the capacity to make decisions (Caepenter, 1999). There is evidence that more than 90% of patients with schizophrenia have sleep problems. Sleep problems may exacerbate existing psychopathology by causing, distress and other negative effects on psychosocial rehabilitation and general functioning (Dursun et al., 1999).

Internationally, the factors commonly associated with relapse include poor adherence treatment –which is thought to be the most crucial issue, substance abuse (Kazadi et al., 2003), co-morbid psychiatric illness, co-morbid medical and/or surgical condition, stressful life events (Weiden, 1997), and treatment setting (Kazadi et al., 2003). The medication compliance for psychiatric illness is 58%. More specifically, about half of the patients with schizophrenia are non-adherent to treatment. This non-adherence may be due to factors that are patient-related (e.g. substance abuse, forgetfulness, anxiety about side-effects, inadequate knowledge, lack of insight , lack of motivation, fear of stigma); health care-related (e.g. poor

patient/health care provider relationship, poor services and access to services, and poor staff training); socio-economically related (e.g. illiteracy, low level of education) or treatment-related (e.g. polypharmacology, complex treatment regimens)(Kazadi et al., 2003).The number of individuals in the population receiving antipsychotic drugs that have been grouped into older and newer classes(Maguire et al., 2002)is surprisingly high(Lean, et al , 2003) and most of whom treated with these antipsychotic medications are unmarried and unemployed, and may live with persistent psychotic and negative symptoms and cognitive impairments(Stover et al., 2008). The compliance is often assessed by subjective or indirect methods such as patient self-report, care provider reports, other significant report and chart view, whereas direct objective methods, such as pill count, blood or urine analysis, electronic monitoring and electronic refill records are used infrequently (Rummel-Kluge et al., 2008). The degree to which an individual follows medical advice is a major concern in every medical specialty (Mitchell et al., 2007).

Much attention has focused on methods to persuade patients to adhere to recommendations, without sufficient acknowledgement that avoidance of sometimes complex, costly and unpleasant regimens may be entirely rational (Mitchell et al., 2007). Numerous studies demonstrated that inadequate compliance and non persistence with prescribed medication regimens result in increased morbidity and mortality from a wide variety of illness, as well as increased health care costs (Cramer et al., 2008). Preventing rehospitalization of schizophrenia patients, the identified modifiable factors suggest further need for development and implementation of integrated mental health services in the community (Suzuki et al., 2003). The term 'compliance', 'adherence' and 'concordance' are not used consistently in the literature; some authors use them synonymously (Rummel-Kluge et al., 2008) whereas others define compliance (adherence: synonym) (Cramer et al., 2008) as the extent to which person complies with medication (Rummel-Kluge et al., 2008) in accordance with the prescribed interval, dose and dosing regimen (Hughes et al., 2007). On the other hand, concordance is defined as a wider concept, including habits and attitudes towards therapeutic strategies (Rummel-Kluge et al., 2008). Medication persistence may be defined as "the duration of time from initiation to discontinuation of therapy (Cramer et al., 2008), non-compliance is a major problem in schizophrenia (Rummel-Kluge et al., 2008).

The aim of the present study is to provide data on the frequency of partial adherence in patients with schizophrenia and to identify patient-related factors, among patients with schizophrenia that may be contributing to medication relapses.

Methods

During 14 days period in May 2012, psychiatrists and registered nursing working in a psychiatric hospital in Amman were asked to participate in this study. The participating physicians were requested to anonymously evaluate the compliance in patients with schizophrenia diagnosed according to ICD10, using a questionnaire consisting of 11 questions (question A-K, possible answers were 'yes' or 'no'; Table 1). The term 'compliance' in the present study was defined as the extent to which a person complies with the prescribed medication.

Question A asked about the patient's negligence of taking his medicine due of dissatisfaction or denial of illness. Question B asked about patient's negligence and intentional discontinuation of prescribed medication because he is convinced that there are other ways to treatment such as spiritual or Para-medical treatment. Questions C-H evaluated the patient-related factors contributing to partial compliance; questions C, D and E are related to patient's negligence due to inadequate ideas about his illness or lack of knowledge about his medicine and the medication side-effect, whereas question F is related to concerns regarding cognitive problem or addiction to the medicine. Questions G and H are related to complex and costly treatment regimens related to intentional partial compliance due to

Living conditions and fear from stigma, and satisfaction of recovering due to symptoms disappearance. Question K assessed the frequency of partial compliance because the physicians suspected that the patients had forgotten unintentionally to take their medication once or more during the past month.

The participating physicians

A total of 12 psychiatrists and 35 registered nurses had been asked to participate, using the questionnaire and data were included in the analysis. All participants are working in Marka psychiatric hospital which is affiliated to Royal Medical Services in Jordan, 6 psychiatrists (2 of them are consultants in the psychiatry department , two senior specialists and two specialists), 6 third year resident psychiatrists, and 35 nurses (6 of them are specialists psychiatric nurse and the rest are trained psychiatric practical nurse).

Statistical analysis

Several statistical measures were used such as the arithmetic mean, T-test, Cronbach's Alpha test, and standard deviation. As for the standard of paragraph or question acceptance, the arithmetic mean should be greater than (0.5), and to be of a significant value, T must be greater than the tabular value or the significance level be less than 0.05.

Results

All participants completed the patient's compliance assessment; data on the assessment of compliance are, therefore, available for 179 patients with schizophrenia (Table 1). 29 patients are not included in the study because they comply with medication.

Table 1. physicians responses for 179 patients with schizophrenia

Questions:	**Yes n (%)**
A. Do you suspect that your patient doesn't comply with medication because he is not convinced that he is sick?	144(80.4)
B. Do you think that your patient isn't compliant with medications because he seeks an alternative spiritual Medication?	116 (64.8)
C. Do you think that your patient has partial compliance because he doesn't have enough idea about his illness?	134 (79.9)
D. Do you think that your patient has partial compliance because he doesn't have knowledge about the prescribed medications?	132 (73.7)
E. Do you think that your patient is partially compliant because he was incapable of noticing deterioration in his health after omitting the treatment?	116 (64.8)
F. Does your patient suffer from problems of cognitive dysfunction that is affecting his daily compliance with his medications?	85 (47.5)
G. Do you think that your patient has partial compliance because of the non availability of, or medicine's high cost?	113 (63.1)
H. Do you think that your patient has partial compliance because of the long period of taking medicine?	109 (60.9)
I. Do you think that your patient has stopped taking medication because of the patient's dissatisfaction and upset of Response or expectation of cure?	68 (38.0)
J. When your patient felt better and symptoms disappeared, did they at any time think that the medication was not necessary and stopped taking it?	72 (40.2)
K. Do you suspect that your patient has forgotten to take the prescribed medication in the past month and nobody reminded him to take medicine?	133 (74.3)

Factors contributing to partial compliance

Patient-related factors possibly contributing to partial compliance(Table 2), denial of illness or patients dissatisfaction of illness (question A)were the most important problems (80.4%), followed by inadequate knowledge about illness, and medication 79.9% and 73.7% respectively (question C and D). A total of 74.3% of patients needed someone to remind

them to take their medication (question K).The psychiatrists reported that 64.8% of patients had anxiety about side-effects(question E) and other problems such as cognitive dysfunction and medication addiction (question F). Cost and availability of medicine were assumed in 63.1% of the patients (question G), followed by duration and complexity of regimen 60.9% (question H). Another factor related to partial compliance was satisfaction of patients with other ways for treatment which we called as paramedical or spiritual treatment question B (64.8%). The psychiatrists also reported that 40.2% of the patients who stopped taking medication after the disappearance of symptoms and they decide the medication is not necessary (question J) followed by dissatisfaction of getting better (question I) 38%. Patients who were considered to be partially compliant (question A and C) were statistically significant more likely to fall in the 'yes' category of questions B and D-K than those who were considered to be compliant.

Table 2. Non/ partial adherence due to factors that are patient-related
• Concerns about the side-effects. • Adjustment to suit daily routine. • Misunderstanding instructions. • Concerns about availability. • Concerns about cost. • Duration and complexity of regimen. • Cognitive dysfunction. • Lack of support.

Discussion

To our knowledge this is one of the largest studies among psychiatrists to assess the medication compliance of their patients with schizophrenia (Rummel-Kluge et al., 2008). Almost 12 psychiatrists and 35 RN assessed the compliance of 200 patients with schizophrenia. The fact that patients having compliance problems might appear high but they do not seem to represent an overestimation because physicians tend to overestimate compliance of their own patients. Difficulties with medication compliance are considered to be one of the most important risk factors for relapse and rehospitalization among patients with schizophrenia and to cause approximately 40-50%of relapse (Weiden, 1997). Rummel-Kluge *etal*. found some differences between psychiatrists working in a hospital assessed their patients as having more compliance problems compared to the patients of psychiatrist working in private practice. Patients with schizophrenia are usually discharged from hospitals to follow-up at their nearest community mental health clinics which focus mainly on

pharmacotherapy, with little psychosocial support services owing to lack of human and material resources (Maidment et al., 2002). Rummel-Kluge *etal*. study found possible reasons for the differences in the assessments of schizophrenic patients by hospital physicians and psychiatrists in private practice. Hospital physicians are confronted with readmissions due to relapses more than psychiatrists in private practice.

There are several strategies that consider the factors derived from questions and contribute to partial compliance, appear promising to improve compliance. **First**, making regular reminders via mail, email or telephone, telephone reminders by families or counseling can be helpful in assisting patients with mental disorders to adjust medication timing (Rummel-Kluge et al., 2008). The figure in this study shows that 74.3% of patients needed someone to remind them to take their medication. **Second,** Explaining the benefits and hazards of treatment option and take into account the patients' preference, Lack of insight/denial of illness contributed to a 5.2-times increase in the risk relapse (Kazadi et al., 2003). Patients' understanding of their conditions and their need to treatment is positively related to adherence. This studyshowsthat 74.9% of the patients needed to know information about their disease and 80.4% of patient's denial his illness. Low insight may be linked to poorer cognitive function and one study suggest that during the first year of treatment, patients with poorer premorbid cognitive functioning are more likely to discontinue (Robinson et al., 2002). It is possible that the lack of insight in this population might be related to lower level of formal education and lack of understanding of mental illness (Stover et al., 2008). Psychosocial interventions such as psychoeducation were shown to reduce rehospitalization, the lack of insight into the illness and into the need for prophylactic medication for relapse prevention. **Third**, considering adherence aids such as medication boxes and alarm and minimize adverse effects, medication side-effects and complex regimens; in which this study shows that 64.8% of the patients fear from deterioration in their health and 60.9% of them are depressed of the long and complexity of regimens. Patients who default on their treatment have said that treatment side-effects (Maguire et al., 2002), together with complex costly regimens and durations (Mitchell et al., 2007) are the main reasons for their poor adherence because most of them do not feel involved in treatment-decision and state that they take medication only because they are told to (Gray et al., 2005).

Recent data suggest that patients with schizophrenia participating in research are able to understand and retain consent information (Caepenter, 1999). Patients typically leave the clinic with a poor understanding of the rational for therapy (Mitchell et al., 2007).Gray *etal* report that most of the participants prescribed antipsychotics did not feel of being involved in

treatment decisions and had not been given written information about their treatment, warned about side-effects or offered non-pharmacological alternatives. The more information that is given, the better adherence is (Maidment et al., 2002). Taking one daily dosage or monotherapy and the use of 'dosette boxes', where medication can be kept in daily order for 7 days (Rummel-Kluge et al., 2008) reduces adherence relapse. So equally regimens that require disruption to lifestyle, or special techniques or arrangements are less welcome by patients (Mitchell et al., 2007).Thus the patient is not always acting irrationally if they attempt to allow for adverse effects or minimize stigma by adjusting doses or times of administration (Lambert et al., 2004). **Another** strategy which improves compliance is: establishing a therapeutic relationship and trust. Perkins (2002) reviewed article published up to December 2002 correlates poor adherence included patients beliefs about their illness and the benefits of treatment (insight into illness, belief that the medication can ameliorate symptoms), perceived cost of treatment (medication side effects), and barriers to treatment (ease of access to treatment, degree of family or social support). The figures in this study show that 80.4% of the patients are not convinced that they are sick. The importance of good communication between patient and health professional is increasingly acknowledged in relation to adherence (Stevenson et al., 2005). At its essence this means forging a jointtherapeutic agreement with full patient involvement, for example discuss mental health issues with a doctor, is predicted largely by the perceived helpfulness of and trust in that doctor (Mitchell et al., 2007). Other process of making a joint therapeutic plan is often abbreviated.

Conclusion

Strategies to improve partially compliant patients with antipsychotic drug are needed. The importance of good communication between patients and health professional is increasingly acknowledged in relation to adherence. Poor adherence owing to lack of insight, medication side-effects, complex regimen and lack of sufficient information about disease were the most likely factors which increase the relapse in patients with schizophrenia.

Limitations

Small sample size might have limited our ability to detect statistically meaningful differences. In any retrospective study design, some data might not have been recorded in case notes and patients might have been erroneously included or excluded. Another limitation is that the questions focused on partial compliance which might have increased the number of patients being considered partially compliant.

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