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A review of Factors affecting for non- adherence to medication for patient with Schizophrenia

Soontareeporn Thongsai

Mental Health and Psychiatric Nursing Department, Naresuan University, Phitsanulok, Thailand

Abstract

BACKGROUND: A number of potential determinants of non-adherence to medication for patient with schizophrenia have been investigated so far. However, the data regarding the factors affecting were neglected.

PURPOSE: 1.To review the factors that affecting to non-adherence to medication for patient with schizophrenia 2.To identify its prevalence and the risk factors that associated with defaulting to adherence for medication in patient with schizophrenia

DATA SOURCES: The authors searched multiple sources dated published through September, 2013, including the Cochrane Library, MEDLINE, PsycINFO, EMBASE, CINAHL Nursing and Allied Health databases, and the bibliographies of 40 previous reviews

METHODS AND DATA EXTRACTION: All, Cochrane Library, MEDLINE, PsycINFO, EMBASE, CINAHL Nursing and Allied Health databases were systematically search for systematic reviews published between Electronic databases were searched for controlled studies in English, published from 1987 to 2013, assessing the non-adherence to medication for patient with schizophrenia. Reviewers extracted study data using a structured abstraction form. Aggregated information about having non-adherence to medication prescribed by the health professional was used for making adjustments in the review.

RESULTS: Thirty reviews were included for the final review. The evidence supports that the key essence of the non-adherence to medication for patient with schizophrenia were related to lack of insight, medication belief and difficulty for to assess to the medication.

Conclusion: To improve the non-adherence to medication for patient with schizophrenia may have to consider on specific factors that may effect to non-adherence

Keywords: *non-adherence, systematic review, schizophrenia*

1. Background

Non adherence to antipsychotic medication is one of the greatest challenges in psychiatry¹⁷. It is rarely an all-or-nothing phenomenon. It may include errors of purpose, errors in dosage and timing, and the occasional use of inappropriate combinations^{4, 8, 18}. It can vary from “taking medication irregularly” to “complete discontinuation”²⁰. The majorities of patients tend to be partially adherent rather than completely adherent or fully non adherent¹⁹. Obviously, non-adherence has a major impact on the effectiveness of therapeutic interventions and presents many problems in routine clinical practice.^{23, 24} Patients who adhere to treatment recommendations have lower relapse rates^{25, 26}

In term of Schizophrenia patient, it is a major mental illness that causes prominent psychological dysfunction, and it is among the top 10 causes of long-term disability in the world. It affects about 1% of the population worldwide.²⁹ Even though people with the various symptoms and domains of impairment associated with schizophrenia are responsive to a range of pharmacologic and psychosocial treatments, partial or complete non-adherence to treatment commonly interferes with optimal recovery. Indeed, lack of adherence to medications for schizophrenia after discharge from an acute hospitalization has been described as the single most significant risk factor for relapse.³⁰ this demonstrates the need for special attention and evidence-based interventions designed to enhance adherence. Non-adherence among patients receiving psychiatric services leads to an increased rate and length of re-hospitalization²⁷ as well as increased costs of care.³¹ Although the prevalence of partial or complete non-adherence is known to be extremely high in schizophrenia, it is likely that both patients and their clinicians overestimate adherence to treatment regimens.³²

The rates of non- adherence in people with schizophrenia varies from 0% to 100%^{1, 3, and 5,6,11,12,13,16} with an average of approximately 50%. The non-adherence rate for psychotic patients (42%) is higher than that for physically ill patients (24%)⁶. Accurately estimating adherence is difficult because there is no agreed upon definition or gold standard for measuring adherence. Some studies treat adherence/non adherence as dichotomous, whereas others define adherence as one point on a continuum, and they may use an ordinal scale to measure it. None of the measures currently used in the literature, such as patients’ self-reports, clinicians’ ratings, pill counts, and serum assays, have proven accurate. In addition, the duration of observation could affect adherence rates. For example, it has been shown that 50% of psychotic patients remain adherent at one year⁸. Within two years after discharge, the adherence rate can decrease to 25%²¹. Medication adherence is a complex and challenging issue. Partial or non-adherence can negatively influence the course of schizophrenia and it can cause personal and socioeconomic problems.

In term of factors affecting non-adherence, it has been suggested that many factors affecting attendance should be taken into account in the first stage of any adherence intervention. There have been many factors identified in the literature as a key reason Problems with treatment adherence among psychiatric patients can encompass a variety of behaviors, including (1) taking

medication regimens incompletely, (2) discontinuing medications altogether, (3) failing to attend the first outpatient appointment after psychiatric hospitalization, (4) missing other scheduled appointments, and (5) dropping out of outpatient follow-up also may include a failure to follow the structure of the unit and refusal to participate in a group therapy program.

In addition, one study using the 1999 Study of Psychiatric Patients and Treatments from the Practice Research Network of the American Psychiatric Institute for Research and Education investigated the characteristics associated with psychiatrist-reported treatment non-adherence, among 1843 patients in routine US psychiatric practice. Using logistic regression modeling to study characteristics associated with a broad range of adherence problems, researchers found that of the 22 potential predictors, all but 3 (age, gender, and problems with primary support group) were found to be significantly associated with treatment adherence problems in bivariate analyses. A predictive model consisting of 8 independently significant predictors from diagnostic, clinical, psychosocial, and treatment history domains was then developed. The 8 predictors were: substance use disorder diagnosis; medication side effects; moderate-to-severe psychotic symptoms; personality disorder diagnosis; economic problems; prior hospitalization; current Global Assessment of Functioning scale score; and duration of treatment with the current psychiatrist. In a subsample of 100 patients randomly drawn from the dataset prior to model construction, this predictive model correctly identified the presence or absence of treatment adherence problems in 91% of patients. Such findings on risk factors may be useful to clinicians, researchers, and program planners who address the important issue of treatment non-adherence in psychiatric care settings.

Therefore, Researching the factors of non-adherence may be of great value in identifying those patient groups at greatest risk and would also allow researchers to design more efficient and targeted treatment adherence interventions for them. Identifying variables that place patients at high risk for treatment adherence problems is the first step in designing and targeting such interventions.

2. Objective

1. To review the factors that affecting to non-adherence to medication for patient with schizophrenia
2. To identify its prevalence and the risk factors that associated with defaulting to adherence for medication in patient with schizophrenia

3. Theoretical framework

The problem of medication non-adherence is multidimensional and can be influenced by several factors. Figure 2 shows the conceptual framework of medication adherence. The major factors influencing patients' medication adherence are (a) illness-related, (b) treatment-related, (c) professional-related, (d) patient-related, (e) significant-others related, and (f) cultural. The individual factors may be related to each other, and the patient-related factor in particular may be influenced by the remaining factors. Healthcare professionals play a crucial role in enhancing medication adherence in people with schizophrenia. Healthcare professionals should be non-judgmental, as patients have their own perceptions regarding medication treatment. A number of factors such as severities of symptoms, levels of insight into their illness, attitudes towards, or satisfaction with medication can provoke uncertainty about the efficacy of medication. Family members who take care of patients at home are significant stakeholders, and they should be involved in the health care process. If necessary, professionals should integrate cultural or traditional beliefs with current mental health treatments, so long as they are not harmful or do not interfere with the modern mental health treatments the patient is currently receiving. It must also be remembered that patients and their families are likely to be susceptible to stigmatisation. Healthcare professionals should accordingly be empathetic and support them in reaching the treatment goals.

4. Search Methodology

Sources

Electronic databases were searched in 2014 using OVID; they were last updated in July 2013. The databases searched include PsycINFO (1806 to week 4 of June 2013), MEDLINE (1950 to week 3 of June 2013), EMBASE (1980 to week 26 of 2013), and the Cochrane Database of Systematic Review (2nd quarter of 2013). The databases of the Thai Department of Mental Health and the electronic libraries of universities were accessed. The grey literatures were retrieved using "Google". In addition to the synonyms of key words, truncation symbols (\$) or *) was used to increase the sensitivity of the search. The Boolean operators "OR" and "AND" enabled multiple terms to be combined in a single search.

Search Criteria

Guidelines were used which described the seven steps of the review process for finding information from research papers and documents. These consisted of a three-step screening process, and it was used as described below for the study:

- Step 1: Classifying (locate all of the documents by using search strategies to classify)
- Step 2: Screening for the selection of abstracts, Documents and full texts
- Step 3: Classifying papers by relevance for the systematic review and randomized controlled trial.

Question for the review

What factors associated to non-adherent to medication for schizophrenia patient?

Object of the review

The objective of this systematic review is to investigate the reasons that intended to effected on medication non-adherent in patient with schizophrenia

Selection of Studies (Key Criteria Identified)

Both published and unpublished studies were included in this review. Original research and review articles relevant to the topic under discussion, published in English from January 2009 through June 2013, and were identified by searching the MEDLINE database using the search terms "schizophrenia or psychosis" combined with "compliance, noncompliance, adherence, or non-adherence." Together with "Factors influencing adherence rates" "Consequence of non-adherence" The author screened all citations and reviewed the full text of peer-reviewed journal articles considered relevant. Bibliographies were scanned to locate additional relevant publications. Because eligible studies varied prominently in methodology, a narrative synthesis was deemed more appropriate than a formal quantitative meta-analysis. This Clinical Update is not intended to be systematic or comprehensive, and due to the large amount of literature on this topic, some relevant articles may not be discussed or referenced.

Validity and Reliability

The strength of the studies will be an important feature, because if any studies have an effect on the assessment and process of search strategies then the result will be shown in the validity and reliability of the studies. On the other hand, if any studies show weakness in the process, then the quality of the studies will be inconsistent. To avoid this error, the validity and reliability of the studies must be looked at carefully. Due to this, the review stage is intended to find the best and strongest available evidence that has been shown.

However, there are some variations and differences in study quality that may affect the final results. In order to get the best quality evidence, we will be develop a method for the standardized process of quality appraisal and working together as a team work to decrease individual bias of the paper.

Data Extraction

All studies that met the relevant criteria were retained for the data extraction stage of the review process. A data extraction form was developed based on a guideline developer's handbook for systematic review, randomized controlled trial and case control studies. The data

extraction based on the study design, intervention approaches and comparison if they were comparing interventions or drugs which were not of interest; outcomes including factors influencing adherence rates and consequence of non-adherence; and epidemiologic studies, meta-analyses and qualitative reviews; and a focus of studies with larger sample sizes and more recent publications due to the large expected number of studies identified.

However, section three (the pilot stage by second observers and third observers) of each guideline needed to be adapted by piloting with secondary observers who will be involved in this stage as consultants for the study, to be able to avoid primary author bias and for making decisions about which criteria need to be added in order to extract more relevant information.

Data Synthesis: Presenting the Findings and Results

The final decision on how to present the results was made at the last stage of data summarization of the included papers. The decision was based on the nature of the results of the different studies.

The databases searched include PsycINFO (1806 to week 4 of June 2013), MEDLINE (1950 to week 3 of June 2013), EMBASE (1980 to week 26 of 2013), and the Cochrane Database of Systematic Review (2nd quarter of 2013) Identification of abstracts: All of documents in Total were count from Cinah and Pro Quest Nursing Journal in sequence.

5. Results:

Study selection

At this point, Figure 1. Show the flow chart of identified studies. The OVID search identified 2,967 abstracts for screening. Due to the large number of abstracts that need to answer 3 different research questions, the 1st screening form were involved for sorting the abstract according to the 3 outcome of the interest that have been address including, Schizophrenia or psychosis, factors influencing adherence rates, consequence of non-adherence. At this stage, any abstracts that did not clearly state and did not match the inclusion criteria were excluded. Follow by the 2nd screening form, there were 73 articles were excluded due to repeat abstract, studies design out of scope, patient population out of scope, comparison study. However, section three (the pilot stage by second and third observers) of each guideline needed to be adapted by piloting with secondary and third observers who involved in this stage as consultants for the study, incase to avoid primary author bias and for making decisions about which criteria need to be added in order to extract more relevant information. Unfortunately, this systematic review study was limited by time, and this part will be based solely on adapting my understanding. Thus, 20 full papers were obtained for the final reviewing.

Factors related to non-adherence

Severity of the disease. Some symptoms of schizophrenia may inhibit the patient's ability to cooperate during their treatment process such as, the severity symptom, lack of illness insight, as these may influence to the medication adherence. In consistence with the previous statement that the symptom severity and adherence, there were 2 studies that supported a directional relation, in which symptom severity was associated with worse adherence. (Acosta et al. 2009; Hudson et al. 2004). A study of Loffler stated that reasons for noncompliance among patients with schizophrenia was that patients with more severe symptoms were less likely to consider relapse prevention as an important factor for their compliance (Loffler et al. 2003). On the other hand, there was another study conducted by the Linden reported that they was no prognostic relation between symptom severity and adherence (Linden et al. 2001). The author states that this contrary finding which may be due to the inclusion in the study which may, in turn, influence the overall findings concerning patient adherence.

Lack of illness insight. Many individuals with schizophrenia have poor or no insight regarding their illness, in the other word we could said that they are not aware of the symptoms and consequences of their illness. Four studies were endorsed at this point that a directional relation in which lack of illness insight was associated with worse adherence (Acosta et al. 2009; Loffler et al. 2003; Olfson et al. 2006; Velligan et al. 2009). Additional, the surveys study of Velligan those work in the clinical experts (Velligan et al. 2009) rated poor illness insight as the most important factor contributing to non-adherence. At this point, the author assumed that patients who declined to accept and being ill may not believe that their symptoms are something that can be managed and cure. Therefore, may be less motivated to take steps to resolve their symptoms, such as taking medication. There was only one prospective study of Linden reported no relation between adherence and lack of insigh (Linden et al. 2001).

Patient-related factors. In term of patient-related factors there were 2 main types of patient-related factors were reviewed such as, socio-demographic factors, beliefs about medication due to the previous study that there were many study have been studied on the certain area of those factors.

Socio-demographic factors: Four studies did not show a relation between adherence and socio-demographic variables such as gender and marital status (Acosta et al. 2009; Linden et al. 2001; Loffler et al. 2003; Aldebot and de Mamani, 2009). Whereas, three prospective studies of [Hudson et al. 2004; Janssenet al. 2006; Linden et al. 2001; Valenstein et al. 2004) did found a positive relationship between socio-demographic factors and adherence for people with schizophrenia for instance, a positive relationship with older age was reported in the study of Linden and Valenstein Linden et al. 2001; Valenstein et al. 2004. However, a negative relationship with low education level were identified in the study of Hudson and colleagues (Hudson et al. 2004)

Beliefs about medication: Patient perception about their medication were appeared as contribute to adherence rates. A cross-sectional study of Rettenbacher and colleagues found that the variable which best predicted compliance was “positive effect on everyday life” as a reason for taking the drug ($p = 0.01$) (Rettenbacher et al. 2004). In addition, another survey study (Velligan et al. 2009) reported that one of the important predictors of adherence problems was “patient’s belief that their medication does not work”. Together with the evidence suggests that the patient’s belief and trust in the effectiveness of medication may take a positively role to the medication adherence for patient with schizophrenia.

Environment-related factors such as, difficulty to assess to the medication. As we are known that Non-adherence to medication can lead to relapse, which can mean more visits to the emergency room, re-hospitalizations and increased need for clinician intervention and all of these were lead to increased costs to healthcare systems and may effected to the patient prognosis. Furthermore, was that relationship with physician, stigma of disease, living situation and family supports. The evidence suggests that a relationship with guidance in drug intake are important and may contributors to good adherence (Loffler et al. 2003; Rettenbacher et al. 2004; Velligan et al. 2009). Whereas, family support, poor insight and lack of illness awareness were no longer contributed to the medication adherence for patient with schizophrenia (Velligan et al. 2009)

6. Conclusion

Our systematic review were identified several factors and consequences of poor adherence in schizophrenia. It were based on the evidence that have been found on a certain time, the most frequently reported driver and consequence of non-adherence appeared to be involved in several factors such as, illness insight a good therapeutic relationship with physician and perceiving the benefits of medication. The factors that should be aware of the importance of the physician and relationship with the patient based on trust as well as educating the patient on the medication’s impact on the symptoms and illness. Considering the substantial burden of non-adherence in schizophrenia on patients and society as a whole, improved adherence in schizophrenia is of great value to patients and society. As our review shows, to improve the non-adherence to medication for patient with schizophrenia may have to consider on specific factors that may effect to non-adherence.

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