Original article

COMPARISON OF METHODS USED IN MEASURING NONADHERENCE AND THE BARRIERS AGAINST ADHERENCE TO ANTIPSYCHOTIC DRUGS IN OUTPATIENTS WITH SCHIZOPHRENIA

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Abstract

Background Although patient self-reporting was the method used most commonly to measure adherence to antipsychotic drugs in schizophrenia, it may underestimate the degree of nonadherence. In addition, little is known about barriers against adherence in patients with schizophrenia in Thailand.

Methods A prospective study was conducted at Chiang Mai University Hospital, Thailand, in which 75 patients with schizophrenia were followed up from a pervious study for three months to evaluate their adherence to antipsychotic drugs measured by self-reporting, psychiatrist rating and pill count. The nine domains of barriers against adherence were assessed, and risk factors associated with high barriers were analyzed using the chi-square and independent t-tests.

Results Of the 75 participants in the previous study, four were lost to follow-up. In this study the prevalence of nonadherence reported by the 71 remaining patients and psychiatrists was only 5.1% and 16.9%, respectively, while that measured by pill count was 46.5%. The three most common barriers reported by patients with schizophrenia were memory problems, stigma, and adverse drug reactions.

Conclusion Subjective methods such as self-reporting and psychiatrist rating might underestimate nonadherence to antipsychotic drugs. Objective methods such as the pill count should be added to evaluate nonadherence. Furthermore, barriers against adherence in Thailand may differ in some aspects from those in western countries.

Keywords: adherence, schizophrenia, antipsychotic drugs, barriers

Antipsychotic drugs have been proven as effective in treating patients with schizophrenia, yet nonadherence ranges from 20% to 89%.(1,2) Nonadherence often leads to negative consequences, including relapse, rehospitalization, poor functional outcomes, and suicide.(3,4) Therefore, effective methods to identify adherence is needed for both psychiatrists and researchers.

According to a review by Velligan et al., patient self-reporting is the method most commonly used to measure adherence,(5) however, it may be unreliable. Velligan et al. found that while 55% of patients reported good adherence, only 40% were adherent, based on pill count.(6) A number of methods have been created to identify adherence, one of which is Medication Event

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Monitoring (MEMS®), which involves pill bottle caps that can record time and date whenever the bottle is opened. Although MEMS® is believed to be a gold standard for measuring adherence, it has been argued that this method might lead to high rates of missing data. In addition, its price is too expensive, especially for those in developing countries.

Several aspects have been found to associate with nonadherence including illness-related (e.g., severity of symptoms, insight, duration of illness), treatment-related (e.g., type of antipsychotic, adverse drug reactions), and patient-related factors (e.g., stigma, level of education, attitude toward illness, substance abuse).(7) Hudson et al. studied nine domains of barriers against adherence in patients with schizophrenia and found that the most commonly reported ones were stigma, adverse drug reactions, memory problems, and lack of social support. Patients with high barriers had lower adherence to antipsychotic drugs when compared to those with low barriers.(8)

In Thailand, there are a limited number of studies about the barriers against adherence in patients with schizophrenia. Our previous study of outpatients with schizophrenia in Chiang Mai found that depression and social support deficits were significantly associated with nonadherence to antipsychotic drugs. Other risk factors were receiving typical antipsychotic drugs, having more than one side effect, and being less satisfied with the treatment.

The purpose of this study was:
1. To compare adherence rates measured by pill count with self-reporting and psychiatrist rating.
2. To identify the most common barriers against adherence to antipsychotic drugs in patients with schizophrenia.
3. To assess the risk factors associated with high barriers against adherence in patients with schizophrenia.

Methods
This was a prospective study conducted at an outpatient clinic of a university hospital in Chiang Mai, Thailand. Seventy-five patients with schizophrenia from a previous study were followed up for three months to evaluate adherence measured by self-reporting and pill count. The inclusion criteria from the previous study were Thai-speaking, aged 18 years or over, diagnosed as schizophrenic according to DSM-IV-TR and receiving oral antipsychotic drugs. The exclusion criteria were receiving depot antipsychotic drugs/therapy within the past month. This study received prior ethical approval from the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University (No. 383/2552). All patients provided written informed consent.

In this study, a patient-rated visual analog scale (0-100%) and pill count were used to compare results from the three-month follow-up with those from the psychiatrist-rated visual analog scale (0-100%) in the previous study. An 80% cut-off point was used to designate nonadherence.

The nine domains of barriers against adherence from the study of Hudson et al. were used to assess those in the sample of this study as follows:
1. Memory problems
2. Problems with the medication regimen
3. Patient fear of medications
4. Adverse drug reactions
5. Denial of illness
6. Stigma of taking medication
7. Lack of trust in the provider
8. Lack of social support
9. Other issues not listed in the previous eight domains

Patients with schizophrenia were split into two groups based on the number of barriers reported; high barriers (≥2) and low barriers (<2). This is defined a priori following the study of Hudson et al. Associations between dichotomous variables (gender, marital status, comorbid psychiatric disorder) and barriers were assessed using chi-square tests, while the associations between continuous variables and barriers were assessed using independent t-tests.

Results
Of the 75 participants in the previous study, 4 (5.35%) were lost to follow-up. Of the remaining 71 participants in this study, 25 (35.2%) were male, 22 (31.0%) were married, 47 (66.2%) had completed at least a high school education, 36 (50.7%) were working and 37 (52.1%) were
receiving typical antipsychotic drugs. The mean age was 45.8±13.4 years and the mean duration of illness was 13.8±11.5 years.

The prevalence of nonadherence at the 80% cut-off point measured by self-reporting and psychiatrist rating, was 5.1% and 16.9%, respectively, while that measured by pill count was 46.5%. However, when treated as continuous variables, adherence rates measured by self-reporting, psychiatrist rating, and pill count were 7.3%, 9.1% and 24.1%, respectively.

The mean number of barriers per participant was 1.1 (range 0-5). The three most common barriers against antipsychotic drugs, reported by patients with schizophrenia, were memory problems, stigma, and adverse drug reactions (Fig.1). No patients reported lack of trust in the provider or difficulty with the regimen.

Patients with high barriers tended to be younger, female, married, lower in educational level, and possessing psychiatric comorbidity, although none of these differences were statistically significant. Only low income was found to associate with high barriers to a statistically significant degree. Those with high barriers were more likely to be nonadherent when measured by self-reporting. However, adherences measured by psychiatrist rating and pill count were not significantly associated with the barriers (Table 1).

Discussion

This study shows 46.5% nonadherence to antipsychotic drugs measured by pill count. This is comparable to 48% reported by Byerly et al(11) and 52% reported by Remington et al(12) However, it sharply contrasts with 5.1% rated by patients and 16.9% rated by psychiatrists in this study. Therefore, it can be assumed that psychiatrists missed about 30% of the patients with nonadherence, and most of the patients with schizophrenia over-reported their adherence.

This inconsistency between adherence measured by self-reporting, psychiatrist rating and pill count is in line with studies in western countries. (12,13) Byerly et al. and Remington et al., used MEMS®, and found that psychiatrists’ assessment dramatically underestimated nonadherence in patients with schizophrenia.(11,12) A possible ex-

**Figure 1.** Frequency of barriers against adherence reported by patients with schizophrenia. “Other” barriers include substance abuse, finding that drugs are not effective, and being afraid of drug dependence.
planation is that a psychiatrist’s judgment of adherence can be biased by a patient’s clinical state. In addition, psychiatrists may evaluate adherence based on self-reporting by patients. Although we did not use MEMS® in this study, it is suggested that there is a significant correlation between MEMS® and pill count, while pill count is more available and can be used in developing countries.

Of the nine barriers against adherence, we found that memory problems (i.e. forgetting to take antipsychotic drugs) was the most common one for patients with schizophrenia. This is consistent with a previous study, which found that nearly 30% of patients with schizophrenia reported memory problems. Impaired cognitive functioning is common in patients with schizophrenia and may affect their ability to follow through with treatment. Memory problems might also be the result of poor support from family, i.e. no one is reminding patients to take their medicine. Stigma was reported in a western study as the most common barrier found and this was an important issue seen in other disorders, including depression and acquired immune deficiency syndrome.

Our previous study found that adherence is affected by the choice of antipsychotic drugs. About half of the patients in this sample received typical antipsychotic drugs, which are more likely than atypical ones to produce extrapyramidal side effects and akathisia. This may lead directly to nonadherence and might explain why we found that adverse drug reaction was reported as one of the top three barriers against adherence. This parallels a study of Yamada et al., which found that the most common reason for nonadherence in Japanese patients with schizophrenia was “distressed by side effects”.

Lack of social support was found to be relatively low in this study, but common in western ones. This might be because social support varies from one culture to another. In Thailand, patients with schizophrenia generally live with their family members, as less than 10% of them were found to live alone.

This study shows that low income is significantly associated with high barriers. The outcome also suggested that patients with psychiatric co-morbidity were more likely to have high barriers, although the association was not statistically significant. High barriers were found to be significantly associated with lower self-reported adherence. While psychiatrist rating and pill count tended to be in the same direction, the relationships were not statistically significant. This inconsistency could be due to a small sample size. The fact that the barriers themselves were reported by patients could also make a correlation

| Table 1. Comparison of baseline characteristics of patients with schizophrenia and high versus low barriers against antipsychotic drug adherence |
|-------------|-----------------|-----------------|-----------------|
|              | High barriers (≥2) (N=13) | Low barriers (<2) (N=58) | p-value |
| Age (mean, years) | 40.4 | 47.0 | 0.105 |
| Gender (% male) | 23.1 | 37.9 | 0.311 |
| Marital status (% married) | 46.2 | 27.6 | 0.191 |
| Educational level (% college or above) | 38.5 | 48.3 | 0.521 |
| Duration of illness (mean, years) | 10.9 | 14.4 | 0.325 |
| Income (mean, baht) | 3,384.6 | 6,908.5 | 0.042 |
| Alcohol or drug problem (%) | 7.7 | 15.5 | 0.464 |
| Having psychiatric comorbidity (%) | 23.1 | 8.6 | 0.156 |
| Medication adherence (%) | | | |
| Patient | 79.5 | 95.7 | 0.023 |
| Psychiatrist | 78.9 | 93.6 | 0.064 |
| Pill count | 74.2 | 76.3 | 0.777 |
Comparison of methods measuring adherence 101

with patient-reported adherence more likely.

Although this study leads to a better understanding of the barriers against adherence in patients with schizophrenia, and highlights the issue of underestimated nonadherence by patients and psychiatrists, certain limitations exist. Firstly, since we followed the same sample as in the previous study,\(^9\) the small sample size might limit our positive findings and could explain why we did not find significant associations between alcohol or drug problems, psychiatric comorbidity, and high barriers.

Secondly, studying in the hospital setting might lead to selection bias, as non-adherent individuals are more likely to be lost to follow-up during the treatment process. In addition and the particular sample characteristics from a university hospital in Thailand might reduce generalization to include other patients with schizophrenia in different settings. However, the attrition rate was relatively low and those who were lost to follow-up did not differ in demographic characteristics, so selection bias is unlikely to explain our findings.

Thirdly, the use of a visual analog scale, although easily assessed and commonly used to assess adherence, may have limited validity and might explain the underestimated nonadherence by patients and psychiatrists.

In conclusion, this study suggests that subjective methods such as self-reporting and psychiatrist-rating might underestimate the problem of adherence in patients with schizophrenia. An objective method such as pill count should be added in evaluating nonadherence. This study also shows that barriers against adherence in Thailand may differ in some aspects from those in western countries, although memory problems, stigma, and adverse drug reaction also play major roles.

Future research of a larger number of patients with schizophrenia or other psychotic disorders is necessary for a better understanding of nonadherence. Methods that decrease memory problems, such as short mobile phone messages, should be emphasized in intervention to improve adherence in patients with schizophrenia.

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การศึกษาเปรียบเทียบวิธีประเมินความไม่ร่วมมือในการรับประทานยาต้านโรคจิต และอุปสรรคที่มีผลต่อความร่วมมือในการรับประทานยาต้านโรคจิตในผู้ป่วยจิตเวช

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บทความ

ความเป็นมา แม้ว่าการประเมินความร่วมมือในการรับประทานยาต้านโรคจิตโดยสอบถามจากผู้ป่วยเป็นวิธีที่ใช้กันมากที่สุดในผู้ป่วยโรคริดสีหน้าแต่อาจทำให้ประเมินปัญหาบางความเป็นจริง

นอกจากนี้ ในประเทศไทยยังมีการศึกษาเกี่ยวกับอุปสรรคที่มีผลต่อความร่วมมือในการรับประทานยาต้านโรคริดสีหน้า

วิธีการ การศึกษานั้นเกิดขึ้นที่โรงพยาบาลสมรักษ์นครเชียงใหม่ โดยติดตามผู้ป่วยโรคจิตเวชจำนวน 75 รายเป็นเวลา 3 เดือน เพื่อเปรียบเทียบความร่วมมือในการรับประทานยาต้านโรคจิตจากการประเมินโดยผู้ป่วย จิตแพทย์ และการนำเม็ดยา และสอบถามเกี่ยวกับอุปสรรคที่มีผลต่อความร่วมมือในการรับประทานยาต้านโรคจิตของผู้ป่วย

ผลการศึกษา จากผู้ป่วย 75 ราย มี 4 รายที่ไม่ได้มารับการรักษาตามนัด ความชุกของการไม่ร่วมมือในการรับประทานยาต้านโรคจิตจากการประเมินโดย ผู้ป่วย จิตแพทย์ และการนำเม็ดยา เป็นร้อยละ 5.1, 16.9 และ 46.5 ตามลำดับ อุปสรรคที่มีผลต่อความร่วมมือในการรับประทานยาต้านโรคจิตที่พบบ่อยที่สุด ได้แก่ ลืมรับยา รู้สึกว่าการรับประทานยาทำให้ดูเป็นผู้ป่วย และหลีกเลี่ยงของยา

สรุป ความร่วมมือในการรับประทานยาต้านโรคจิตและการนำเม็ดยาอาจทำให้ประเมินเป็นผู้ป่วย ความไม่ร่วมมือในการรับประทานยาต้านโรคจิตอาจทำให้ประเมินเป็นผู้ป่วย ซึ่งควรใช้วิธีอื่น เช่น การบันทึกวิธีร่วม ด้วย และอุปสรรคที่มีผลต่อความร่วมมือในการรับประทานยาในผู้ป่วยจิตเวชชาวไทยแตกต่างจากในต่างประเทศในบางแง่มุม เช่นทางพยาบาลศาสตร์ 2553;49(3):97-103.

คำสำคัญ: ความไม่ร่วมมือในการรับประทานยา ยาต้านโรคจิต โรคริดสีหน้า