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การศึกษาความร่วมมือในการใช้ยาของผู้ป่วยซึมเศร้า ด้วยการหาอัตราการครอบครองยาแบบดัดแปลง

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บทคัดย่อ

วัตถุประสงค์ : เพื่อหาวิธีที่ใช้วัดความร่วมมือในการใช้ยาของผู้ป่วยโรคซึมเศร้า

วัสดุและวิธีการ : งานวิจัยนี้เป็นงานวิจัยเชิงพรรณาแบบย้อนหลัง โดยใช้ข้อมูลจากฐานข้อมูลของสถาบันจิตเวชศาสตร์สมเด็จเจ้าพระยาในช่วงวันที่ 10 มิถุนายน 2547 ถึง 14 สิงหาคม 2555 ซึ่งวัดความร่วมมือในการใช้ยาของผู้ป่วย ด้วยวิธีการวัดอัตราการครอบครองยาแบบปรับปรุง โดยค่าอัตราการครอบครองยามากกว่าหรือเท่ากับร้อยละ 80 จะแสดงว่าผู้ป่วยให้ความร่วมมือในการใช้ยาดี

ผล : จำนวนผู้ป่วยนอกที่ได้รับการวินิจฉัยเป็นโรคซึมเศร้าทั้งหมด 2,834 คน ซึ่งเป็นเพศหญิงร้อยละ 70.25 และอายุอยู่ในช่วง 40-49 คิดเป็นร้อยละ 22.12 ซึ่งในงานวิจัยนี้มีการศึกษารายการยาที่ใช้ในผู้ป่วยโรคซึมเศร้าจำนวน 21 รายการ โดยยาฟลูอ็อกซิทีนเป็นยาที่นิยมใช้มากที่สุด รองลงมาคือยาอมิทริปไทลีน (ปริมาณการใช้ยาเป็นร้อยละ 49.75 และร้อยละ 23.82 ตามลำดับ) อย่างไรก็ตามรายการยาที่ศึกษามี 16 รายการเป็นยารักษาโรคจิตเภท ซึ่งใช้เป็นยาที่ใช้ร่วมกับยารักษาโรคซึมเศร้าเพื่อประสิทธิผลในการรักษา โดยยาเปอร์เฟนนาซีน เป็นยาที่นิยมใช้มากที่สุด รองลงมาคือยาฮาโลเปอร์ริดอน (ปริมาณการใช้ยาเป็นร้อยละ 15.81 และร้อยละ 8.47 ตามลำดับ) จากการวัดความร่วมมือในการใช้ยาพบว่าผู้ป่วยให้ความร่วมมือในการใช้ยาดี คิดเป็นร้อยละ 43.40 ซึ่งจะพบว่าผู้ป่วยอายุมากจะให้ความร่วมมือในการใช้ยามากกว่าผู้ป่วยที่มีอายุน้อย

สรุป : ในการศึกษานี้พบว่าผู้ป่วยโรคซึมเศร้าส่วนใหญ่เป็นผู้ป่วยที่ไม่ให้ความร่วมมือในการใช้ยา นอกจากนี้พบว่า ผู้ป่วยที่มีอายุมากจะให้ความร่วมมือในการใช้ยามากกว่าผู้ป่วยที่มีอายุน้อย

คำสำคัญ : ความร่วมมือในการใช้ยา, การวัดอัตราการครอบครองยา, ข้อมูลการใช้ยา

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DETERMINING MEDICATION ADHERENCE IN DEPRESSED PATIENTS BY MODIFIED MEDICATION POSSESSION RATION

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Abstract

Objective : This was to identify the measurement method of medication adherence in patients with depression.

Material and Method : This was a retrospective descriptive study. The samples were recruited from the medical database of SomdetChaopraya Institute of Psychiatry duting June 10th 2004 – August 14th 2012. The medication adherence rate was assessed by modified Medication Possession Ratio (modified MPR). In this study, good MPR was defined as the medication adherence was equal to, or greater than 80%.

Results : 2,834 records of patients with diagnosis of depression from out-patient department was recruited. 70.25% were female, 22.12 % were found between 40-49 year of age. There were 21 items of different antidepressant medication used in this study. Most of the antidepressant used was Fluoxetine followed by Amitriptyline (49.75% and 23.82%, respectively). However, there were 16 items of antipsychotics drugs that used in adjunctive with antidepressants and the most frequent used of antipsychotics was Perphenazine followed by Haloperidol (15.81% and 8.47%). In case of medication adherence, we found that medication adherence as followed the criteria of this study was 43.40%. The medication adherence was found more cooperative in older ages than in younger ages.

Conclusion : Medication adherence of patients with depression in this study was less than half. We found the cooperativeness in taking medication in older age than in younger age.

Keywords : adherence, medication possession ratio, medical record

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Introduction

Nowadays, more than 350 million people worldwide suffered from depression, one of the major causes of committed suicide[1]. In 1990, depression was ranked as the fourth of burden of disease by world health organization (WHO) and was predicted as the second rank in 2020[2]. In 2004, depression in Thailand was ranked as the first for the burden of diseases in women and the third in men as the cause of disability adjusted life years (DALYs)[3]. Statistic data showed an increased in number of patients with depression during 2008 and 2011[4]. The results suggested that the number of depressed patients in Thailand was trend to be high.

One of the important factors to help decreasing the number patients with depression was medication adherence. Previous data showed that there was three times of ratio of the non- medication adherence to the medication adherence[5] and some data also showed that only 23 % of depressed patients adhered to medication[6].

There are several tools and methods that were used to classify non-adherence. Though none of them is considered as gold standard[7], some of these methods have been used in researches[8]. They can be classified into two groups which were direct methods and indirect methods.

The direct methods evaluate the adherence by observation technique, measurement of the level of medicine, biologic marker and metabolite in blood. The indirect methods are more popular for measuring adherence in research because they are easy to use. Such techniques are patient self-reports, pill counts, rates of prescription refills[8] etc.

Some of the popular techniques to study the medication adherence in the database are Proportion of Days Covered (PDC) and Medication Possession Ratio (MPR). These two measurements are appropriate measuring adherence for long-term medication treatment and they are suitable for measuring adherence when the number of patients is large[9]. The reason is that they can calculate medication adherence quicker than other tools. The PDC is more rigid than the MPR because once the patient forgets to take medicine; the patient will be classified as a non-adherent. So when applied with PDC, too many non-adherent patients will be found. Although the MPR is less rigid than the PDC, the original MPR method is not flexible enough to differentiate non adherent from adherent group. Therefore, the modified MPR method which is more flexible for classifying non-adherent group to adherent group is introduced to help healthcare professionals set an appropriate intervention for each patient to calculate the percentage of adherence.

Material and Method

Sample and data collection

This study was retrospective descriptive study which used electronic medical record from a database of the Somdet Chaopraya Institute of Psychiatry, Thailand during of 10 June 2004 to 14 August 2012. The modified Medication possession ratio (MPR) was applied to assess adherence rate. If the value of medication adherence by patient is greater than or equal to 80%, it will be accepted as good medication adherence. All of the samples must be diagnosed as depression using International Classification of Diseases, Tenth Edition Thai Modification (ICD-10TM) codes of F32 (Depressive episodes), F33 (Recurrent depressive disorder) and F34.1 (Dysthymia). The medications used in this study were grouped as in national list of essential medicines (2011) including 4.2.1 antipsychotic drugs, 4.2.2 anti-manic drugs and 4.3 antidepressant drugs and we excluded the medicine that was used prn. (pro re nata, when necessary for). And we also excluded medication possession ratio (MPR) of medicines which was over 110 percent for each medicine.

Measuring medication adherence

Data collected from a database were used to calculate adherence by Medication Possession Ratio (MPR). The MPR could be calculated with the general equation (MPR = Number of days supplied within refill interval/ Number of days in refill interval). However, the concept of the MPR in our proposed method can be represented in the equation 1.

$$MPR_{ij} = \frac{NM_{ij}}{ND_{ij}} \qquad (1)$$
$$= \begin{bmatrix} 0 \text{ when the ratio is} < 0.8 \\ 1 \text{ when the ratio is} \geq 0.8 \end{bmatrix}$$

Here, the MPR of the ith medicine for the jth patient is defined as the number of days supplied the ith medicine for the jth patient (NM_{ij})/ the number of treatment day for the ith medicine for the jth patient (ND_{ij}). In this paper, a medicine is a set of drugs with same generic names for all strengths. For example, two strengths for fluoxetine are available, i.e., 20 mg. and 40 mg. These two strengths are grouped as the same medicine. If the value of the ratio in equation 1 is greater than or equal to 0.8, the MPR is set to 1. On the other hand, when the value of the ratio was less than 0.8, the MPR was set to 0. With the MPR_{ij}, medication adherence by patient was proposed in this paper. The medication adherence by patient (MA-P) is the ratio of medication possession by equation 1 from all medications for a patient to the number of medications which were taken by the patient. The MA-P was shown in the equation 2 which was the modified MPR method.

Table 1 Levels of medication adherence grouped by MA-P

Percentage of MA-P	Level of Adherence
80 to 100	Adherent Patient
60 to <80	Non-adherent Patient Level 1
40 to <60	Non-adherent Patient Level 2
20 to <40	Non-adherent Patient Level 3
0 to <20	Non-adherent Patient Level 4

$$MA\text{-}P_j = \frac{\sum_i MPR_{ij}}{TM_j} \quad (2)$$

Here, $MA\text{-}P_j$ is the medication adherence of the jth patient and TM_j is the total number of medicines that were taken by the jth patient. The level of medication adherence for a patient was shown in table 1.

If the value of MA-Pj was greater than or equal to 0.80, the jth patient would be accepted as a medication adherence patient. Non-adherent patient level 4 was the most severe non-adherence patients.

Experimental settings

7,346 depressed outpatients were found in database. However, 2,834 depressed outpatients were collected according to the inclusion criteria. The total numbers of medications were 39 items. Data of medications and patients were recorded in a database which is constructed by PostgreSQL, open source database management software. The PHP language is used for creating a program which is applied for calculating medication adherences.

Results

In this section, three experimental results, as statistics of selected patients, the result of medication adherence by patient and the distribution of non-adherent patients on each level, was shown below.

Statistics of selected patients

The distributions of selected outpatients are grouped by gender and age and shown in table 2. Moreover, the selected medicines are shown in table 3. From the result, some observations can be made. For gender, the percentage of female patients was greater than male patients. The interval of ages which obtained the most frequent patients was the 40-59 years old. For medicines on depressed patients, fluoxetine is the most popular medicine for treatment depression. Antipsychotic was also used for treatment of depression. Perphenazine is the most popular medicine of antipsychotic group. Furthermore, Lithium is the most popular medicine of anti-manic group.

Table 2 Background information of depressed outpatients

Descriptions	Number of patients (patients)	Percent (%)
All patients Gender	2,834	100.00
Male	843	29.75
Female	1,991	70.25
Age		
15-19 years old	36	1.27
20-29 years old	300	10.59
30-39 years old	533	18.81
40-49 years old	627	22.12
50-59 years old	621	21.91
60-69 years old	427	15.07
70-79 years old	237	8.36
More than 80 years old	53	1.87

Medication adherence by patient

In this section, the values of medication adherence by patient were calculated using MA-P from 2,834 depressed outpatients, selected according to the inclusion criteria. The results are grouped by adherence's groups (adherence and non-adherent patients), gender and average age, and shown in table 4. From the result in table 4, some interesting information can be concluded. The numbers of adherent patients and non-adherent patients were 1,230 (43.40%) and 1,604 (56.60%), respectively. The result using the original MPR is also calculated which was shown in table 5, the numbers of adherent patients and non-adherent patients were 1,215 (42.87%) and 1,619 (57.13%), respectively. For gender, distribution of non-adherent patient in males and female were 58.84% and 55.74%, respectively. It was not highly different among male and female. Some interesting information can be drawn from age groups, the average from non-adherent groups from the age interval of 15-19 years old, 20-29 years old and 30-39 years old were 61.11%, 69.00% and 63.04%, respectively. These values were higher than the average from all patients. From this result, more than half of outpatients were non-adherent patients. Distribution of non-adherent patients on each level is shown in table 6.

Discussion

Since the modified MPR method in this research was more flexible than the original MPR, then it could classify patients into different non adherent level based on the number of

Table 3 A set of selected medicines

No.	Generic name	Number of patients use medicine (patients)	Percentage of medicine use (%)
Antidepressant drugs			
1	Fluoxetine	1,410	49.75
2	Amitriptyline hydrochloride	675	23.82
3	Mianserin	413	14.57
4	Trazodone	253	8.93
5	Nortriptyline	228	8.05
6	Imipramine	204	7.20
7	Sertraline	185	6.53
8	Escitalopram	132	4.66
9	Venlafaxine HCL	108	3.81
10	Mirtazapine	96	3.39
11	Flupentixol/Melitracen	68	2.40
12	Duloxetine Hydrochloride	29	1.02
13	Fluvoxamine	29	1.02
14	Paroxetine	28	0.99
15	Clomipramine	14	0.49
16	Tianeptine	12	0.42
17	Reboxetine	10	0.35
18	Agomelatine	7	0.25
19	Desvenlafaxine	7	0.25
20	Bupropion Hydrochloride	5	0.18
21	Doxepin Hydrochloride	4	0.14

medicine used. We found that the non adherence to medication patients were higher in young and middle age groups than in old age. This result was consistent to the result of survey about the depressed patient in Japan.[10] This study also showed that the adherence to medication in patients with depressive disorder was lower than those who were non adherent which was quite similar to previous studies.[5,6]

We also found that the rate of adherence using the modified MPR and the rate of adherence using the original MPR were not different (43.40% and 42.87% respectively. This might be counted that the modified MPR in this study could be used interchangeably with the original MPR.

Table 3 A set of selected medicines (continue)

No.	Generic name	Number of patients use medicine (patients)	Percentage of medicine use (%)
Antipsychotic drugs			
1	Perphenazine	448	15.81
2	Haloperidol	240	8.47
3	Risperidone	122	4.30
4	Chlorpromazine	102	3.60
5	Quetiapine	55	1.94
6	Thioridazine	39	1.38
7	Trifluoperazine	38	1.34
8	Amobarbital/Chlorpromazine	35	1.24
9	Olanzapine	31	1.09
10	Clozapine	19	0.67
11	Aripiprazole	15	0.53
12	Paliperidone	9	0.32
13	Flupenthixol	7	0.25
14	Ziprasidone Hydrochloride	5	0.18
15	Pimozide	4	0.14
16	Bromperidol	3	0.11
Anti-manic drugs or Mood stabilizer			
1	Lithium carbonate	72	2.54
2	Lamotrigine	17	0.60

Fluoxetine was the most frequently used medication in this study. Fluoxetine is the antidepressant which is recommended as the first choice medication for depression.[11] To treat psychotic symptoms, it is recommended that the antipsychotic medication be used in conjugate with antidepressant. In this study, perphenazine which is antipsychotic medication was the most frequently used.

Limitations

Though the modified MPR technique is easy and more flexible than the original MPR, this technique does not take account for those who are prescribed as prn.. so some data might be lost for this reason. Moreover, this is a retrospective study, data may be recorded incompletely as well.

Table 4 The result of medication adherent patient by the modified MPR

Descriptions	Number of adherent patient (patients)	Percentage of adherent patient (%)	Number of non-adherent patient (patients)	Percentage of non-adherent patient (%)
All patients Gender	1,230	43.40	1,604	56.60
Male	347	41.16	496	58.84
Female	883	44.35	1,108	55.65
Age				
15-19 years old	14	38.89	22	61.11
20-29 years old	93	31.00	207	69.00
30-39 years old	197	36.96	336	63.04
40-49 years old	265	42.26	362	57.74
50-59 years old	287	46.22	334	53.78
60-69 years old	218	51.05	209	48.95
70-79 years old	125	52.74	112	47.26
More than 80 years old	31	58.49	22	41.51

The averages of non-adherent patients from young and middle-aged groups were higher than those of older-aged groups.

Table 5 The medication adherence by MPR

Percentage of adherent patient (%)	Number of patients (patients)	Percentage of patients (%)	Number of non-adherent patient (patients)	Percentage of non-adherent patient (%)
Adherent Patient	1,230	43.40	1,619	57.13
Non-adherent Patient Level 1	134	4.73		
Non-adherent Patient Level 2	262	9.24		
Non-adherent Patient Level 3	111	3.92		
Non-adherent Patient Level 4	1,097	38.71		

Conclusion

Modified MPR in this study can be used interchangeably with the original MPR. The result showed that there was more non adherence to medication patients than adherent ones. Young and middle age groups found to be prone to be non adherent than old aged group. To prove the efficacy of the modified

MPR, the better than descriptive study design should be performed.

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