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Original Article

A short term outcomes of pharmaceutical care in Thai patients with schizophrenia: a randomized controlled trial

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Abstract

The purpose of this experimental study was to examine the outcomes of pharmaceutical care in schizophrenic patients. Ninety-three patients from three psychiatric hospitals were randomly assigned to receive pharmaceutical care (intervention group) and ninety-five patients received usual care (control group) matched by the severity of disease. Drug related problems (DRPs), patient knowledge and quality of life (QOL) were assessed in both groups. Costs of care were measured in both groups. The number of DRPs decreased significantly more in the intervention group than in the control group ($p<0.001$). The mean knowledge score increased greater in the intervention group ($p<0.001$). The mean QOL score showed a trend towards improvement in the intervention group (both $p<0.001$). Cost-effectiveness ratios (CER) of pharmaceutical care and usual care for achieving good medication adherence was 16.54 and 16.06 USD/successful patient, respectively and CER for improved QOL was 17.30 and 14.98 USD/successful patient, respectively.

Keywords: pharmaceutical care, schizophrenia, clinical outcomes, humanistic outcomes, cost-effectiveness, Thailand

1. Introduction

Schizophrenia is a chronic psychiatric disease characterised by disorders of thought, perceptions, mood and behavior lasting for at least 6 months with the potential to result in suicide. The Diagnostic and Statistical Manual of Mental Disorders fourth revised edition (DSM IV-TR) defines positive and negative symptoms of schizophrenia, which are present for a period of at least between 1 and 6 months. Positive symptoms are bizarre thoughts, delusions and hallucinations. Negative symptoms refer to a loss typically of emotion, speech, or motivation.

The median lifetime morbidity risk for schizophrenia was 7.2/1,000 persons (McGrath *et al.*, 2008). People with schizophrenia have a two- to threefold increased risk of dying (median standardized mortality ratio = 2.6 for all-cause mortality), and this differential gap in mortality has increased over recent decades (McGrath *et al.*, 2008). The WHO reported 24 million patients with schizophrenia in the world population, and that more than 50% receive inappropriate treatment. Approximately 90% of patients with schizophrenia in developing countries were not treated (WHO, 2012). The prevalence of schizophrenia in the Thai people is 0.7-0.9 per 1000 (Lhautrakul and Suchanit, 2005). The prevalence of psychiatric disease in the Thai population was 581 per 100,000 (Mental Health Department, 2007). Schizophrenia has many economic and social effects (Wu *et al.*, 2005).

Pharmacological treatment is the most important procedure for management of psychiatric diseases. Antipsychotic drugs must be used for a long time, so that the most common drug related problem (DRP) is nonadherence (54%) (Dulprapa, 2004). One of the reasons for nonadherence is failure to tolerate adverse drug reactions. Adverse drug reactions associated with antipsychotics are weight gain, drowsiness, orthostatic hypotension, anticholinergic effects, and extrapyramidal side effects (EPS) (APA, 2004). These

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vary between drugs with atypical antipsychotics being less likely to cause extrapyramidal reactions than typical drugs. DRPs in patients with schizophrenia may cause an increase in the recurrence rate, the suicide rate and also increases the cost of treatment. Pharmaceutical care is a process designed to identify, resolve and prevent DRPs and improve patient's QOL (Hepler and Strand, 1990). A systematic review study for effectiveness of pharmaceutical care process by evaluating 22 randomised controlled trials (RCTs) published between 1990 and 2003 showed obviously improved medication use and surrogate endpoints, but improvement in other outcomes was less conclusive (Roughead *et al.*, 2005). Pharmaceutical care is not routinely provided for patients with schizophrenia in Thailand. The usual care provided by pharmacists in hospitals for patients with schizophrenia consist only of dispensing and providing education for using their medications. Therefore, this study set out to pilot and evaluate the provision of pharmaceutical care in Thai patients with schizophrenia.

2. Aim of The Study

The objective of this study was to investigate the effect of pharmaceutical care in Thai patients with schizophrenia on the following three outcomes, clinical (DRPs), humanistic (QOL), and economic (cost/patient with good adherence).

The hypothesis investigated was that "patients with schizophrenia who received pharmaceutical care would have better outcomes than those receiving usual care.

3. Methods

This study consisted of an open, randomised experimental design using two comparison groups and was approved by the Ethical Committee of Mahasarakham University (document number 0056/2008, 0071/2008, 0080/2008). The study was conducted between January 2009 and December 2009.

3.1 Subjects

One hundred and eighty-eight outpatients with schizophrenia in the stabilization phase or maintenance phase were selected for participation in the study and were recruited from the three largest psychiatric hospitals in North-East Thailand: Prasrimahabhodi Psychiatric Hospital (750 beds), Khon Kaen Rajanagarindra Psychiatric Hospital (372 beds) and Nakhon Ratchasima Rajanagarindra Psychiatric Hospital (300 beds). The patients must have been taking antipsychotic drugs for at least 1 month before participating in the study. They were randomly divided into two groups to receive either usual care (control group) or the pharmaceutical care (intervention group) by research pharmacist by a drawing lots.

Patients were excluded if they could not be followed-up throughout the study, had dementia, or were in acute phase during the study. All patients included were given information about the study by research pharmacists and were willing to sign a consent form. The research pharmacists were all 6th year pharmacy students who received training for providing pharmaceutical care for patients with schizophrenia and worked with a registered pharmacist. Patients were followed up 1 month after receiving the intervention.

3.2 Interventions

The research pharmacists developed a pharmaceutical care manual for patients with schizophrenia. The manual described the process of pharmaceutical care for patients with schizophrenia and the patient profile form. All patients in the intervention group received pharmaceutical care, provided by one of the trained research pharmacists.

The provision of the pharmaceutical care process carried out by the research pharmacists had the following steps (designed to take 30 minutes to 1 hour once for each patient):

- Obtaining medication history
- Performing physical assessment of patient s to assess ADRs (such as EPS)
- Evaluating laboratory data
- Reviewing current drug therapy for appropriateness
- Identifying the patients' DRPs
- Consulting with the patient or physician and recommending relevant changes in drug therapy to physicians to resolve or prevent DRPs
- Providing patient education and consultation regarding the disease, its management and drug therapy to resolve or prevent DRPs
- Monitoring patients for desired and undesired outcomes and adherence for 1-month after receiving the therapy review

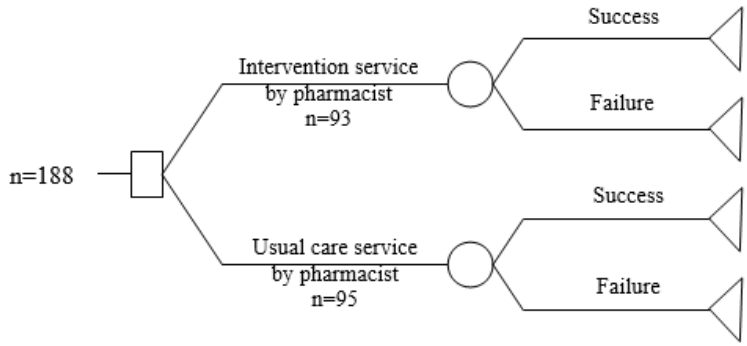
The data were recorded on the pharmaceutical care profile form. The data collection and intervention process were conducted at psychiatric clinics.

3.3 Comparator

Patients in the usual care group received the standard service provided by registered pharmacists working in the three hospitals, of dispensing and giving medicine information to patients or their carers. No attempt was made to control delivery of standard care.

3.4 Cost-effectiveness analysis

A decision analysis model was used to analyze the costs and effectiveness of pharmaceutical care compared with usual care (see Box.1). This model was evaluated from the health care provider's perspective. The direct costs of the two alternatives were composed of three parts, labor cost, material cost and capital cost. Effectiveness was the number



Effectiveness = Success = Medication adherence ≥ 80% (good level) or Quality of Life score was improved from baseline

$$\text{CER} = \frac{\text{Cost of service}}{\text{Effectiveness from service}} \qquad \text{ICER} = \frac{\text{Cost of intervention} - \text{Cost of usual care}}{\text{Effectiveness of intervention} - \text{Effectiveness of usual care}}$$

Cost of service = Labor cost + Material cost +Capital cost

$$\text{Labor cost} = \frac{\text{time spent for service (minutes)} \times \text{monthly salary of pharmacist providing service}}{30 \text{ days/month} \times 8 \text{ hours/day} \times 60 \text{ minutes/hour}}$$

Material cost = Cost of educational materials+ cost of telephone monitoring (if have) + acquisition drugs cost

$$\text{Capital cost} = \frac{\text{time used with equipment (minutes)} \times \text{Depreciation cost of equipment}}{30 \text{ days/month} \times 8 \text{ hours/day} \times 60 \text{ minutes/hour}}$$

$$\text{Depreciation cost of equipment (Straight-line method)} = \frac{\text{Acquisition cost of equipment}}{\text{Useful life time of equipment*}}$$

Figure 1. Decision model and cost calculation formulas

of successful patients whose medication adherence was ≥ 80% (designated as being a good level) or who showed improved quality of life at the end of providing care.

An innovative technology is judged to be cost-effective when its Cost Effectiveness Ratio (CER) is similar to or less than that of the usual technology, or when it has higher costs but shows greater effectiveness or when the Incremental Cost-Effectiveness Ratio (ICER) is in a range that the hospital administration can accept for the additional cost per additional patient with positive outcome. The threshold ICER for a preventive program for this study was defined at the start as less than 500 THB per additional patient with good adherence (or 16.67 USD/patient). All costs are displayed in USD based on the Thai National Bank's average exchange rate in 2009, 1 USD = 30.00097 THB.

3.5 Instruments

1. Patient record forms consisted of demographic data, history of present illness, medication profile, laboratory data, and patient counseling data

2. Costs record form

1) Labor costs included time spent on patient counseling by pharmacists and other health professionals and their monthly salaries

2) Material costs included costs of all materials used in pharmacy counseling such as education media, information booklet, disease and drug indication leaflet, cost of telephone monitoring, and acquisition drug costs

3) Capital costs included depreciation of equipment used in pharmacy counseling such as computer, counter and benches

3.6 Classification of drug-relatedproblems

DRPs were classified according to Hepler and Strand classification (1990). DRPs categorizations used were:

- Untreated Indications
- Improper Drug Selection
- Sub-therapeutic Dosage
- Failure to Receive Drug
- Over-dosage
- Adverse Drug Reactions
- Drug Interactions
- Drug Use without Indication

The DRPs were collected by the research pharmacists before and after the period of 1-month provision of pharmaceutical care.

1. Adherence evaluation questionnaire (Putkhao, 1998) : an interview questionnaire designed for use by pharmacists with patients with schizophrenia and their carers, composed of 7 items, each having yes or no responses. Each item scored one, giving a total score of 7. Good adherence was defined as a score of at least 4 out of 7.

2. Knowledge of schizophrenia and antipsychotic drugs evaluation Questionnaire (Putkhao, 1998): composed of 10 items, with yes or no questions, each item scoring one giving a possible total score of 10.

3. WHOQOL-BREF-THAI (Suntimaleeworakul, 2004): comprising 26 items in 4 domains; physical domain 7 items, psychological domain 6 items, social relationship domain 3 items, environmental domain 8 items, overall QOL 2 items.

The DRPs, knowledge, and QOL were measured before and one month after the intervention. The costs were measured throughout the study.

3.7 Statistical analysis

A database was established and analyzed using SPSS for Windows (V.11.5, IBM corporation). Descriptive statistics are shown as means with standard deviations for continuous variables and frequencies (with percent) for categorical variables, CER and ICER. The scores of QOL, knowledge and adherence in the periods before and after the provision of pharmaceutical care were compared, using the paired t-test or Wilcoxon signed rank test. The scores of QOL, knowledge, number of DRPs, characteristics and adherence in the control group and the intervention group were compared, using the independent t-test or Mann-Whitney U Test at baseline and after the intervention. Statistical significance was considered as $p<0.05$.

4. Results

Demographic details and characteristics of patients are shown in Table 1. Ninety-three patients were in the intervention group and 95 patients were in the control group. No significant differences were found in patients' characteristics between groups before providing pharmaceutical care.

The common DRPs identified in the two groups were failure to receive the drug and adverse drug reactions. In the intervention group, the number of DRPs decreased from 170 problems to 63 problems (62.9%) or an average of 1.83±0.73 problems/person to 0.68±0.49 problems/person (decreased DRPs pre-post = 1.15±0.55 problem/person, $p<0.001$), while the control group decreased from 105 to 90 problems (14.3%) or an average of 1.11±0.45 problems/person to 0.95±0.39 problems/person (decreased DRPs pre-post =0 .16±0.49 problem/person, $p<0.001$). The mean difference between group are statistically significant ($p<0.001$). Most of the DRPs which decreased in the intervention group were failure to receive the drug and adverse drug reaction type A. The details of DRPs are shown in Table 2.

Before giving pharmaceutical care, the mean knowledge score in the intervention group was similar to that in the control group. After giving pharmaceutical care, the knowledge scores of the intervention group (6.7±1.68 to 8.2± 1.48) increased significantly more than in the control group (7.1±1.73 to 7.6±1.75). Before giving pharmaceutical care, most of the patients in both groups had knowledge in the moderate level. After giving pharmaceutical care, most of them had knowledge in the high level. Details of the knowledge of schizophrenia and antipsychotic scores are shown in Table 3.

Before giving pharmaceutical care, the mean adherence score in the intervention group was not significantly different from that in the control group. After giving pharmaceutical care, the adherence scores of the intervention group (5.2± 1.24 to 5.6±0.74) significantly increased while the adherence scores of the control group (5.5±1.42 to 5.0±1.38) significantly

Table 1. Demographic details and characteristics of patients in the intervention and control group

Characteristics	Number of patients (%)		P-value[a]
	Intervention group (n=93)	Control group (n=95)	
Gender Male	68 (73.1)	67 (70.5)	0.693
Age (year) (Mean, ±SD)	36.2 ± 8.37	37.5 ± 9.10	0.325[b]
BMI (kg/m^2) (Mean, ±SD)	22.4 ± 2.98	22.5 ± 3.06	0.931[b]
Alcohol drinking	18 (19.4)	13 (13.7)	0.295
Smoking	35 (37.6)	36 (37.9)	0.971
Marriage status			
Single	68 (73.1)	66 (69.5)	0.854
Married	15 (16.1)	17 (17.9)	
Divorced	10 (10.8)	12 (12.6)	
Relationships in family			
Very good	38 (40.9)	27 (28.4)	0.082
Good	49 (43.0)	59 (62.1)	
Moderate	12 (12.9)	8 (8.4)	
Not good	3 (3.3)	1 (1.1)	

[a] Chi-square, [b] Independent t-test

Table 2. Number of drug related problems of patients in the intervention group and the control group

Types of DRPs	Number of DRPs (%)					
	Before			After		
	Intervention group (n = 93)	Control group (n = 95)	p-value	Intervention group (n = 93)	Control group (n = 95)	p-value
Untreated indication	1 (0.6)	0 (0.0)	0.311 [a]	0 (0.0)	0 (0.0)	-
Medication used without indication	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Improper drug selection	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Sub-therapeutic dosage	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Over dosage	0 (0.0)	0 (0.0)	-	0 (0.0)	0 (0.0)	-
Adverse drug reaction type A	42 (24.7)	19 (18.1)	**< 0.001** [a]	26 (42.3)	23 (25.6)	0.559 [a]
Drug interaction	11 (6.5)	3 (2.9)	**0.024** [a]	5 (7.9)	3 (3.3)	0.451 [a]
Type of non-adherence						
Stop using drugs	17 (10.0)	16 (15.2)	0.796 [a]	3 (4.7)	6 (6.7)	0.321 [a]
Forget to take the drugs	36 (21.2)	23 (21.9)	**0.032** [a]	12 (19.0)	19 (21.1)	0.190 [a]
Taking more tablets than in the prescription	10 (5.9)	12 (11.4)	0.689 [a]	1 (1.6)	10 (11.1)	**0.006** [a]
Taking less tablets than in the prescription	19 (11.2)	12 (11.4)	0.150 [a]	2 (3.2)	13 (14.4)	**0.004** [a]
Not taking drug on time	14 (8.2)	8 (7.6)	0.157 [a]	8 (12.7)	10 (11.1)	0.654 [a]
Cannot take the drug at the time in the prescription	12 (7.0)	9 (8.6)	0.455 [a]	4 (6.3)	3 (3.3)	0.679 [a]
Cannot take all types of drugs in the prescription	8 (4.7)	3 (2.9)	0.112 [a]	2 (3.2)	3 (3.3)	0.668 [a]
Total	170 (100.0)	105 (100.0)	-	63 (100.0)	90 (100.0)	< 0.001

[a] Chi-square test , One patient may have several problems

decreased. Before giving pharmaceutical care, over 90% of patients in both groups had adherence scores at the good level. After the intervention, the adherence scores of 6 patients in the intervention group which were poor had improved, but 4 patients in the control group had scores which changed from good to poor. Details of the adherence scores are shown in Table 4. After providing pharmaceutical care, the scores for quality of life in the intervention group increased significantly in two domains; physical domain (23.4±2.86 to 24.3±2.91; $p< 0.001$) and mental domain (19.1± 3.21 to 21.1±3.54; $p<0.001$), while the scores of quality of life of the control group increased only in the mental domain (20.0±3.49 to 21.0±2.94; $p=0.004$). Furthermore, the total quality of life scores of the intervention group increased significantly (83.8±8.56 to 86.5±8.68; $p=0.002$), but there was no difference in the control group (85.4±11.07 to 85.8± 9.23; $p=0.675$). Quality of life scores are shown in Table 5.

4.1 Cost-effectiveness analysis

The average time for providing usual services was 3.62 minutes/person while the average time for giving pharmaceutical care in the intervention group was 18.73 minutes/person. Labour costs for pharmaceutical care and usual care were 1.07 USD/patient and 0.71 USD/patient respectively. Material costs for pharmaceutical care and usual care were 15.05 USD/ patient and 13.32 USD/patient. Capital costs for pharmaceutical care and usual care were 0.07 USD/patient and 0.004 USD/patient. Thus the total costs for pharmaceutical care and usual care was 16.19 USD/patient and 14.03 USD/patient.

Comparing between pharmaceutical care and usual care, total costs were 1,537.67 and 1,332.76 USD, respectively. Each group showed effectiveness in terms of the number of patients with good level of medication adherence (≥ 80%), which was 93 (97.8%) and 83 persons (87.4%). The CER of pharmaceutical care and usual care for good medication adherence were 16.54 and 16.06 USD/successful patient, respectively. The ICER of pharmaceutical care compared with usual care for improved medication adherence patient was 20.58 USD/successful patient which was higher than the acceptable threshold of 16.67 USD/successful patient. Therefore providing a pharmaceutical care intervention in order to improve medication adherence did not meet this cost-effectiveness criterion. For quality of life, ICER was dominated by usual care because it consumed less cost (1,332.76 vs 1,537.67 USD) but showed almost the same effectiveness as

Table 3. The scores of the knowledge of schizophrenia and antipsychotics used of patients in the intervention group and the control group

Knowledge of disease and antipsychotic used	Before			After			p-value of comparing before and after in each group	
	Intervention group (n = 93)	Control Control (n = 95)	p-value	Intervention group (n = 93)	Control group (n = 95)	p-value	Intervention group (n = 93)	Control group (n = 95)
Knowledge scores (total scores 10) (Mean ± SD)	6.7 ± 1.68	7.1 ± 1.73	0.097[a]	8.2 ± 1.48	7.6 ± 1.75	0.009[a]	< 0.001[b]	0.010[b]
Knowledge level (number of patients (%))								
high (8 – 10)	32 (34.4)	41 (43.2)	0.179[c]	70 (75.3)	54 (56.8)	0.008[c]	< 0.001[d]	0.037[d]
moderate (4 – 7)	57 (61.3)	52 (54.7)		22 (23.7)	39 (41.1)			
low (0 – 3)	4 (4.3)	2 (2.1)		1 (1.1)	2 (2.1)			

[a] Independent t-tests, [b] Paired t-tests, [c] Chi-square, [d] McNemar tests

Table 4. Compliance scores of patients in the intervention group and the control group

Compliance	Before			After			p-value of comparing before and after in each group	
	Intervention group (n = 93)	Control Control (n = 95)	p-value	Intervention group (n = 93)	Control group (n = 95)	p-value	Intervention group (n = 93)	Control group (n = 95)
Compliance scores (Mean ± SD) (total scores 7)	5.2 ± 1.24	5.5 ± 1.42	0.115[a]	5.6 ± 0.74	5.0 ± 1.38	0.010[a]	0.020[b]	< 0.001[b]
Compliance level Number of patients (%)								
Good (4-7 score)	85 (91.4)	87 (91.6)	0.965[c]	91 (97.8)	83 (87.4)	0.060[c]	0.070[d]	0.344[d]
Poor (1-3 score)	8 (8.6)	8 (8.4)		2 (2.2)	12 (12.6)			

[a]Mann Whitney U tests , [b]Wilcoxon sign Rank tests, [c]Chi-square, [d]McNemar tests

Table 5. Quality of life scores of patients in the intervention group and control group

Quality of life (total scores)	Mean score of quality of life (Mean ±S.D)					
	Intervention group (n=93)			Control group (n=95)		
	Before	After	P-value	Before	After	P-value
Physical (35)	23.4 ± 2.86	24.3 ± 2.91	< 0.001[b]	23.7 ± 2.72	23.8 ± 2.83	0.748[b]
Mental (30)	19.1 ± 3.21	21.1 ± 3.54	< 0.001[a]	20.0 ± 3.49	21.0 ± 2.94	0.004[b]
Social (15)	8.8 ± 1.73	9.1 ± 1.99	0.064[b]	8.8 ± 2.27	9.0 ± 2.01	0.503[b]
Environment (40)	25.3 ± 3.68	25.3 ± 4.13	0.873[a]	25.3 ± 4.80	25.4 ± 3.94	0.784[b]
Total scores (120)	83.8 ± 8.56	86.5 ± 8.68	0.002[a]	85.4 ± 11.07	85.8 ± 9.23	0.675[a]

[a] Paired t-tests, [b]Wilcoxon Sign Ranks tests

pharmaceutical care (89 or 95.7% vs 89 persons or 93.6%). These results showed that pharmaceutical care was not cost-effective after one month. From one-way sensitivity analysis, we found that the pharmaceutical care service will reach cost-effectiveness when the pharmaceutical care can make 20 additional patients with good drug adherence compared with the usual care.

5. Discussion

This study showed that pharmaceutical care could reduce DRPs, increase patient knowledge and quality of life in patients with schizophrenia. Most of the drug related problems identified were non-adherence and adverse drug reactions. Most of the causes for non-adherence were "forget to take drug" and "cannot use drug as in the prescription". These may occur as the result of the disease itself or adverse drug reactions affecting the patients' memory. Moreover, because of the long duration of treatment, patients with schizophrenia may feel unhappy taking the drug, patients may not have knowledge related to the disease and antipsychotics used, or they may experience adverse drug reactions.

Adverse drug reactions are an important drug related problem. Most ADRs are type A and therefore preventable DRPs. This is especially the case with typical antipsychotic drugs which have anticholinergic effects (dry mouth, blurred vision, urinary retention) and extrapyramidal symptoms. After giving pharmaceutical care the number of ADRs decreased significantly in the intervention group, presumably because the pharmacists identified the ADRs, gave counseling for preventing ADRs and made recommendations to the physician to resolve the problems such as decreasing dose or change to alternative drugs.

Our patients with schizophrenia had an adherence rate of about 70% (5/7*100) in both groups, both before and after giving pharmaceutical care, which was higher than expected. Despite this, sufficient patients in the intervention group showed improved adherence to a good level after receiving pharmaceutical care to demonstrate statistical significance. Some patients in the control group had poor adherence levels after the study for one month. Good adherence requires continuously remembering to take medications. Medication non-adherence is common and difficult to detect in patients with schizoaffective disorder and schizophrenia particularly, because of their poor memory and recall. Approximately 50% of patients take less than 70% of prescribed doses. Many factors contribute to non-adherence, including poor illness insight, a negative attitude toward medication, substance abuse and disorganization. Interventions to improve adherence consist of advising acceptance of illness, drawing analogies. Interventions which offer more sessions over a longer period of time with a continuous focus on adherence are most likely to be successful, as well as pragmatic interventions that focus on attention and memory problems (Barkhof, 2011). The adherence rate in this study was evaluated by using a questionnaire specifically developed for use in patients with schizophrenia. The questions ask about the consistency of taking drug, how often they increase or decrease dose by themselves, how often patients forget to take drug, and how often they see the doctor in the hospital before the appointment for follow up. The adherence rate translates from the adherence score, so the adherence rate may be different from other studies. Improvements in scores in the intervention group derived mainly from not changing doses by themselves, and taking the drug with higher consistency, whereas some patients in the control group showed increases in forgetting to take their drug. Similarly most patients' knowledge was moderate to high at baseline, but a significant increase was found after receiving pharmaceutical care. When patients have increased the knowledge, adherence has been shown to be increased correspondingly (Xia, 2011).

Total quality of life scores increased significantly after receiving pharmaceutical care, as did scores in the physical domain and mental domain. Although quality of life in social and environmental domains were not changed, these effects may be more likely to change after a longer period of intervention. Furthermore quality of life scores in the mental domain of the control group also increased significantly, suggesting that this domain may be more sensitive than other domains in this population. In addition, WHOQOL-BREF-THAI questionnaire is not specific for patients with schizophrenia and may not be sensitive to change over a short time. Further studies are needed to develop a quality of life measure which is specific for Thai patients such as by modifying S-QoL (Auquier *et al.*, 2003; Lancon *et al.*, 2007) or S-QoL 18 (Boyer *et al.*, 2010). The quality of life scores slightly increased but changes were not significant statistically. It is not clear why changes occurred but it could be hypothesized that patients such as these, who have psychological problems, are often lonely and may need sympathy. Pharmacists in the process of providing pharmaceutical care could thus have contributed to them feeling better. In addition, if psychological well-being increased, the physical well-being will be better.

The labour costs, material costs, capital costs and total costs for giving pharmaceutical care activities for patients with schizophrenia were, as expected, more than for usual care activities. The labour costs and capital costs of pharmaceutical group were higher than those of the usual care group because the pharmacists spent more time to identify, resolve and prevent and give drug counseling for patient. In addition, the pharmacists used more educational media for the pharmaceutical care group than for the usual care group, so that the material costs of pharmaceutical care was higher than the usual care.

CER of pharmaceutical care was similar to that of usual care for good medication adherence. Damen and others (2008) have studied the impact on adherence with atypical antipsychotics using a pharmacoeconomic discrete-event simulation (DES) model, adapted to the Swedish treatment

setting (Damen *et al.*, 2008). Improved adherence among patients with schizophrenia resulting in health improvements and cost savings are in balance with the additional costs. However, CER for improved quality of life for one successful patient in pharmaceutical care was higher than for usual care. Although the costs of pharmaceutical care group were higher than the usual group, the scores of quality of life in physical and mental domains were also higher than the usual care, which may be clinically significant. In this study we considered cost per patient with good medication adherence or improved quality of life as the clinical outcomes, for comparison with other health technologies, that may report cost per quality-adjusted life-year (QALY), which will be cost effective when ICER is less than 3 times of gross domestic product (GDP).

If pharmaceutical care could have been provided for a longer time, the number of successful patients would be increased. That shows an improve in medication adherence over usual care. Sensitivity analysis showed that a minimum of 20 successful cases was required for pharmaceutical care to be cost-effective with an ICER of 3.96 USD/successful patient, which is less than the agreed acceptable ICER of 500 THB/ successful patient (or 16.67 USD/successful patient from the hospital administrator's viewpoint).

A systematic review has evaluated the quantity and quality of medical literature examining the impact of pharmacists in mental health from 1972-2003 (Finley, 2006). The 16 studies evaluating the impact of pharmacists in mental health demonstrated improvements in outcomes, prescribing practices, patient satisfaction and resource use. Nine of the studies examined the role of pharmacists in providing treatment recommendations and patient education, five featured pharmacists as providers with prescriptive authority, and two studies described the impact of pharmacists in delivering education to the psychiatric staff. However, most of the studies were small, and significant limitations in study design limit further comparison. Other studies measuring the impact of medication information for adult psychiatric patients on adherence, knowledge, economic, clinical and humanistic outcomes were recently reviewed. Adherence was 11-30% higher in the intervention groups than in the control group and knowledge was increased by 14-28% in intervention groups in comparison with controls. No significant differences were seen for frequency of side-effects, relapse or admission rates, symptoms or quality of life. Not one of the 17 studies in this review explored the economic impact of the intervention (Desplenter *et al.*, 2006). In contrast, our study has shown the potential success of pharmacists in mental health care settings and indicated the level of outcome required to demonstrate cost-effectiveness in supporting the role of the psychiatric pharmacist.

This is the first randomized controlled trial studying the outcomes of pharmaceutical care in patients with schizophrenia. The study covered all the three types of outcomes: clinical, humanistic and economic outcomes. A major limitation of this study was that intermediate outcomes were used and not endpoints, because measurements of end points would have required longer studies. Generalization of the results of this study is limitated because our patients were recruited from only three psychiatric hospitals in northeast of Thailand, where standard practices may differ from elsewhere. Furthermore, the unblinded design may have lead to bias, as the research pharmacists both provided the pharmaceutical care and gathered the data for analysis. Patients included had to have only one month of antipsychotic treatment, but were required to be in a stable phase of the illness. Details of duration of treatment, symptom severity and specific diagnoses were not obtained, hence there may have been differences between groups in these parameters. Follow-up questionnaires were administered after only one month interval, which may have been inadequate to demonstrate any benefits of pharmaceutical care. Future studies should ensure comparable patient groups, and examine the provision of pharmaceutical care over more prolonged periods. The study was a small pilot project and, as such, had no power to detect specific differences in a single primary outcome measure. Further work is required to design and conduct a more robust study which has power to detect a clinically significant difference in either adherence or quality of life.

Based on the results, despite the limitations, we advocate further expansion of pharmaceutical care services over standard care for patients with schizophrenia in the future.

6. Conclusions

Pharmaceutical care in schizophrenia can reduce the number of drug related problems, and increase knowledge of schizophrenia, adherence to antipsychotic use and quality of life in the physical and mental domains. However, 1-month of pharmaceutical care was not cost-effective in terms of improving medication adherence or quality of life from the provider perspective. If in the long term pharmaceutical care can increase the number of successful patients compared with the usual care by at least 20 cases, it will become cost-effective.

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