

FACTORS RELATED TO DECISION-MAKING TOWARDS PARTICIPATION IN CLINICAL TRIALS IN DIABETES PATIENTS AT KING CHULALONGKORN MEMORIAL HOSPITAL, BANGKOK, THAILAND

Rakjit Kanlayanatam, Naowarat Kanchanakhan*

College of Public Health Sciences, Chulalongkorn University, Bangkok, 10330, Thailand

ABSTRACT:

Background: In aspects of ethics and human rights, all clinical trials must be conducted according to the International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) to ensure that the patient is always well-being and safe during participating in the clinical trials; patient's comprehension should be enhanced with a clear understanding of clinical trial participation before their decision to enter a clinical study. The number of Thai patients participating in clinical trials has increased. There are several factors that affect patient decision making whether to participate or decline to participate in a clinical trial, and to enable better decision making it is important to enhance health professionals' role to provide better support to their patients. It is therefore imperative to assess patient's knowledge and attitude about clinical trials before patient's participation, and to learn and focus more about the factors related to patients' decision-making towards participation in clinical trials.

Methods: A cross-sectional study through self-questionnaire data collection method described factors related to the decision making process regarding participation in clinical trials. The study was conducted in diabetes patients at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. 110 diabetes patients was included. Multiple logistic regression analysis was used to examine factors that influence phase III clinical trial participation.

Results: Majority was female patients and age range 61-80 years. Some factors that were associated with a positive decision making outcome. Good knowledge and attitude on clinical trial participation was significantly associated with patients' acceptance of clinical trial participation. Collected data also represented diabetes patients with good knowledge at 60.7% and high level of attitude at 94.6% influencing their acceptance to participate in the clinical trial. Logistic regression analyses showed that the factors best explaining participation were knowledge about clinical trial ($p=0.007$), attitude towards clinical trial participation ($p<0.001$), and patient with single status ($p=0.025$). 56/110 (50.9%) patients accepted to participate in Phase III clinical trials and the therapeutic benefits (60.9%) as primary reason and helping the future of clinical trials as secondary reason for acceptance to participate in Phase III clinical trial in diabetes patient. The influential factors that was significantly associated with decision-making of patient include age ($p=0.001$), knowledge ($p=0.001$ by Chi-square, $p=0.003$ by t-test), and attitude ($p=0.001$ by Chi-square and t-test).

Conclusion: The findings can make a difference in the study towards patients' knowledge and attitude towards clinical trial participation.

Keywords: Clinical trials; Decision making; Clinical trial participation; Diabetes; Factors related to decision-making

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INTRODUCTION

Over the past decade, the number of clinical trials in Asian countries has increased rapidly due to

* Correspondence to: Naowart Kanchanakhan
E-mail: Naowarat.K@chula.ac.th

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the importance of evidence based on ethnic diversity and cost-effectiveness in clinical trials. Nowadays (year 2015), Thailand is one of the most rapidly growing in Southeast Asian countries, ranking number one and most active region for industry-sponsored clinical trial (1,739 studies of total 3,956 studies in Southeast Asia, as of 25 June 2015) [1]. The globalization of phase III clinical trials can bring both benefits and risks to research subjects. Depending on the study design, during participating in clinical trial patients may be asked to receive an investigational new drug (IND) or alternative treatment as either monotherapy or combination with a standardized regimen, to accept treatment assignment by randomization, to undergo additional study procedures, laboratory tests, exams, and interviews, and, in the blinded trial, to remain unaware of what drug they are taking for the duration of the study. Although the risks resulting from participation is not known and there may be other side effects of drug or study procedures that may happen that are not known, it is evident that subjects or sick volunteers often participate in clinical trials for many reasons; for example hope for better treatment, financial, and altruism. However, beyond the risks and benefits from clinical trial participation, there are other factors that influence patient's decision to participate or declining to participate in clinical trials [2, 3].

Previous studies reported that patients' knowledge and attitudes on clinical trials are important influential factors in their decision-making process to participate in clinical trials [2, 4, 5]. The factors are varied in individual patients depending on; for example patients' health status, socio-demographic characteristics, medical insurance plan, and their experience in clinical trial participation [2]. Even patients decide to take part in clinical trials with many reasons, however it was found that patients' knowledge about clinical trial and attitude were related to their decision-making for clinical trial participation and other influential factors is necessary to be investigated in future study. Furthermore, a previous study reported that patients who had a high level of understanding of clinical trials were likely to have a more positive attitude toward participation than were those with lower levels of understanding, which impacted their decision-making to participate in clinical trials respectively. This means the positive attitudes can lead to decide for participating in the clinical trial [6]. The relationship between attitudes and decision-

making in patients for participation in clinical trials is correlation. In previous studies also reported the positive attitudes is a major factor for patients' decision-making to participate in clinical trials [3, 6-8]. However, the difference of individual demographic data, knowledge, and understanding of clinical trial is still varied and it is the factors related to decision-making in patients. The specific cancer trials and cancer patients were frequently studied in the literature which may be a gap in research because of limited study area [9]. Mostly cancer patient participated in clinical trials with alternative treatment reason, patients' health status, medical insurance plan, and economic purpose which were not broaden to non-clinical trial patient or patient in different therapeutic area those who may have more alternative and the clinical trial is not their best option [3, 5, 6, 9-12]. Therefore, to further research in non-clinical study specific and in different therapeutic area beyond cancer patient is recommended to be more focused; and due to the number and percentage of deaths among Thai people, diabetes stands on the top 12 causes of death especially in female that is in the top 5 causes of death. Diabetes is one of chronic diseases that are major health problems among Thai people 1991-2009 with its prevalence has been risen every year as well as rate of hospitalization of patients with diabetes [13]; and management of diabetes in providing greater efficacy of treatment in diabetic patient is continuously developed in medical field for discovering a new drug that would be more efficacy and better response to metabolic mechanism in diabetic patient than the existing medicine and treatment; in addition to find a new techniques in therapeutic procedure in order to prolong glucose control and decrease complications in the patient which would need more studies in clinical trials, therefore diabetes patient was studied in this research. The results of this research can make a difference in the study towards patients' knowledge and attitude towards clinical trial participation.

METHODOLOGY

A cross-sectional descriptive study was conducted at King Chulalongkorn Memorial Hospital, Bangkok, Thailand [14] during 5-17 November 2015. Diabetes patients aged 18-80 years were eligible to participate in this study.

A convenient sample of individual patient was recruited from out-patient of the Endocrinology

Metabolism and Thyroid Clinic and study population included patients who are non-participant in any clinical trials during last 6 months. The sample size was determined using Fisher's (1998) formula [15] and 110 patients were approached to complete the questionnaire. Data collection was implemented through self-administered questionnaire and face-to-face interview for some case like elderly patients. All questionnaires are administered in Thai language. The questionnaire was adapted from the literature and the existing questionnaires from the previous studies [4, 5, 9] with similar points to focus on assessment of patients' knowledge on clinical trial and attitude towards clinical trial participation. The measurement methods for each variable using the questionnaire which consists of 4 sections (Section 1: Socio-demographic characteristics with 13 items; Section 2: Knowledge about clinical trials, 12 items [Yes/No choice]; Section 3: Attitude towards clinical trial participation, 10 items with 5-point Likert scale; and Section 4: Decision-making to participate in clinical trial, 4 items which comprises one key statement (Yes/No choice to explore whether patients will participate in clinical trial or not). The questionnaire was pilot-tested and retested with 30 sampling patients at least, whose socio-demographic data and criteria is equivalent to study population. Cronbach's alpha coefficient was used to measure reliability of the questionnaire for attitude. Reliability test result is 0.734.

DATA ANALYSIS

Data analysis was performed through the licensed SPSS statistical package. Descriptive statistics was used to describe and analyze the patients' socio-demographic characteristics level of knowledge about clinical trials, level of attitude towards clinical trial participation, patients' decision-making to participate in phase III clinical trials, and study variables. It includes central tendency (mean, median) and dispersion (standard deviation, 95% CI), frequency and percentage. A Chi-square test was conducted to determine differences in categorical data, and the t-test was used to compare the mean values of variables. Univariate analysis and multiple logistic regression model were used for analytical statistics in this research. Results were considered statistically significant at a p -value <0.05 .

ETHICAL CONSIDERATION

This study was approved by the Institutional

Review Board of the Faculty of Medicine, Chulalongkorn University (COA no. 771/2015). Prior to patient participation in this study, written informed consent was obtained by the researcher or designated research assistants from each patient in the waiting area of OPD, Endocrinology Metabolism and Thyroid Clinic. The purpose of the study, methods, how many questions and estimated time of completing a questionnaire, the anticipated benefits, and that study participation is voluntary for the patients were explained to the patients. The patients were given sufficient time to consider whether to participate in the study.

RESULTS

The socio-demographic characteristics of diabetes patients are listed in Table 1. In total, 110 patients completed the questionnaire. The socio-demographic factors include age, gender, marital status, religion, education, occupation, monthly income, health status, medical insurance plan, living area, and distance from home to hospital. Majority of the patients were female in the age group "61-80 years" (46%) and minority were in the age group "18-30 years" (11%) and living in Bangkok (85.5%). Collected data described patient with diabetes (56.4%) and patient with concomitant disease (43.6%). Most patients had rather moderate and good knowledge on clinical trials (70.9% and 23.6%); and the level of attitude towards clinical trial participation in diabetes patients showed 80% high level. The proportion of patient's decision-making for clinical trial participation was acceptance rate at 50.9% and decline rate at 49.1%. The therapeutic benefits (60.9%) was the patient's main reason for their decision to participate in clinical trial, and decision for clinical trial participation whether or not will be made by themselves the most (71.8%); and family members (20%) is a secondary influential person for their decision. The demographic variables, age and transportation are the influential factors which were significantly associated with patients' decision for clinical trial participation ($p=0.001$, $p=0.046$ respectively) as shown in Table 1.

Table 2, the relationship between patients' attitude towards clinical trial participation (attitude score range 10-50 points) and their decision-making for clinical trial participation, the mean score was 36.88 (SD=3.45) as Good Attitude which was associated with acceptance of clinical trial participation ($n=56$). As a result, good attitude was

Table 1 Relationship between socio-demographic characteristics of diabetes patients and clinical trial participation

Variables	No. of patients	Accepted		Declined		p-value
		No.	%	No.	%	
Age, (years)						0.001
18 - 30	11	11	19.6	0	0.0	
31 - 40	22	7	12.5	15	27.8	
41 - 60	31	18	32.1	13	24.1	
61 - 80	46	20	35.7	26	48.1	
Gender						0.525
Male	21	12	21.4	9	16.7	
Female	89	44	78.6	45	83.3	
Marital status						0.174
Single	13	9	16.1	4	7.4	
Married	81	37	66.1	44	81.5	
Widow, separate	16	10	17.9	6	11.1	
Religion						1.000
Buddhism	106	54	96.4	52	96.3	
Others	4	2	3.7	2	3.6	
Education						0.484
≤ Primary school	34	14	25.0	20	37.0	
High school	21	11	19.6	10	18.5	
Certificate / diploma	13	8	14.3	5	9.3	
≥ Bachelor's degree	42	23	41.1	19	35.2	
Occupation						0.477
Employee	24	11	19.6	13	24.1	
Self-employed	15	6	10.7	9	16.7	
Government officer	7	5	8.9	2	3.7	
Dependent	38	18	32.1	20	37.0	
Others	26	16	28.6	10	18.5	
Monthly income (THB)						0.484
< 10,000	37	21	37.5	16	29.6	
10,000-30,000	51	24	42.9	27	50.0	
30,000-50,000	11	4	7.1	7	13.0	
> 50,000	11	7	12.5	4	7.4	
Health status						0.548
Diabetes	62	30	53.6	32	59.3	
Concomitant disease	48	26	46.4	22	40.7	
Medical insurance plan						0.281
Universal Coverage (UC)	17	12	21.4	5	9.3	
Civil Servant Medical Benefits Scheme (CSMBS)	37	19	33.9	18	33.3	
Social Security Scheme (SSS)	24	13	23.2	11	20.4	
Private insurance	3	1	1.8	2	3.7	
Others	29	11	19.6	18	33.3	
Living area						0.644
Bangkok	94	47	83.9	47	87.0	
Other provinces	16	9	16.1	7	13.0	
Transportation						0.046
Bus	29	19	33.9	10	18.5	
Taxi	23	10	17.9	13	24.1	
Own vehicle	44	17	30.4	27	50.0	
Others	14	10	17.9	4	7.4	
Travel time from home to hospital (hour)						0.162
≤ 2 hours	101	49	87.5	52	96.3	
>2 hours	9	7	12.5	2	3.7	

Table 2 Relationship between attitude and clinical trial participation

Variables	Accepted		Declined		p-value
	No.	%	No.	%	
Attitude score: Mean \pm SD	36.88 \pm 3.45		33.72 \pm 3.92		<0.001 ^a
Low level of attitude	0	0.0	2	3.7	<0.001 ^b
Moderate level of attitude	3	5.4	19	35.2	<0.001 ^c
High level of attitude	53	94.6	35	64.8	

a Two-sample t-test

b Pearson's chi-square test (By grouping low and moderate attitude row because of too small number)

c Fisher's exact test

Table 3 Multiple logistic regression model of acceptance to participate in clinical trials

Variables	b	p-value	Adjusted OR	95% CI
Attitude score	0.268	<0.001	1.31	1.13 - 1.51
Knowledge score	0.541	0.007	1.72	1.16 - 2.55
Marital status				
Single	1.620	0.025	5.05	1.22 - 20.91
Widow, separate	1.286	0.076	3.62	0.87 - 15.01

highly related to decision-making for clinical trial participation in diabetes patients ($p < 0.001$ by Chi-square).

DISCUSSION

The major findings of this study were the proportion of patient's decision-making for clinical trial participation with acceptance rate at 50.9% and refusal rate at 49.1%. Majority of diabetes patients was range 61-80 years and female. This study reported some factors that were associated with a positive decision making outcome (say 'yes' to join the trial in the future). Good knowledge and attitude on clinical trial participation was significantly associated with patients' acceptance of clinical trial participation. Collected data also represented diabetes patients with good knowledge at 60.7% and high level of attitude at 94.6% influencing their acceptance to participate in the clinical trial.

Attitude was significantly associated with decision-making for CT participation ($p < 0.001$) which were a factor related to patients' decision-making to take part in the trial. This result is in line with previous studies that reported the positive attitude is a major factor for patients' decision-making to participate in clinical trials. It was also indicated that the attitude could predict future behavior according to Kraus's study, Attitudes and the Prediction of Behavior [16].

To identify the relationship between socio-demographic characteristics of patients, patients' knowledge about clinical trial, patients' attitude towards clinical trial participation, and their

decision-making for participation in phase III clinical trials, multiple logistic regression models was used for analysis. Using backward elimination (with log-likelihood ratio test), the final model comprised only 3 variables i.e., marital status (Married, Single, Widow/Separated), knowledge score and attitude score as shown in Table 3. Moreover, it was interestingly reported in this study that the most frequency of incorrect response to a question on patient knowledge assessment was "*The physician can convince or persuade you to participate in clinical trials*" which represented 28.2% (31/110) for correct response. This implied mostly patients (71.8%) always trust in their doctor and the doctor can convince them to join the trials; it described patient's belief and point of view to their doctor. Similar to another study [5], reported that 47.2% of patients discussed with doctor for their decision to take part in the clinical trial.

However, in this study, the proportion of acceptance (50.9%) and refusal (49.1%) rate of clinical trial participation was not significant difference in this small sample size. Therefore, similar studies with a larger sample size will help to confirm the result of this study. A total of 110 patients in this study is a small sample size and limited power. The study was conducted at only one public hospital in the center of Bangkok and findings cannot be extended to other hospitals in different region of Thailand. The target population in this research was only out-patient with diabetes diagnosis which is not extent to in-patient and another disease indication. Therefore, the factors to

influence in-patient and patients in other diseases for clinical trial participation were not identified and their knowledge and attitude towards clinical trial participation was not investigated. Study outcome would be a primary data for future studies with a larger sample size and further studies in different therapeutic area is recommended.

CONCLUSIONS

A total of 110 diabetes patients completed the structured questionnaire in the study and they have never participated in a clinical trial during last 6 months or currently participating in any clinical trials. This study reported that 50.9% of the patients will participate in the phase III clinical trial if they will be asked to join in the future. Majority of the patients were female in the age group "61-80 years" (46%) living in Bangkok (85.5%). Collected data represented patient's health status as diabetes (56.4%) and diabetes with concomitant disease (43.6%). Mostly patients (60.9%) gave reason of therapeutic benefits (hope to get better treatment) as their main reason for clinical trial participation. 79 of 110 patients (71.8%) decided to participate in the trial by themselves and 20% by family. Interestingly, 27 of 110 patients (24.5%) is optimistic with altruism reason.

Overall knowledge about clinical trials indicated that 70.9% of patients had moderate knowledge on clinical trials and 23.6% had good knowledge. Another findings of attitude towards clinical trial participation in this study, it showed that 80% of patients had good attitude and low attitude represented just only 1.8%. Logistic regression analyses showed that the factors best explaining participation were knowledge about clinical trial ($p=0.007$), attitude towards clinical trial participation ($p<0.001$), and patient with single status ($p=0.025$). Furthermore, the data findings also represented the significant relationship between age and decision for clinical trial participation ($p=0.001$), transportation and decision ($p=0.046$), and relationship between moderate knowledge and decision for clinical trial participation ($p=0.003$), and relationship between good attitude and decision for clinical trial participation ($p<0.001$) respectively.

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