



ปัจจัยในการทำนายการตอบสนองต่อการรักษาของผู้ป่วยโรคซึมเศร้าที่ได้รับการรักษาทางจิตเวชในกรุงเทพมหานคร

รณชัย คงสกนธ์ *

Guy Edwards**

บทคัดย่อ

วัตถุประสงค์ เพื่อศึกษาปัจจัยในการทำนาย การตอบสนอง ต่อการรักษาของผู้ป่วยโรคซึมเศร้าที่ได้รับการรักษาด้วยกระบวนการรักษาทางจิตเวชในโรงพยาบาลรามาธิบดี

วิธีการ Cohort study ศึกษาในผู้ป่วยโรคซึมเศร้า จำนวน 96 คน ที่มารับการรักษาแผนกจิตเวช โรงพยาบาลรามาธิบดี ติดตามการรักษา 3 เดือน ด้วยแบบวัด Hamilton rating scale for depression ฉบับภาษาไทย ประเมินผลก่อนและหลังการรักษา ศึกษาผู้ป่วยที่มีคะแนนลดลง 50% ที่ถือว่าตอบสนองต่อการรักษา และใช้สถิติในการวิเคราะห์ปัจจัยตอบสนองต่อการรักษา ด้วย chi-square test

ผลการศึกษา อัตราการตอบสนองต่อการรักษาทางจิตเวชระยะเวลา 3 เดือน ร้อยละ 67.7 (95% C.I.=58.18-77.23) จากการวิเคราะห์ทางสถิติ ไม่พบปัจจัยที่เป็นตัวทำนายการตอบสนองในระยะเวลา ได้อย่างมีนัยสำคัญทางสถิติในการศึกษาครั้งนี้

สรุปผลการศึกษา โรคซึมเศร้า เป็นปัญหาทางสาธารณสุขที่สำคัญที่เกี่ยวข้องควรตระหนักถึงการสูญเสียความสามารถทางหน้าที่การงานทั้งก่อนและหลังการรักษาอย่างชัดเจน แต่เป็นโรคที่ให้การรักษาได้โดยมีอัตราการตอบสนองที่ดี ในระยะเวลาเพียง 3 เดือน ภายใต้กระบวนการรักษาทางจิตเวช แม้ว่าปัจจัยการทำนายผลต่อการรักษา จะไม่พบในการเก็บข้อมูลในขณะนี้ จึงมีความจำเป็นต้องมีการศึกษาในระยะเวลาที่นานขึ้น ในผู้ป่วยจำนวนมากขึ้นต่อไป

คำสำคัญ โรคซึมเศร้า การตอบสนองต่อการรักษา ปัจจัยทำนาย

วารสารสมาคมจิตแพทย์แห่งประเทศไทย 2549; 51(2): 107-116.

* ภาควิชาจิตเวชศาสตร์ คณะแพทยศาสตร์ โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล กทม 10400.

** Southampton University Hospitals Trust, Southampton, Hampshire, SO16 6YD, UK.



Predictors of Response to Antidepressant Treatment in a Cohort of Bangkok Patients

Ronnachai Kongsakon M.D., LL.B., M.Sc.^{a*}

J Guy Edwards M.D.^{**}

Abstract

Objective To assess the value of commonly elicited and recorded demographic characteristics and clinical data as possible predictors of a therapeutic response to treatment of depression in a Bangkok university hospital.

Patients and Methods After initial screening, 96 outpatients diagnosed on DSM-IV criteria as having depressive disorders by the psychiatrists responsible for their treatment were rated on a Thai version of the Hamilton rating scale for depression (HAM-D (Thai)) before and after three months treatment. Those with a 50% or greater reduction in score on the HAM-D (Thai) were regarded as responders. The statistical association between the demographic and clinical data and response to treatment was assessed by the chi-square test.

Results The response rate following 3-month psychiatric care was 67.7% (95% C.I.=58.18-77.23). There was no statistically significant association between any of the demographic and clinical data and the outcome of treatment.

Conclusion The treatment outcome in the Thai psychiatric setting described is comparable to that reported in other countries and had shown a good response rate. Much routinely elicited demographic and clinical information recorded in this population of Thai patients appears to be unhelpful in predicting the response to three months treatment of depression.

Key words Depression, Treatment response, Predictors, Thai patients

J Psychiatr Assoc Thailand 2006; 51(2): 107-116.

^a **Address for correspondence:** *Ronnachai Kongsakon, M.D., LL.B., M.Sc.,*

Department of Psychiatry, Faculty of Medicine, Ramathibodi Hospital,

Mahidol University, Bangkok, 10400, Thailand.

Tel: (662) 2011098 E-mail: rarks@mahidol.ac.th

Submitted: 24 March 2006

* Department of Psychiatry, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, 10400, Thailand.

** Southampton University Hospitals Trust, Southampton, Hampshire, SO16 6YD, UK.

Introduction

Clinical and biological predictors of a therapeutic response to antidepressant treatment (especially pharmacotherapy) have been studied since shortly after the introduction of antidepressant drugs into clinical practice in the late 1950s. The many studies that have been carried out since then have been reviewed by Bielski & Friedel (1976), Ananth (1978), Tyrer et al (1980), Joyce & Paykel (1989), Kocsis (1990), Goodwin (1993) and others. Practically all of the studies were undertaken in Western populations. None of them was carried out on Thai patients. The aims of the present study were therefore to assess the value of a range of commonly documented clinical predictors in Thai patients treated in a Bangkok hospital.

Methods

Patients

All out-patients referred to Ramathipodi Hospital, Bangkok, are assessed by senior doctors and those with psychiatric disorders are diagnosed on the basis of conventional DSM-IV criteria (American Psychiatric Association, 2000). Patients of both sexes, aged 17 to 65, with new episodes of depressive disorders diagnosed on these criteria were considered for possible inclusion in the study. Only those with severe cognitive dysfunction and learning disability were excluded.

The patients were then screened with a self-administered questionnaire that had previously been shown to have good validity and reliability (Lotrakul & Sukanich, 1999). All patients with a score of 15 or more on this questionnaire were rated by one of us (RK) on a

Thai version of the Hamilton rating scale for depression (HAM-D (Thai); Lotrakul and Sukanich, 1996) and only those with a score of 18 or more on the HAM-D (Thai) were included in the study. A total of 96 patients met the inclusion criteria. A wide range of baseline data were collected on these patients (see Table 1).

Treatment

The choice of treatment was determined by the 13 staff psychiatrists at Ramathibodi Hospital who were caring for the patients. These psychiatrists had had an average of 10.7 years experience in psychiatry. In view of the large number of patients referred to the hospital and a shortage of staff trained in psychological therapies, treatment was predominantly pharmacological (Table 1). The choice of treatment was uninfluenced by the undertaking of the study. Only a small minority of patients were admitted to hospital.

Treatment response

At the end of three months treatment the patients were again rated by RK on the HAM-D (Thai). They were then categorized as responders and non-responders. For the purpose of the study responders were defined as those with a 50% or more reduction in the HAM-D (Thai) score over the three months period. Twelve patients (14.5%) did not complete three months treatment or were lost to follow-up. Attempts were made to contact each of these patients by telephone. It was apparent from speaking to them on the phone that ten of them had not responded to treatment. These too were regarded as non-responders. Two other patients could not be traced.

Table 1 Baseline characteristics and clinical data

Characteristics/ Clinical data		Number (N=96)	%
Age	Mean (S.D.)	39.2 (13.39)	
	Range	17-65	
Sex	Men	15	15.6
	Women	81	84.4
Marital status	Married	49	51.0
	Single/Separated/Divorced	30	31.3
	Widowed	17	17.7
Occupation	Government officer	15	15.6
	Business owner	9	9.4
	Employee in private section	22	22.9
	Agricultural worker	3	3.1
	Other employees	22	22.9
	Student	11	11.5
	None	14	14.6
Monthly income (Thai baht)	0-4999	41	42.7
	5000-9999	24	25
	10000-19999	18	18.8
	20000	13	13.5
Education level	None	6	6.3
	Elementary	35	36.5
	Secondary	16	16.7
	College	11	11.5
	University	26	27.1
	Post-graduate	2	2.1
Type of Depression	Major depressive disorder	46	47.9
	Dysthymic disorder	19	19.8
	Depressive disorder NOS*	12	12.5
	Mood disorder with atypical features	12	12.5
	Mood disorder with psychotic features	2	2.1
	Double - depression	4	4.2

Table 1 Baseline characteristics and clinical data (cont.)

Characteristics/ Clinical data		Number (N=96)	%
Suicidal thoughts	Yes	53	55.2
	No	43	44.8
Alcohol	None	74	77.1
	Seldom	20	20.8
	Often	2	2.1
Previous depression	Yes	35	36.5
	No	61	63.5
Death in family (past year)	Yes	21	21.9
	No	75	78.1
Family history of depression	Yes	14	14.6
	No	81	84.4
Family history of other psychiatric illness	Yes	20	20.8
	No	76	79.2
Stressors (past 3 months)			
-Marital	Yes	41	42.7
	No	55	57.3
-Family	Yes	53	55.2
	No	43	44.8
-Employment	Yes	41	42.7
	No	55	57.3
-Financial	Yes	53	55.2
	No	42	43.8
- Social	Yes	14	14.6
	No	81	84.4
- Legal	Yes	7	7.3
	No	88	91.7
Main treatment			
TCA	Yes	30	31.2
	No	66	68.8
SSRI	Yes	45	46.9
	No	51	53.1

Table 1 Baseline characteristics and clinical data (cont.)

Characteristics/ Clinical data		Number (N=96)	%
TCA+Antipsychotic	Yes	8	8.3
	No	88	91.7
SSRI+Antipsychotic	Yes	1	1.0
	No	95	99.0
TCA+SSRI	Yes	3	3.1
	No	93	96.9
Admission to hospital	Yes	3	3.1
	No	93	96.9

* Not otherwise specified

** Tricyclic antidepressant

*** Selective serotonin reuptake inhibitor

Some patients were given a benzodiazepine, mostly as a hypnotics in addition to their antidepressant treatment.

Statistical analysis

The results are expressed as numbers and percentages. The range and means + SD are given where appropriate. The association between the demographic and clinical data and therapeutic response to treatment was assessed by the chi-square test and a P-value of < 0.05 was considered statistically significant.

Ethics

The study was approved by the ethics committee of Ramathibodi Hospital. Each patient gave his or her informed consent to participate.

Results

The numbers of responders and non-responders, chi-square values and p-value for the differences between groups are shown in Table 2. It can be seen that

none of the baseline variables was significantly associated with a positive therapeutic response.

Discussion

The results of this study suggest that much demographic and clinical information routinely collected in Ramathibodi Hospital is unhelpful in predicting the outcome of treatment in a population of Thai outpatients suffering from depressive disorders. The findings are in keeping with the results of much previous research carried out in Western countries (Bielski & Friedel, 1976; Ananth, 1978; Joyce & Paykel, 1989; Kocsis, 1990; Goodwin, 1993.).

The results of this earlier research were largely inconsistent, but with some exceptions. Conspicuous among these exceptions was 'neurosis', which was found to be a negative predictor of a therapeutic

Table 2 Baseline characteristics, clinical data and therapeutic response

	Responders	Non-responders	X ²	P
Age				
< 30	19 (29.2)	4 (12.9)	3.07	0.08
≥ 30	46 (70.8)	27 (87.1)		
Sex				
Men	11 (16.9)	4 (12.9)	0.26	0.61
Women	54 (83.1)	27 (87.1)		
Domestic status				
Without partner	36 (55.4)	11 (35.5)	3.33	0.07
With partner	29 (44.6)	20 (64.5)		
Education				
Elementary	28 (43.1)	13 (41.9)	0.46	0.79
Undergraduate	17 (26.2)	10 (32.3)		
Post graduate	20 (30.8)	8 (25.8)		
Monthly income				
< 5000 baht	17 (26.2)	4 (12.9)	4.19	0.12
5000-9999 baht	31 (47.6)	13 (41.9)		
≥ 10000 baht	17 (26.2)	14 (45.2)		
Category of depression				
Major	38 (59.4)	14 (45.2)	1.81	0.41
NOS*	15 (23.4)	9 (29.0)		
Dysthymia	11 (17.2)	8 (25.8)		
Suicidal thoughts				
Yes	35 (53.8)	18 (58.1)	0.15	0.69
No	30 (46.2)	13 (41.9)		
HAM-D (Thai)** Score				
< 30	57 (87.7)	27 (87.1)	0.01	0.93
≥ 30	8 (12.3)	4 (12.9)		
Stressors (past 3 months)				
Marital				
Yes	28 (43.1)	13 (41.9)	0.01	0.92
No	37 (56.9)	18 (58.1)		
Family				
Yes	32 (49.2)	21 (67.7)	2.91	0.09
No	33 (50.8)	10 (32.3)		

Table 2 Baseline characteristics, clinical data and therapeutic response (cont.)

	Responders	Non-responders	X ²	P
Employment				
Yes	27 (41.5)	14 (45.2)	0.11	0.74
No	38 (58.5)	17 (54.8)		
Financial				
Yes	36 (56.3)	17 (54.8)	0.02	0.90
No	28 (43.8)	14 (45.2)		
Social				
Yes	11 (17.2)	3 (9.7)	0.937	0.333
No	53 (82.8)	28 (90.3)		
Legal				
Yes	4 (6.3)	3 (9.7)	0.359	0.549
No	60 (93.8)	28 (90.3)		
Main treatment				
TCA***	12 (38.7)	26 (44.1)	0.270	0.874
SSRI****	17 (54.8)	29 (49.2)		
	2 (6.5)	4 (6.8)		
Death in family (past 1 year)				
Yes	16 (24.6)	5 (16.1)	0.885	0.347
No	49 (75.4)	26 (83.9)		
Drinks alcohol				
Yes	51 (78.5)	23 (74.2)	0.216	0.642
No	14 (21.5)	8 (25.8)		
Previous depression				
Yes	25 (38.5)	10 (32.3)	0.349	0.555
No	40 (61.5)	21 (67.7)		
FH of psychiatric disorder				
Yes	15 (27.3)	5 (16.1)	1.379	0.240
No	40 (72.7)	26 (83.9)		

*Not otherwise specified

**Thai version of Hamilton rating scale for depression

***Tricyclic antidepressant

****Selective serotonin reuptake inhibitor

response. Specific drug choices for some categories of depression were considered to be negative or positive predictors of a response. Thus, the choice of tricyclic antidepressants predicted a negative response in 'atypical depression', whereas the use of alternative antidepressants predicted a positive response in this disorder. Prescribing an antidepressant alone predicted a negative response in psychotic depression, while using a combination of an antidepressant and an antipsychotic predicted a positive response. A very early age of onset of depression, co-morbid anxiety and current alcohol use were possible predictors of a negative response to fluoxetine (Nierenberg, 2003)

In our study, we could not assess the effect of 'neurosis' as a possible predictor, as this disorder is not included in the diagnostic classification of depression used in Ramathibodi Hospital (DSM-IV). Twelve patients were given a diagnosis of atypical depression by the psychiatrists responsible for their treatment. This number was insufficient for a meaningful statistical analysis. Similarly, there were too few patients with a depressive psychosis to allow for a meaningful comparison with previous research.

Research into the predictors of a response to treatment of depression (like many other studies of depression) is fraught with methodological problems. These include the tendency of many cases of 'depression' to remit spontaneously or in response to non-specific aspects of care; lack of a truly objective biological marker or instrument for diagnosing depressive disorders; and the large number of variables that can influence the outcome of treatment. These formidable difficulties, together with the small sample size, undoubtedly contributed to the negative results of our

study. However, in everyday clinical practice it appears that much of the information on Thai patients with a variety of depressive disorders that is routinely collected in Ramthibodi Hospital does not allow psychiatrists to predict the response to treatment with a statistically significant degree of accuracy.

Acknowledgements

We thank the patients for kindly agreeing to participating in the study; our psychiatric colleagues for providing data on their patients; Mrs. Umaporn Udomsubpayakul for her statistical advice; and Miss Sukalin Wanakasemsan for her secretarial assistance.

References

1. Bielski RJ, Friedel RO. Prediction of tricyclic antidepressant response: a critical review. *Arch Gen Psychiatry* 1976;33:1479-89.
2. Ananth J. Clinical prediction of antidepressant response. *Int Pharmacopsychiatry* 1978;13:69-93.
3. Tyrer PJ, Lee A, Edwards JG, Steinberg B, Elliot EJ, Nightingale JH. Prognostic factors determining response to antidepressant drugs in psychiatric out-patients and general practice. *J. Affective Disorder* 1980;2:149-56.
4. Joyce PR & Paykel ES. Predictors of drug response in depression. *Arch Gen Psychiat* 1989;46:89-99.
5. Kocsis JH. New issues in the prediction of antidepressant response. *Psychopharmacol Bull* 1990;26:49-53.
6. Goodwin FK. Prediction of antidepressant response. *Bull Menninger Clin* 1993;57:146-52.
7. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition,

- Text Revision. Washington, DC: American Psychiatric Association, 2000.
8. Lotrakul M, Sukanich P. Development of the Thai Depressive Inventory. J Med Assoc Thai 1999; 12:1200-7.
 9. Lotrakul M, Sukanich P. The reliability and validity of Thai version of Hamilton Rating Scale for Depression. J Psychiat Assoc Thai 1996;41: 235-46.
 10. Nierenberg AA. Predictors of response to antidepressants: general principles and clinical implications. Psychiat Clin North Am 2003;26: 345-52.