FLUOXETINE IN THE TREATMENT OF DEPRESSION IN ASIAN (CHINESE AND INDIAN) PATIENTS IN SINGAPORE

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ABSTRACT

The aim of this paper is to study the efficacy and side-effects of fluoxetine. Fluoxetine is a specific serotonin reuptake inhibitor. Nineteen Asian (Chinese and Indian) patients who satisfied the DSM-3R criteria for major depressive episode were treated with fluoxetine 20 mg daily for 12 weeks. They were monitored two weekly. The results showed that during the period of treatment there was significant improvement in depressive symptoms and no serious side-effects. There were no significant changes in weight, temperature, blood pressure and pulse rate throughout the 12 weeks. This study showed that fluoxetine was well-tolerated and relieved the symptoms of depression effectively. Most of the results are supported by other studies.

Keywords: *Asian, Chinese, depression, fluoxetine, Singapore*

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INTRODUCTION

The aim of the study is to evaluate the efficacy and side-effects of fluoxetine hydrochloride on Asian (Chinese and Indian) patients in Singapore. Fluoxetine hydrochloride, is a specific serotonin reuptake inhibitor chemically unrelated to the tricyclic, tetracyclic or the monoamine oxidase inhibitor antidepressant[1]. It is a straight-chain phenylpropylamine with much greater pharmacological specificity than first or second generation antidepressants and very minimal anticholinergic, antihistaminergic or cardiac activity[2,3]. Diminished serotoninergic function has for some time been regarded as playing a major part in the aetiology of depression. At clinical relevant doses, fluoxetine inhibits the neuronal reuptake of serotonin allowing the serotonin to remain longer in the synaptic cleft, thereby enhancing its action[4-6]. Inhibition of serotonin reuptake is the basis for the efficacy of fluoxetine in major depressive disorder. Fluoxetine and similar antidepressants have been studied extensively in humans. The clinical experience showed a high degree of clinical efficacy and safety for fluoxetine for major depressive disorders[7-14], in the elderly depression[15,16] and in the treatment of depression in general practice[17].

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METHOD

This is an open-label design clinical trial. The subjects were recruited from the Department of Psychological Medicine, National University of Singapore, and a private psychiatric clinic at Mount Elizabeth Hospital in Singapore. They were outpatients at the time of recruitment. They gave informed consent and fulfilled criteria for major depressive episode (DSM-3R). Exclusion criteria include: having recent ECT, high suicide risk, significant organic illness, substance abuse or schizophrenia, and having taken antidepressant drugs within the past 5 days. The patients took fluoxetine capsules 20mg daily for 12 weeks.

A history and physical examination was carried out to confirm the diagnosis and to rule out exclusion criteria. Before the treatment and at each subsequent visit (1, 2, 4, 6, 8, 10 and 12 weeks later), the subjects were evaluated with the following rating scales:

1 Hamilton Rating Scale for Depression (HAM-D) [18]

2 Clinical Global Impression (CGI) (Appendix 1)

For evaluation of safety, the following were measured:

1 Side-Effects Scale (Appendix 1)

2 Physiological changes: in weight, temperature, pulse rate and blood pressure.

3 Changes in blood chemistry: alanine transferase, alkaline phosphatase, creatinine and glucose levels.

The following statistical tests were used:

1 For the Hamilton Rating Scale for Depression (HAM-D), the Clinical Global Impression (CGI), and the Side-Effect Scale, a p value of <0.05 (two-tailed) on the Wilcoxon Signed Ranks Tests on difference in score is considered statistically significant.

2 For changes in weight, temperature, pulse rate and blood pressure, a p value of <0.05 (two-tailed) on the paired student t-test is considered statistically significant.

The study was approved by the hospital ethical committee, and was carried out under a certificate issued by the Medical Drug Trial Committee of the Ministry of Health, Singapore.

Appendix 1

Clinical Global Impression (CGI)

1 = normal, not at all depressed
2 = borderline depressed
3 = mildly depressed
4 = moderately depressed
5 = markedly depressed
6 = severely depressed
7 = among the most extremely depressed patients

Side-Effects Scale

Item	Symptoms	Range of Scores*			Scores
1	dry mouth	0	1	2	
2	constipation	0	1	2	
3	weakness	0	1	2	
4	giddiness	0	1	2	
5	drowsiness	0	1	2	
6	blurred vision	0	1	2	
7	nausea	0	1	2	
8	jitteriness	0	1	2	
9	others	0	1	2	

* 0 = nil, 1 = elicited, 2 = reported spontaneously.

RESULTS

A total of 21 patients were enrolled into the study. Two patients did not turn up after 2 weeks. The remaining 19 patients who completed at least 4 weeks of treatment were analysed. The mean age of these 19 patients was 42.6 years (SD = 14.5 years). There were 16 Chinese (84%) and 3 Indians (16%); 9 males (47%) and 10 females (53%). Seven (37%) had no previous episodes of depression, and 10 patients (53%) reported experiencing from 1-2 previous episodes of depression. The mean age of onset of the first episode of depression was 36.2 years (range 19-73 years). The mean duration of the present depression was 9.5 months (range 1-38 months). Most of them (65%) had symptoms less than 3 months. The mean scores for Hamilton Rating Scale for Depression (HAM-D)[18] and Clinical Global Impression (CGI) and the Side-Effects Scale before treatment and at 1, 2, 4, 6, 8, 10 and 12 weeks, are shown in Table I. Intake of fluoxetine was associated with improvement in the patients' condition as evidenced by the drop in the HAM-D scores. The mean HAM-D score before treatment was 21.2 (range 13-35) and it dropped steadily to 6.9 (range 0-20) at the 6th week (mid-point), and to 1.1 (range 0-14) at the 12th week (end of trial). The improvement in the patients' condition was confirmed in scores of the CGI.

Table I - Scores on improvement and side-effects

Visit	HAM-D*		CGI		SE	
	Mean	SD	Mean	SD	Mean	SD
0 week	21.21	7.2	4.5	0.77	2.30	1.80
1 week	17.16	7.3	3.7	1.05	3.21	2.68
2 week	11.79	8.3	2.8	1.18	2.21	2.18
4 week	7.53	5.7	2.2	0.89	1.95	1.65
6 week	6.94	5.9	2.1	0.99	1.77	1.89
8 week	4.94	5.0	1.8	1.07	1.35	1.97
10 week	2.39	2.8	1.5	0.77	0.92	1.55
12 week	2.15	3.7	1.1	0.95	0.62	0.77

all differences between week 0 and subsequent weeks are statistically significant at $p < 0.05$

HAM-D = Hamilton Rating Scale For Depression
CGI = Clinical Global Impression
SE = Side-effect Scale

The side-effects reported spontaneously by the patients in this study were agitation/jitteriness (3 occasions), insomnia (2), nausea (2), weakness (2), loss of appetite (1), dry mouth (1) and headache (1). Some of these side-effects were symptoms of depression and some were reported before treatment. They were well tolerated by the patients and were not severe enough to warrant withdrawal of the study drug. The mean total "Side-effect" score before treatment was 2.30. It rose to 3.21 after one week of treatment. Thereafter it was below the original level of 2.30. On the 12th week (last visit) it was only 0.77.

The usual side-effects due to intake of tricyclic antidepressants (ie dry mouth, blurring of vision, drowsiness, and weakness) were not experienced by most of the patients in this study. There was no statistically significant difference in weight, temperature, pulse rate and blood pressure of the patients before and at subsequent visits (on 1, 2, 4, 6, 8, 10 and 12 weeks) (Table II). Among the laboratory tests performed, two patients were found to have changes from normal at baseline to abnormal at the 12th week. In one patient the alanine transferase rose from 19 to 88 units/litre, and in another, from 9 to 70 units/litre (upper normal - 56 unit/litre).

Table II - Changes in weight, temperature, pulse rate and blood pressure

Visit	Weight Rate	Temperature	Pulse	Blood Pressure	
				supine	standing
0 week	59.1kg	36.8°C	81.9/min	125/81	123/82
1 week	58.8kg	36.8°C	84.6/min	128/83	124/83
2 week	58.5kg	36.9°C	83.0/min	129/81	124/81
4 week	58.8kg	36.7°C	82.9/min	129/80	128/82
6 week	58.6kg	36.9°C	85.1/min	129/81	129/80
8 week	58.6kg	37.0°C	84.6/min	126/80	128/82
10 week	59.3kg	36.8°C	80.5/min	136/81	132/83
12 week	59.5kg	36.7°C	82.7/min	130/81	131/84

all differences between week 0 and subsequent weeks are statistically significant

DISCUSSION

The efficacy of fluoxetine in the relief of the symptoms of depression has been well established in many trials. It is superior to placebo[10,12,19], and comparable to the older antidepressants like imipramine[10,12], amitriptyline[9,14-16], maprotiline[17], dothiepin[18] and mianserin[19]. These trials were carried out in the West mainly on Caucasian patients. The present study is one of the few carried out on Asian (Chinese and Indian) patients. At least four other fluoxetine trials were carried on Asians - in Hong Kong[20], Korea[21], Thailand[22], and Taiwan[23]. Their results, were similar to the present trial. They showed a progressive improvement in the patients' condition as documented by measurements of the HAM-D and CGI. In this trial, the improvement was seen as early as the seventh day of treatment. By the sixth week of treatment, the mean HAM-D score had dropped to 6.9, and 90% of the patients were normal or mildly depressed. At the 12th week, apart from one patient having a score of 14 on the HAM-D, the rest had total scores of 4 or less on the HAM-D.

As all controlled trials showed no differences in antidepressant efficacy of standard antidepressant drugs, the more important objective of the study is to report on the relative absence of unpleasant side-effects or serious adverse effects. For this purpose, side-effects, weight, blood pressure, pulse rate and temperature were measured before and during the period of treatment. In an uncontrolled trial, it is necessary to rate the "side-effects" at the beginning of the trial and compare them at each

follow-up visit. For the evaluation of side-effects, a "side-effects" scale was constructed. Eight commonly experienced side-effects were chosen for this scale: dry mouth, constipation, weakness, giddiness, drowsiness, blurred vision, nausea and jitteriness. Some of the items of the "side-effects" could be symptoms of depressions.

Most of the previous studies showed that fluoxetine was better tolerated than the first generation tricyclics [9,10,14-16], and differed from the newer antidepressants (maprotiline, mianserin, dothiepin) in having less sedation [17,18], weight loss instead of weight gain [9,11,13,15-17]. The prominent adverse experiences reported by the patients in most studies were nausea[8,11,14,17]. These studies also showed no significant changes in the physiological and biochemical measurements.

CONCLUSION

This uncontrolled open study showed that in the treatment of major depression in Asian patients, fluoxetine was efficacious and had a low side-effects profile.

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