Malaysian Journal of Medicine and Health Sciences Vol. 3(2) June 2007 : 37-43

Effectiveness of Different SSRI Antidepressants in Combination with CBT for Short-term Management of Panic Disorder

MZ Azhar & KON Noorjan
Department of Psychiatry, Faculty of Medicine & Health Sciences
Universiti Putra Malaysia
43400 UPM, Serdang, Selangor, Malaysia

ABSTRACT

Objective: This paper reports the result of an analysis of data of brief therapy for out-patients with panic disorder referred by physicians in a busy specialist hospital in Kuala Lumpur. **Methods:**The patients were randomly assigned into different groups of SSRI (Specific Serotonin Reuptake Inhibitor) antidepressants i.e. escitalopram, sertraline, or fluoxetine. All patients received cognitive behaviour therapy (CBT). The therapy was aimed for a maximum of twelve sessions. There were 33 patients in the escitalopram group, 31 patients in the sertraline group, and 31 patients in the fluoxetine group. **Results:** The result shows that all the groups were similar in the severity and scores for pre-treatment but for post-treatment, there were significant differences among them. **Conclusion:**All groups showed significant improvements in all modalities of measurements. However, the escitalopram and sertraline groups showed faster overall improvement compared to the fluoxetine group.

Keywords: Panic disorder, antidepressants, cognitive behaviour therapy, psychotherapy

INTRODUCTION

Antidepressants have been used for many years to treat depression with significant success. The most used group of antidepressants is the specific serotonin reuptake inhibitor (SSRI). All the three drugs used in this study that is, escitalopram (ESC), sertraline (STR), and fluoxetine (FXT) are SSRIs. They have all been shown to be very effective in the treatment of major depressive disorders with ESC being the youngest of the three to be used in Malaysia. Of late, they have also been used to treat the anxiety group of disorders including panic disorder and obsessive compulsive disorder, that is, anxiety disorders most likely to be caused by some biological etiology rather than purely psychological entity. Cognitive behaviour therapy has also been shown to be successful in panic disorder treatment especially in the last few years where the technique and theory have been refined.[1] It has also been demonstrated to be very successful in Malaysian patients.[2] In this study, we attempt to demonstrate the effectiveness of this treatment, that is, faster response and overall improvement, when given in combination with SSRI and which SSRI does better in this combination. As far as we know, no such study in Malaysia has been undertaken to compare pharmacotherapy and psychotherapy for panic disorder where psychotherapy is the permanent treatment.

METHODOLOGY

Sample

Subjects selected for the study consisted of male and female patients diagnosed as having panic disorder by a psychiatrist based on DSM IV [3] criteria. The subjects were recruited from among the patients referred by physicians to the psychiatry and psychotherapy clinic of a specialist hospital in Kuala Lumpur. They were then divided at random into three groups, i.e. (i) the escitalopram group (ESC), (ii) the sertraline group (STR), and (iii) the fluoxetine group (FXT). All groups received cognitive behaviour therapy (CBT) as standard treatment by the first author. The treatment was carried out over a period of twelve weeks. The inclusion criteria were (i) aged between 18 to 50, (ii) able to communicate well, and (iii) cooperation to carry out sessions in a group for one hour per week. The exclusion criteria were having other psychiatric disorders besides panic disorder, for example, other neuroses, agoraphobia, psychosis, depression, or Axis II traits or disorders. All patients gave informed consent to participate in the study. They were dropped from the study if they requested to be included in either group or if the medication needed to be changed or if they missed therapy sessions more than once. The duration of inclusion into the study was from January 2004 until June 2007. All together, 33 patients were recruited for the ESC group, 31 for the STR group and 31 for the FXT group.

Procedure

Those in the ESC group received a starting dose of ESC 10 mg per day. They were seen weekly and the doses were increased as necessary to a maximum of 20 mg/day if no side effects occurred. None of the patients needed treatment to be increased to 20 mg/day. Those in the STR group were treated in a similar manner. They received a starting dose of STR 50 mg per day. They were seen weekly and the doses were increased as necessary to a maximum of 100 mg/day if no side effects occurred. Only one patient needed treatment to be increased to 100 mg/day. Those in the FXT group received a starting dose of FXT 20 mg per day. They were seen weekly and the doses were increased as necessary to a maximum of 40 mg/day if no side effects occurred. Only two patients needed treatment to be increased to 40 mg/day. As mentioned earlier, all patients were seen for weekly sessions of CBT

At weekly meetings and at baseline, a research assistant who was blind to the patients' group measured the scores for the following:

1. Hamilton Anxiety Score (HAS) [4]
2. Beck Anxiety Score (BAI) [5]
3. Catastrophic Belief Score
4. Panic Frequency per week
5. World Health Organization Quality of Life Scale-Brief Version (WHOQOL-BREF) [6]. (This was measured only at baseline and at 12 weeks)

All the tests were self-rated but the research assistant was on hand to assist if queries arose.

Analysis

The results of all the tests from the three groups of patients were analysed statistically using chi square, *t*-test, and anova.

RESULTS

The study was conducted over a period of three and a half years. There were all together 95 patients with 33 patients in the ESC group, 31 in the STR group and 31 in the FXT group. The results are shown in the tables below. Table 1 shows that there was no difference in age between the three groups. There was also no significant difference in baseline measurements of BAI and HAS between the three groups. However, after 12 weeks there was a significant difference in all measurements. All patients improved significantly but patients in the ESC group improved better than those in the other two groups. The QOL score also improved in all groups but there was marked improvement in the ESC group compared with the other two groups.

Table 1. Treatment types received by patients and the results of HAS, BAI, and QOL at baseline and at end of 12 weeks

Treatment types	Age Mean (sd)	BAI Pre Rx	BAI 12 sessions	HAS Pre Rx	HAS 12 sessions	QOL Pre Rx	QOL 12 sessions
CBT + ESC	33.44 (6.82)	30.52 (2.13)	21.13 (2.74)	33.63 (2.5)	21.24 (3.86)	63.85 (3.78)	80.16 (2.77)
		p<0.0001		p<0.0001		p<0.0001	
CBT + STR	31.54 (6.17)	31.74 (3.25)	22.45 (3.96)	34.81 (2.34)	21.52 (4.23)	65.37 (4.69)	78.78 (4.50)
		p<0.0001		p<0.0001		p<0.0001	
NFD + FXT	31.67 (7.98)	30.76 (1.89)	26.77 (2.20)	32.98 (2.31)	29.09 (1.92)	63.09 (4.61)	68.81 (3.52)
		p<0.0001		p<0.0001		p<0.0001	

HAS ; Hamilton Anxiety Score
BAI ; Beck Anxiety Inventory
QOL; WHO Quality of life – Brief Version Scale

Table 2. Treatment types received by patients and the results of panic frequency, and catastrophic beliefs at baseline and at end of 12 weeks

Treatment types	Panic frequency Pre Rx	Panic frequency 12 sessions	Catastrophic belief: Pre Rx	Catastrophic belief: 12 sessions
CBT + ESC	16.11 (4.02)	4.01 (3.15) P<0.001	100	23.01
CBT + STR	16.17 (4.23)	7.67 (6.12) P<0.001	100	35.90
CBT + FXT	16.19 (3.89)	9.78 (4.23) P<0.001	100	60.05

Table 2 shows the results of the analysis done for the panic frequency and catastrophic belief scores at baseline and at the end of twelve weeks treatment. There was a significant change in all groups at the end of twelve weeks but the ESC group showed better improvement. The results seemed to indicate that those in the ESC group responded better in all modalities.

DISCUSSION

There is no specific measuring tool to measure panic disorder, but practically all patients would have symptoms of anxiety. As such we decided to measure these symptoms to address the above problem. The HAS and BAI were chosen because they are self-administered, not too time consuming, easy to use by patients and the patients are given CBT which uses these measurements as part of therapy recording. Patients with this disorder also tend to have a low level of quality of life. We thought this measure would be useful to assess overall improvements in patients. It is very difficult to measure quality of life because there are numerous scales available but no one scale is comprehensive enough to measure all the aspects we would like to look at. The most easy to use in our patients seem to be the WHOQOL-BREF as it has only 30 questions and takes a short time to administer and is not difficult for the patients to understand. It also covers rather comprehensively most of the domains we would like to measure.

Findings of a significant reduction were expected in practically all measures in all groups. Using anova, it was clear that the patients in the CBT + ESC did best, *but all three methods were beneficial for all patients.* This could be explained by the anxiety present in these patients. If we assume that panic disorder has a major psychological component and is not a pure biological disorder but a primary psychological disorder which could be maintained by biological factors, then the results fit the model. So if psychological treatment

is used to treat the core issue of the disorder, then the other symptoms which are secondary will improve as well. Based on Clark's model of the panic circle [7,8], catastrophic beliefs are the core problems in patients with panic. Thus those treated with CBT will learn to reduce the catastrophic belief score and this will have a direct effect on reducing the panic. Table 1 shows that patients in all groups could significantly reduce their HAS and BAI scores. However, although the QOL scores show significant changes, the anova test indicates that the ESC and STR groups have better results than the FXT group indicating better overall improvement in the ESC and STR groups compared to the FXT group. Table 2 shows these values clearly through the reduction in panic frequency and catastrophic belief scores. Anova and the *F*-values also indicate superior results in the ESC and STR group with the ESC having better results than the STR group.

It is important for clinicians to understand that anxiety disorder can severely affect the daily life of sufferers. It is well known that suicide rates in anxiety and panic can reach a rate of 20% [9,10] which is very high even in comparison to some depressive conditions. As such this condition must be aggressively treated. As most patients see their family physicians or general practitioners initially, it is highly important that the family doctor makes the right diagnosis and institutes the right treatment. As can be seen from the results, the SSRIs have significant positive results on the patients. However, the results were shown after 12 weeks of treatment. It is therefore very important for family physicians (FP) to be patient when using this drug. Several studies have indicated that CBT + SSRIs are useful or better than CBT alone in treating anxiety. [11,12] As such the FP should attempt to use antidepressants especially SSRI in the treatment of panic disorder. Its efficacy has been proven in this study. The only drawback is that it takes time to work. At 12 weeks, the ESC and STR groups improved in terms of panic frequency and catastrophic belief scores compared to the FXT group. This means that the combination for FPs to use would be the SSRIs and of the SSRIs, ESC and STR should be recommended.

Patients with anxiety have been shown to be particularly sensitive to physical symptoms and medication effects. [13] The serotonin reuptake inhibitors (SSRIs) have an improved tolerability over the traditional tricyclics and most side effects resolve over time and safety in the medically ill and those with overdoses have been established. [14] Panic disorder is also not necessarily an acute condition but can be a chronic and recurring condition requiring long-term management. As such an antidepressant is more acceptable than a benzodiazepine if one wants to use a drug to treat the condition.

Treatment should ideally combine psychological treatment with SSRI especially ESC and STR. Concomitant use of a benzodiazepine if no psychological treatment is used may be helpful but the duration of use should not exceed 2 to 3 weeks. At the moment, there is no evidence to indicate that the dose of SSRI should be reduced once a remission is reached. As such the dose that makes the patient recover should be continued for at least one to two years although studies are still being conducted to ascertain this. If symptoms persist, then the obvious thing is to continue treatment or to add psychological treatment. It is not uncommon for FP to conduct psychological treatment. Studies in the United Kingdom and Germany[15,16,17,18] have shown that FP and non psychiatrists can be trained to achieve remarkable results using CBT in patients.

Using actual CBT techniques will obviously be difficult but counseling using CBT hypothesis might suffice in most patients while the more resistant ones can be sent for further management to a psychiatrist or psychotherapist. Besides, the CBT model for depression is very easy to grasp and can be used to treat all patients since depression is an ingredient present in many patients with the above problems. Also, when used in combination, the dose of the drug can be lower than when the drug is used alone and thereby reduces the possibility of side effects which could further aggravate the misinterpretated beliefs patients hold regarding their health.

In this study, the only drawback is that the clinicians are not blinded to the SSRIs used by patients; only the research assistant who collects all data is blinded. However, based on the above finding, it can be recommended that clinicians use a combination of CBT and SSRIs especially ESC and STR to treat panic disorder and the duration of therapy should not be less than 12 weeks. It is perhaps better to avoid benzodiazepines and use CBT in combination with SSRIs but this can be a focus of another research study.

REFERENCES

[1] Beck AT, Rush AJ, Shaw BF, Emery G. Cognitive therapy of depression. New York: Guilford Press, 1979.

[2] Azhar MZ. Cognitive psychotherapy experience with Kelantan clients. Medical J. of Malaysia 1998; 53(2):165-169.

[3] APA. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders-Revised (4th. Edition). Washington D.C., APA, 1994

[4] Snaith RP, Baugh SJ, Clayden AD *et al.* The clinical anxiety scale: an instrument derived from the Hamilton Anxiety Scale. Br. J. Psychiatry 1982;141:518-523

[5] Beck AT, Epstein N, Brown G *et al.* An inventory for measuring clinical anxiety : psychometric properties. Journal of Consulting and Clinical Psychology 1988; 56: 893-897

[6] The WHOQOL group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. Psychological Medicine 1988; 28: 551-558

[7] Clark DM, Ehlers A. An overview of cognitive theory and treatment of panic disorder. Applied & Preventive Psychology 1993; 2: 131-139

[8] Clark DM. A cognitive approach to panic. Journal of Behavior Therapy and Experimental Psychiatry 1986; 24: 461-470.

[9] Reich J, Warshaw M, Peterson LG *et al.* Comorbidity of panic and major depressive disorder. J. Psychiatric Research 1993; 27: 23-33

[10] Lepine JP, Chignon JM, Teherani M. Suicide attempts in patients with panic disorder. Arch. Gen. Psychiatry 1993; 50: 144-149

[11] Sharp EA. Comparison of fluvoxamine and CBT and placebo in panic disorder. Psychological Medicine 1996; 53: 123-130

[12] Azhar MZ. Comparison of fluvoxamine alone, fluvoxamine and cognitive psychotherapy and psychotherapy alone in the treatment of panic disorder in Kelantan – implications for management by family doctors. Med. J. Malaysia 2000; 55(4): 402 - 408

[13] Salkovskis PM. Somatic problems. In: KE Hawton, PM Salkovskis, J Kirk and DM Clark (eds.) Cognitive behaviour therapy for psychiatric problems: a practical guide. Oxford: Oxford University Press, 1989

[14] Preskorn SH. Comparison of the tolerability of buproprion, fluvoxamine, imipramine, nefazodone, paroxetine, sertraline, and venlafaxine. J. Clin. Psychiatry 1995; 56(Suppl 6): 12 21

[15] Linden M. Cognitive behaviour therapy under conditions of routine treatment in the general health care system. Behav. & Cog. Psychotherapy 1996; 24: 39-50.

[16] Scott CS, Scott JL, Tacchi MJ *et al.* Abbreviated cognitive therapy for depression: a pilot study in primary care. Behav. & Cog. Psychotherapy 1994; 22: 57-64.

[17] Hayward L, MacGregor AD, Peck DF *et al.* The feasibility and effectiveness of computer-aided CBT in a rural area. Behav. & Cog. Psychotherapy 2007; 35 (4): 409-420

[18] d'Ardenne P, Farmer E, Ruaro L *et al.* Interpreter mediated CBT with traumatised people. Behav. & Cog. Psychotherapy 2007; 35 (3); 293- 302