ORIGINAL ARTICLE

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

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Summary

This paper reports the result of a brief therapy attempt at treating panic in a busy outpatient psychiatric clinic. The patients were cases of panic referred from the various outpatient clinics within the hospital complex. The patients were divided into three groups at random using one of three modalities of treatment, i.e. cognitive behaviour therapy (CBT), CBT and Fluvoxamine (FVX), and FVX alone. The therapy was aimed for a maximum of nine sessions after which the patients were to be discharged. There were 14 patients in each group. The results show that all the groups were similar in the severity and scores pre treatment but after the different types of treatment there was a significant difference among them. The FVX alone group, showed significant improvement from the pretreatment levels but did not show as much improvement as the other groups and the mean score was only 9.07 after nine sessions. The best group was the CBT in combination with FVX. This indicates that the best way to treat panic is to combine drug treatment and psychological treatment. It is also shown from the study that the combination group requires less FVX than the FVX alone group. This finding has implications for the treatment of panic at the family physician clinic.

Key Words: Panic disorder, Fluvoxamine, Cognitive behaviour therapy, Family Physicians

Introduction

Fluvoxamine is a selective serotonin reuptake inhibitor (SSRI). Serotonergic mechanisms have been implicated in the aetiology of panic disorder. As such it would be logical to assume that Fluvoxamine would be useful in the treatment of panic. Several studies have indicated this[1,2,3,4]. Cognitive therapy has also been shown to be successful at treating panic especially in the last few years where the technique and theory have been refined[5,6,7]. It has also been demonstrated to be very successful in Kelantan patients[8,9]. In this study we evaluate the effects of the treatment when given alone or when given in combination. Although the effects have been shown in other populations, Fluvoxamine alone or in combination with cognitive therapy has never been evaluated in Kelantan patients or in Malaysian patients. The purpose of this study was to determine the best method or combination of methods for implementation at the family practice level.

Materials and Methods

Sample: - Subjects selected for the study consisted of male and female patients diagnosed as panic disorder by a psychiatrist based on DSM IV[10] criteria. The subjects were recruited from among the patients attending the USM Hospital psychotherapy clinic. They were on a waiting list. They were divided at random into three groups, i.e. (1) the Fluvoxamine only group (FVX) group, (2) a group that were treated with both Fluvoxamine and cognitive behaviour therapy (FVX + CBT) and (3) a group that received only Cognitive Behaviour Therapy (CBT). The other inclusion criterias include; age between 18 to 50, ability to communicate well, cooperation to carry out sessions in a group for one hour per week. The exclusion criterias include having other disorders besides panic, eg. phobias, hypochondriasis, other neuroses. All patients were required to give informed consent to enter the study. They were dropped from the study if they requested to be included in either group.

Procedure: - Those in the FVX group received a starting dose of FVX 50 mg. per day, were seen weekly and the dose increased as necessary to a maximum of 200 mg./day if no side effects occurred. Those in the CBT + FVX group were treated in a similar manner as the previous group with the addition of weekly CBT sessions. In the CBT only group, the patients were seen for weekly sessions of CBT but were never given FVX or any other drugs. All patients were seen weekly for 9 weeks and those in the last two groups received weekly sessions of CBT as described by Clark for panic disorder [11,12].

At weekly meetings and at baseline, the following tests were done/measured by a research assistant who is blind to the patients' group. The scales are all self-reports and the research assistant only guides the subjects.

The tests are

Tests: - The psychological tests included;

a) the Beck Anxiety Inventory (BAI)[13],
b) the Beck Depression Inventory (BDI)[14],
c) the Hamilton Anxiety Scale (HAS)[15],
d) the Hamilton Depression Scale (HDS)[15],

The physical tests included;

a) the blood pressure,
b) the pulse rate, and

Other measurements made include;

a) Panic frequency per week[11,12]
b) Catastrophic belief score[11,12]

Analysis: - The results of all the tests from the three groups of patients were analyzed statistically using Chi Square, t test and Anova.

Results

The study was conducted over a period of two years. Each patient was analyzed after receiving treatment for 9 weeks. There were 66 patients with 22 patients in each group. However a total of 15 patients defaulted follow-up leaving 51 patients who completed 9 weeks of the study period with 17 patients in each group. The results are shown in the tables below. Table I shows that there were no difference in age between the three groups. There was also no significant difference in panic frequency between the three groups. However after 9 weeks there was a significant difference in frequencies of panic. All patients improved significantly but patients in the CBT + FVX and CBT alone groups improved better than those in the FVX alone group (Table II). The catastrophic belief score also improved in all groups but there was more marked improvement in the first two groups compared with the last group. The measurement of HAS which is essentially a measure of biological symptoms of anxiety were also significantly reduced after 9 weeks of treatment in all three groups although the fall was less marked in the FVX alone group.

Table III shows that the same results were seen for cognitive and psychological anxiety symptoms as measured by the BAI. All results show significant reduction from baseline. Remarkable results were also seen with the depressive scores. Both biological depression as measured by HDS and psychological and cognitive depression as measured by the BDI show significant reduction in scores for all groups.

Table IV shows the results of the physical tests done on the patients. Again it was seen that there was significant reduction in pulse rates in all three groups.

Table I
Results of Age, Panic Frequency, Catastrophic belief and HAS before and after 9 weeks of treatment in the three groups of patients.

Treatment types	Age Mean (sd) Range	Panic Freq pre Rx	Panic Freq 9 sess	Catas Belief Pre Rx	Catas Belief 9 sess	HAS Pre Rx	HAS 9 sess
CBT +FVX	31.57 8.00 17-45	16.07 4.01	4.07 3.87	100 18.36	31.79 3.23	37.14 5.93	22.86
		p<0.0001				p<0.0001	
CBT.	31.66 8.09 18-44	16.36 3.08	3.64 2.21	100	30.71 9.97	37.0 3.44	21.50 5.17
		p<0.0001				p<0.0001	
FVX.	31.36. 7.54 18-44	16.07 3.95	9.07 1.98	100	80.71	36.50 3.23	28.71 4.18
		p<0.0001				p<0.0001	

CBT: Cognitive Behaviour Therapy *FVX: Fluvoxamine* *PreRx: Pretreatment*
Sess: session *Catas: Catastrophic* *HAS: Hamilton Anxiety Score*

Measurements of systolic blood pressure also showed significant reduction from baseline in the CBT + FVX group and the CBT alone group but not significantly in the FVX alone group.

Table V shows the dosage of FVX used in the FVX + CBT group and the FVX alone group. The results show that those in the former group required significantly less drug than those in the latter group.

Table II
Comparison of all three groups at pre Rx and after 9 sessions

	Pretreatment	After 9 session
Panic frequency	f-0.11 p=0.89(NS)	f-47.48 p<0.0001
Catastrophic belief		f-961.56 p=0.0001
HAS	f-0.48 p=0.62(NS)	f-40.34 p<0.0001

Analysis of Variance (ANOVA) test
Done for comparison of improvement among the three groups (Pretreatment and After 9 sessions)
All groups were similar in severity and scores pretreatment
After treatment there was significant difference among them
Fluvoxamine group - significant improvement from preRx levels
- did not show as much improvement as other groups
- Mean score 9.07 after 9 sessions

Table III
Results of other psychological tests i.e. BAI, HDS, BDI before and after 9 weeks of treatment in the three groups of patients.

Treatment types	BAI Pre Rx	BAI 9 Sess	HDS Pre Rx	HDS 9 Sess	BDI Pre Rx	BDI 9 Sess
FVX+ CBT	50.5	19.8	35.0	9.2	28.0	1.41
	4.65	3.89	3.41	1.38	0.81	0.81
	p<0.01		p<0.01		p<0.01	
CBT	52.8	17.5	33.4	10.0	26.0	5.0
	4.25	3.78	2.53	0.57	2.16	1.29
	p<0.01		p<0.01		p<0.01	
FVX	54.2	32.4	34.4	12.2	26.4	16.8
	2.87	1.81	2.82	4.46	1.71	1.06
	p<0.01		p<0.01		p<0.01	

BAI =Beck Anxiety Inventory *HDS= Hamilton Depression Scale* *BDI= Beck Depression Inventory* *Sess= session*
CBT= Cognitive Behaviour Therapy *FVX= Fluvoxamine* *PreRx= Pretreatment*

Table IV
Results of physical tests i.e. pulse rate and systolic blood pressure before and after 9 weeks of treatment in the three groups of patients.

Treatment Types	Pulse Rate Pre Rx	Pulse Rate 9 Sess	Systolic BP Pre Rx	Systolic BP 9 Sess
FVX +CBT	93.1	83.4	123.5	115.0
	3.2	2.99	3.82	4.08
	p<0.01		p<0.05	
CBT	95.4	82.0	126.0	115.7
	2.76	2.0	4.47	4.49
	p<0.01		p<0.05	
FVX	96.0	89.4	125.7	118.6
	1.63	1.51	4.49	2.44
	p<0.01		p=(NS)	

FVX= FluvoxaminePreRx= Pretreatment
Sess= session *BP= blood pressure*
CBT= Cognitive Behaviour Therapy

Table V
Dosage of FVX required in different groups

Treatment Type	Mean	S.D.
FVX + CBT	64.286	30.562
FVX	153.571	30.786
	p < 0.0001	

CBT= Cognitive Behaviour Therapy
FVX= Fluvoxamine

Discussion

The finding of significant reduction in practically all measures in all groups was very unexpected. It is however cautioned that the duration of the illness of the subjects was not included in the data collection and this may affect results. Using Anova it was clear that the patients in the FVX+CBT and the CBT alone groups were generally better than those in the FVX alone group. This is easily explained with regard to panic disorder if it is assumed that panic is not a pure biological disorder but a primary psychological disorder, which could be maintained by biological factors. So if psychological treatment is used to treat the core issue of the panic then the other symptoms which are secondary will improve regardless of the use of drugs or not. Hence

the almost similar results of the FVX + CBT and CBT alone groups. Based on Clark's model of the panic circle[11,12] the catastrophic beliefs are the core problems in patients with panic. Thus those treated with CBT in either the FVX + CBT group or CBT alone group will learn to reduce the catastrophic belief score and this will have a direct effect on reducing the panic. Table I shows that those in the first two groups could significantly reduce their catastrophic scores more than those in the third group (31.79 and 30.71 against 80.71) and thus the reduction in panic frequency was much better in the first two groups as well (4.07 and 3.64 against 9.07). It seems that there is a correlation between catastrophic belief and panic frequency. Similarly the results for the HAS, BAI, HDS, BDI showed a similar pattern and can be similarly explained. What is important is that although the reduction in the FVX alone group is not as much as in the other two groups, they are nevertheless significant. The only non-significant change was the systolic blood pressure. However Table V shows that if the patient gets psychological help the dosage of drugs can be significantly reduced. This is obviously good for the patient as it helps to reduce cost as well as potential side effects.

All results seem to favour non-drug treatment for panic or judicious use of drugs (low dosages) together with psychological treatment. But not all doctors can afford to do psychological treatment. It can be time consuming and patients may not stay in treatment. So how can the family physicians make use of the results of this study? It is believed that they can choose one of two options. The best would be to combine SSRI and CBT but if they are not keen on CBT then they ought to use SSRI for long duration.

At the present time, based on referrals from family doctors, our experience tells us that in Malaysia the majority of family physicians use benzodiazepines to treat panic disorders. These are very good drugs which help to calm the patient and has a very fast onset of action. However their side effects far outweigh their usefulness. If used for a very short period, they are very useful but the tendency to use it for longer than 6 weeks is evident and tolerance and withdrawal are very common with these drugs especially those with a short half life. At the present moment, to treat panic disorder (PD) one has to ensure improvement in at least 5 domains i.e.

1. Panic attacks (frequency), including limited-symptom attacks,
2. Anticipatory anxiety
3. Panic related phobias (including agoraphobia)
4. Well-being/overall severity of illness, and
5. Disability in terms of work, social, and family impairment.

It is important for clinicians to understand that panic disorder can severely affect the daily life of sufferers and that the five domains above should always be checked to establish this fact. It is well known that suicide rates in panic can reach a rate of 20%[16,17], 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 initially, it is highly important that the family doctors make the right diagnosis and institute the right treatment. As can be seen from the results, the drug FVX that is a serotonin reuptake inhibitor has significant positive results on the patients. However the results were shown after 9 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 + FVX are equal or better than CBT alone in treating panic[18] and some studies indicate that FVX is as good as CBT[19]. As such the FP should attempt to use FVX instead of benzodiazepines in the treatment of panic disorder. Its efficacy has been proven in this study and in other studies[1,2,3,4,18]. The only drawback is that it takes time to work and as such psychological treatment is an advantageous addition.

Patients with PD have been shown to be particularly sensitive to physical symptoms and medication effects[5]. The serotonin reuptake inhibitors (SSRI) of which FVX is one, have an improved tolerability over the traditional tricyclics and most side effects resolve over time and safety in the medically ill and with overdoses have been established. PD is also not an acute condition but is really a chronic and recurring condition requiring long-term management. As such a SSRI is more acceptable than a benzodiazepine if one wants to use a drug to treat the condition. Published data suggest the SSRIs are better than tricyclics or benzodiazepines in maintaining

improvement and preventing relapse. Also the SSRIs provide single daily dose as opposed to the other two drugs, which give better ease of use of the drug.

However we strongly recommend that family practitioners should attempt to combine psychological treatment with a SSRI and the starting dose should be low. For FVX it should be 50 mg. It is not uncommon for family practitioners to conduct psychological treatment. Studies in the United Kingdom and Germany [20,21] have shown that family practitioners can be trained and have shown remarkable results using CBT in depressive patients. Perhaps our family practitioners can also be trained to do specific CBT treatment for panic. It is perhaps time that our family practitioners should include CBT as part of their repertoire of treatment. Specific CBT techniques for specific disorders like panic have been successfully taught to nurses in Malaysia with encouraging results. It is therefore possible to train family practitioners to conduct CBT for panic. A series of weekend workshops can be conducted for interested family practitioners. CBT knowledge can be an added advantage to family practitioners because the technique can then be used for other psychological problems as well including those related to psychological reactions of physical illnesses and chronic pain.

In the past and perhaps in the present too, the main problem of treating panic in GP practice has always been the overuse of benzodiazepines and the very short duration of total treatment. Now with the increase in the number of family practitioners, it is hoped that the results of this study will help family practitioners to treat panic better.

The important message for family practitioners and their patients is that panic disorder is a chronic and disabling condition that often requires treatment over several years especially if they choose not to use CBT.

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