Original Article

Comparison between Escitalopram and Pregabalin for Generalized Anxiety Disorder Treatment

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ABSTRACT

Objective: To facilitate the emerging need for investigating the efficacy of escitalopram compared to pregabalin for treating generalized anxiety disorders

Methods: This was a quasi-experimental study having a pre and post-test design conducted on patients before and after treatment with Pregabalin and escitalopram, carried out for twelve weeks on 90 patients in the year 2021 between January to June on visiting Mayo Hospital in Lahore, within the age range of 18 to 60 years. They were divided into 2 equal groups by purposive sampling. The 20 mg dose of escitalopram per day was given to the participants of group A while a dose of 150-200mg per day of pregabalin was given to group B and the level of anxiety before and after the experiment was measured by Hamilton Anxiety Baseline. A record of all clinical signs and symptoms was also maintained throughout the time of medication. After 12 weeks, follow-up data was taken from the patients and the scores were compared with the baseline.

Results: : Efficacy, defined as ≥2% reduction in the scores of anxiety among the participants after 12 weeks was significantly higher in Escitalopram group A than in Pregabalin group B: (92.8% vs. 82.5%) with p-value= 0.003. Gastrointestinal symptoms were seen in 11.9% of patients in Group A and 27.5% of patients in Group B. In Group A 14.2% of patients reported headaches, as compared to 22.5% of patients in Group B. Sleep disturbances, were reported by 10% of patients in Group A and 15% of patients in Group B. Sweating was seen by 19% of patients in Group A and 50% patients in Group B. Urinary symptoms were experienced by 4.7% patients in Group A and 7.5% patients in Group B.

Conclusion: : Escitalopram is a better option and efficacious for the Pakistani population in treating psychological issues including depression, bipolar and other affective disorders despite the minor side effects compared to Pregabalin.

Keywords: Escitalopram, Pregabalin, Generalized Anxiety Disorder, Diagnostic and Statistical Manual of Mental Disorders (DSM-5), Hamilton Anxiety Rating Scale (HAM-A). 5), (HAM-A).

Introduction

Generalized anxiety disorder is a condition that leads to extreme uncontrollable physical and emotional distress due to excessive worry.[1] The worldwide prevalence of generalized anxiety disorder with comorbid disorder ranges from 48% to 98%.[2] Even in Pakistan, not only clinical but local population including teenage to geriatrics is suffering from generalized anxiety disorder and comorbid physical or mental health disorders.[3] The purpose of the management of anxiety disorders is emotional regulation[4] and the focus is a reduction in the central nervous system that elicit disturbing physiological responses.[5] Systematic reviews and meta-analyses have added to the factors responsible for generalized anxiety disorder and highlighted the genetic, psychological and environmental factors that have gained attention.[6]

A common form of medication, selective serotonin reuptake inhibitor (SSRI) helps in decreasing amygdala reactivity to control anxiety.[7] Escitalopram is the most common psychopharmacological drug with a proven response to treatment for generalized anxiety disorder in different countries without the comorbid disorder.[1] However, another drug Pregabalin has also been proved the effective management of generalized anxiety disorders along with an early response to treatment,[8] reduction in the level of severity and relapse prevention.[9] Other similar treatments paroxetine, and agomelatine has satisfactory effects for comorbid disorders with generalized anxiety disorder in all age groups with approved doses by FDA from around 10-20mg/day and 10-50mg/day respectively.[10] Depression is seen more often as a comorbid mental health disorder with a generalized anxiety disorder and coronary heart disease in the anxiety population has been linked with a worse prognosis.[11]

Studies have shown that long-term use of such medications for the treatment of generalized anxiety disorder is cost-effective as well as the continuation may prevent relapse rate among the patients.[12] The comparative studies between escitalopram and other medicines like tandospirone have revealed that the patient's condition and the level of severity might produce different results for the individuals[13] as the effectiveness may differ with different anxiety disorders i.e. social anxiety disorder and comorbid disorders i.e. bipolar disorder.[14] There is a scarcity of studies that specifically compare the efficacy of escitalopram with pregabalin in the context of Pakistani population. The objective of the study is to find out the difference between the outcome of escitalopram and pregabalin among patients with generalized anxiety disorder, as there is a need to provide the studies about the efficacious pharmacotherapy for

the treatment of generalized anxiety disorder with comparative studies for different available drugs in specifically Pakistani clinical population.

Material and Methods

This study was conducted in the year 2021 in the Department of Psychiatry and Behavioral Sciences, Mayo Hospital affiliated with King Edward Medical University, Lahore after approval of the research proposal by the Ethical Review Committee. The research followed the methods that comply with the ethical boundaries while dealing with the human subjects and throughout the study process until the report writing.

This quasi-experimental study with pre and post-test design was carried out for twelve weeks. A sample of 90 patients, both males and females were selected based on the diagnosis of generalized anxiety disorder defined in Diagnostic and Statistical Manual of Mental Disorders (DSM-5) suffering from a severe level of anxiety since the last 10 -12 months with a score of 17 or above as the anxiety measure used for this study. The patients were divided into 2 equal groups; group A Escitalopram treated and group B Pregabalin treated, both equally for 12 weeks. in which the follow-up was done between 13^{th} – 15^{th} week by comparing with baseline data. Non probability purposive sampling technique was used.

The study was comparison of effectiveness between escitalopram and pregabalin in the clinical population diagnosed with generalized anxiety disorder based on the symptoms given in Diagnostic and Statistical Manual of Mental Disorders (DSM-5). The efficacy score was defined as ≥2% decrease in anxiety disorder score by using the Hamilton Anxiety Rating Scale (HAM-A) after treatment. This scale is a 5-point Likert scale from 0 - 4 ranging from not present to severe with scores 0 - 56. It takes 15 minutes only and rated for the symptoms of anxiety. The physical and cognitive symptoms are given to rate as outcome score. The reported levels are acceptable because the scale is reliable and validated.[15]

The recording of scores was done at baseline before treatment and after treatment. The data was collected quantitatively from a public institute's OPD, the Department of Psychiatry and Behavioral Sciences, Mayo Hospital Lahore, Pakistan. The scores were attained for the comparison between the two groups using the Hamilton anxiety rating scale. Purposive sampling method was used to allocate the sample from indoor wards and outdoor services and then assigned to either of the intervention groups named group A or group B. The 20 mg dose of escitalopram per day was supplied to the participants of group A while a dose of 150-200mg per day of pregabalin was given to group B and the baseline data was collected. After 12 weeks, follow-up data was taken, from the patients and the scores were compared with the baseline.

Those within the age range between 18 and 60 years (N=90), either males or females within each study group (n=45), who met the DSM-5 criteria for diagnosing generalized anxiety disorder and a score of 17 or more on the HAM-A rating scale were included. The participants were diagnosed with generalized anxiety disorder as the main inclusion criteria. On the other hand, patients having Intellectual disabilities, a history of head injury, epilepsy, ongoing psychotherapy, drug abuse and a history of psychosis, bipolar affective disorder and dementia on clinical examination were excluded.

The participants were selected by purposive sampling from indoor and outdoor patients. Informed consent was obtained. The demographic data including name, age, gender, and duration of symptoms was noted. Patients were assessed with a Hamilton anxiety rating scale score at the time of enrollment. In group A, patients were given escitalopram 10-20mg/day while in group B, patients were given pregabalin150-600 mg/day. Then patients were followed-up in OPD after every 4 weeks. After completion of 12 weeks, patients were again assessed on the HAM-A scoring system and the score was noted. If the score was ≥2% decreased from baseline, efficacy was labelled as positive. On each visit, the patients were asked about any side effects experienced by them during medication and in case of severe side effects, the drug was discontinued. All this information was recorded through the measure of HAM-A.

Data were entered into an excel sheet under Microsoft 10 and then transferred to the SPSS version 23 for analysis. The categorical variables like gender, efficacy and side effects were presented as frequencies and percentages. For the continuous variables like age and duration of symptoms simple descriptive statistics i.e. mean and standard deviation were used. In the inferential statistics for hypothesis testing the chi-square test was applied to compare the efficacy and side effects in both of the study groups. A p-value of (≤0.05) was taken as a significant cutoff score. Data was stratified for age, gender, and the level of severity of anxiety at baseline with the duration of symptoms.

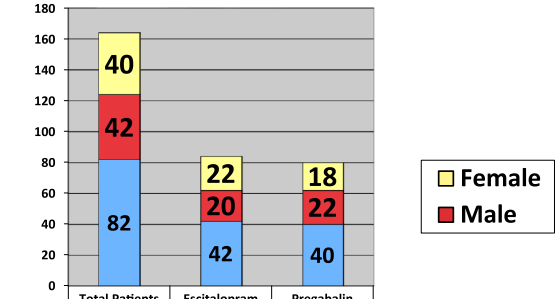
Results

Initially, 90 patients participated in the study but later 8 of them didn't follow up. The Hamilton Anxiety Baseline score at baseline (M=29.47, SD=4.786) and follow up score (M=17.22, SD=6.895) showed a decline in the level of anxiety in both groups, but overall, efficacy of Escitalopram was significantly higher than that of Pregabalin i.e. Group-A: 92.8% vs. Group-B: 82.5%, P-value= 0.003.

Table 1: Combined Pre and Post scores of the HAM-A Scale for both Drugs

	N	HAM-A Min.Score	HAM-A Max. Score	HAM-A Mean Score	Std. Deviation
Before Treatment	90	18	40	29.17	4.786
After Treatment	82	8	37	17.65	6.895

The maximum value of the Hamilton Anxiety Baseline before treatment was 40, while the maximum value of the Hamilton Anxiety Baseline after treatment was 37. The standard deviation before treatment was 4.786 and after the treatment standard deviation was 6.89. That is, there was more variation after the treatment. This may be due to the effectiveness of the medicines. The mean age of all patients was 36.27 ± 10.92 while meaning age in the escitalopram group was 36.55 ± 11.04 years and in the pregabalin group was 35.98 ± 10.92 years. Efficacy was



	Total Patients	Escitalopram group	Pregabalin group
Female	40	22	18
Male	42	20	22
Total	82	42	40

Figure 1: Distribution of sample gender

achieved and group cross-tabulations show that there were 39 persons (92.8%) who achieved efficacy due to Escitalopram, and 33(82.5%) efficacy was achieved due to Pregabalin.

In this study, total of 82 patients were followed out of which 40 were female and 42 were male. In the escitalopram group, 22 were male and 22 were female. In the pregabalin group, 22 were male and 18 were female. To test the association between efficacy achieved (yes, no) and types of medicine taken (Escitalopram, Pregabalin), a Chi-square test is executed with SPSS and the results are shown in the following outputs. There were only 3 (7.2%) patients who had not achieved efficacy due to Escitalopram while 9 (17.5%) patients had not achieved efficacy with Pregabalin. Therefore, Escitalopram remained more effective than Pregabalin.

An independent sample t-test was performed to test the significance of medicines to achieve efficacy. The group statistics show that after the treatment there remained 42 persons who took Escitalopram, while 40 persons took Pregabalin. The Hamilton Anxiety Baseline means after the treatment was 15.33 who took Escitalopram, which was considerably low than the mean after the treatment who took Pregabalin. So Escitalopram remained more effective than Pregabalin. The results of the independent sample t-test show that there is a highly significant difference between the two types of medicine after the treatment as the p-value is 0.005 of the t-test statistic (-2.906) with a mean difference of (-3.867) shows that escitalopram remains more effective that the pregabalin.

To test the association between efficacy achieved (yes, no) and types of medicine (Escitalopram, Pregabalin) a Chi-square test is executed with SPSS and the results are shown in the following outputs. Efficacy was achieved and group cross-tabulations show that there were 39 persons (92.8%) who achieved efficacy due to Escitalopram while 33 (82.5%) of them achieved efficacy due to Pregabalin. There were only 3 (7.2%) persons, who have not achieved efficacy due to Escitalopram while 9 (17.5%) persons have not achieved efficacy due to Pregabalin. Therefore, Escitalopram remained more effective than Pregabalin. The Pearson Chi-Square test value of 2.052 with a P-value of 0.152 shows that the group (a type of medicine) and Efficacy achieved are not associated that is they are independent.

Table 2: Before and after treatment scores

Groups	N	HMA-A	SD	x2	p
Escitalopram	42	15.22	5.63	-3.02	.005
Pregabalin	40	19.20	6.40	-3.86	.005
Efficacy Scores Total %	88				

An independent sample t-test was performed to test the significance of medicines to achieve efficacy. The group statistics show that after the treatment there remained only 42 patients who continued Escitalopram, while 40 patients continued taking Pregabalin. The Hamilton Anxiety Baseline after the treatment was 15.33 mean for those who took Escitalopram, which was considerably lower than the mean of those who took Pregabalin. Therefore, Escitalopram remained more effective than Pregabalin. The results of the independent sample t-test show that there is a highly significant difference between the two types of medicines after the treatment as the p-value is less than 0.005 on t-test (-2.906). The mean difference (t=3.867) shows that Escitalopram remains more effective than Pregabalin.

Table-3: Summary of symptoms after treatment in both groups

			Frequency(%)	Total
GIT	E	Y	5(11.9%)	42
		N	37(88.1%)	
	P	Y	11(27.5%)	40
		N	29(72.5%)	
H	E	Y	6(14.2%)	42
		N	36(85.5%)	
	P	Y	9(22.5%)	40
		N	31(77.5%)	
SI	E	Y	4(10.1%)	42
		N	38(15%)	
	P	Y	6(39.9%)	40
		N	34(40%)	
SW	E	Y	8(19%)	42
		N	34(81%)	
	P	Y	20(50%)	40
		N	20(50%)	
US	E	Y	2(4.7%)	5
		N	3(95.3%)	
	P	Y	40(7.5%)	77
		N	37(92.5%)	

GIT=Gastrointestinal disturbances, H=Headache, SI=sleep issues, SW=sweating, US=Urinary problems, SW: x2= 8.729, p-value=0.003

Discussion

This was a quasi-experimental study having a pre and post-test design conducted on patients before and after treatment with Pregabalin and escitalopram, carried out for twelve weeks on 90 patients in the year 2021 between January to June on visiting Mayo Hospital in Lahore, within the age range of 18 to 60 years. They were divided into 2 equal groups by purposive sampling. The 20 mg dose of escitalopram per day was given to the participants of group A while a dose of 150-200mg per day of pregabalin was given to group B and the level of anxiety before and after the experiment was measured by Hamilton Anxiety Baseline. A record of all clinical signs and symptoms was also maintained throughout the time of medication. After 12 weeks, follow-up data was taken from the patients and the scores were compared with the baseline. A marked reduction in anxiety scores was observed and documented in patients treated with escitalopram compared with pregabalin.

Serotonin reuptake inhibitors including escitalopram and pregabalin are recommended by World Federation of Societies of Biological Psychiatry as first-line treatments for anxiety disorders, but inspite of their recommendation, escitalopram is not the drug of choice in Pakistan for anxiety disorders. Psychotherapy,16 including cognitive / behavioral therapy, auto relaxing treatment is recommended mostly in combination with pharmacotherapy.17 Pregabalin is a structural variable of gamma-aminobutyric acid (GABA) and a new entity in use for treat-

ing Generalized Anxiety Disorders since 2002. It inhibits the release of high levels of neurotransmitters which are excitatory and this action is performed by specific binding sites of this drug to calcium releasing channels. Pregabalin does not directly bind to GABA A, GABA B or benzodiazepine receptors.

One good aspect of Pregabalin is that it is rapidly taken up from the gut via blood vessels to enter the circulation from where it is maximally absorbed within 2 hours via oral administration, but in our study, oral efficacy of Escitalopram was significantly higher than that of Pregabalin i.e. Group-A: 92.8% vs. Group-B: 82.5%, p-value= 0.003 which is consistent with many other relevant studies.18 This is coherent with the study of a total of 273 patients who found a 2-point greater reduction in Hamilton anxiety rating scale score associated with pregabalin than with placebo. There was an improvement in both cognitive and somatic anxiety symptoms. Data is scarce about the relative tolerability of pregabalin when compared to other treatments; however, the adverse event profile of pregabalin[26] differs from that of venlafaxine XL, with pregabalin being associated with more prominent dizziness and vertigo, and venlafaxine XL with more prominent nausea and a pooled analysis of studies that included a benzodiazepine[27] indicates that treatment with pregabalin is more likely to be associated with dizziness, and benzodiazepine treatment more likely to be associated with somnolence and incoordination.[28]

Another research included 356 patients, out of which 180 patients were treated with pregabalin and 176 patients, as a placebo has been closely similar to this study in results.19 The mean difference that brings a change in the Hamilton anxiety rating scale score was significantly greater when compared with the placebo. In this study, the score HAM-A was 0.22 which was higher for escitalopram with an efficacy rate of pregabalin, 67.7%.20

The researcher enrolled a total of 526 patients, 299 of those completed 24 weeks of open-label treatment with escitalopram. About 92% of patients who completed 24 weeks of treatment showed significant improvement in anxious symptoms.21 Results showed that the efficacy percentage of Escitalopram in this study was 92.8%, which is comparable to the efficacy reported by the study as 92%. HAM-A was 0.57 with Escitalopram.22 Some other similar studies have supported the efficacy of escitalopram in 68-69% of cases within 4 weeks.23 It showed that taking of escitalopram as a drug of choice had less adverse effects on the gut and very few patients (about 3.5-8.9%) reported discontinuing it due to its side effects.24 It also claimed that the frequency of side effects such as gastrointestinal upset, headache, sleep disturbance and urinary symptoms was higher in patients who were given Pregabalin than that of Escitalopram but the difference in the frequency of these side effects was not statistically significant for the treatment groups.25

There is very limited data regarding how much of Pregabalin can be tolerated in comparison to other agents used for the same purpose. However, it is a documented fact that the side effects of Pregabalin26 are different from venlafaxine XL. This difference lies in the fact that the patients experience stronger episodes of dizziness and vertigo when compared to the other drug. It has also been observed that in contrast to Pregabalin, venlafaxine XL is linked with stronger episodes of nausea. Another comparative study with benzodiazepines revealed that the latter caused not only dizziness but additionally acute episodes of lack of motor coordination.28

When we go through the most recent literature it is clearly evident that escitalopram is comparatively better tolerated in intensive treatment of anxiety disorders and therefore should be prescribed as a drug of choice for alleviating the symptoms of anxiety.29 Co-administration of eszopiclone with escitalopram in another study on anxiety driven patients showed good results and had a visible effect on the quality of sleep, performance of patients during day time activities, levels of anxiety and magnitude of mood swings in insomniac patients. Selective serotonin reuptake inhibitors are an alternative for treating GAD more than any other medication due to the comparative efficacy, tolerability, and safety in anxious adults.15 Based on the results reported in the Pakistani population, this study concluded that escitalopram (10-20 mg/day) is comparatively safe and better tolerated in short and long-term treatment.

Conclusion

Escitalopram is a better option and efficacious for the Pakistani population in treating psychological issues including depression, bipolar and other affective disorders despite the minor side effects compared to Pregabalin.

Limitations, Implications and Recommendations

This study covers limited data from limited patients. Population from different settings with different ages and clinical comorbidities for Pakistan. Future recommendations also include carrying out different research designs. Implications are wide for clinical, medical professionals dealing with the psychiatric population, non-medical practitioners and researchers.

The increasing trends in the presence of anxiety symptoms among younger children, people with substance use, and people who are still undiagnosed with any medical or mental illness must be tested for anxiety. The prevalence rate is alarming, based on the anxiety level this research would generate in the practitioners in decision making for patients with diverse demographic backgrounds. For the general population, the use of prescription drugs with lesser side effects must be considered for treating anxiety. The findings imply for the pharmacological industry too to generate options that enhance the quality of life.

Author Contributions

NIC helped with literature review and writing of the manuscript. MSZ contributed in data analysis, interpretation of results and final approval of the draft.

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