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SAFETY AND EFFECTIVENESS OF ESCITALOPRAM AND VENLAFAXINE SR IN SOCIAL ANXIETY DISORDER PATIENTS IN MARDAN, PAKISTAN: A PROSPECTIVE COHORT ANALYSIS

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ABSTRACT

Social Anxiety Disorder (SAD) is a widespread psychiatric condition characterized by fear and discomfort in social situations, often leading to panic attacks. SAD is influenced by biological, genetic, familial, and environmental factors and can result in severe mental health issues. It is most prevalent in third-world countries, impoverished communities, and among the unemployed. A prospective cohort study was conducted in the mardan district to assess the effectiveness and safety of escitalopram and venlafaxine in treating SAD. The study included 240 adult participants, with a higher prevalence of SAD in females, especially those aged 18 to 39. Both medications were found to reduce anxiety levels significantly. Venlafaxine was more effective than escitalopram, with a statistically significant reduction in mean social anxiety scores by using Himilton anxiety rating scale. Both drugs demonstrated good compliance rates, but mild adverse effects such as weight gain, xerostomia (dry mouth), and ejaculation dysfunction were reported. Venlafaxine and escitalopram are effective and safe treatments for SAD, with venlafaxine showing superior effectiveness. However, this study had limitations in terms of its sample size, so further multicenter studies with larger and more diverse populations in Pakistan are needed for generalizability.

Keywords: *social anxiety disorder (SAD), Escitalopram, Venlafaxine.*

1. INTRODUCTION

Social anxiety disorder is also called social phobia. Social anxiety (SA) is a common human experience characterized by an intense fear of evaluation from others in social situations (Morrison, A.S et al. 2013). It is also characterized by persistent fear and avoidance of social situations due to fears of evaluation by others. SAD can be highly distressing, and it can interfere with school, work, and social life as sufferers avoid social or performance situations (Schneier F et al. 2015). People with social anxiety disorder are afraid of other people's judgement and avoid it. Individuals with social anxiety disorder are typically feel uncomfortable and shy when meeting new people, silent in groups, and withdrawn in unfamiliar social gathering. When they interact with others, they might or might not show overt evidence of discomfort (e.g, blushing, not making eye

contact), but invariably experience intense emotional or physical symptoms, or both (e.g. fear, heart racing, sweating, trembling, trouble concentrating (Stein, M.B, et al. 2008).

Venlafaxine is the first antidepressant of the innovative generation to be compared to other antidepressants like escitalopram. Venlafaxine has fewer anticholinergic and CNS adverse effects and is well tolerated (Schneier,2011). Venlafaxine mono amine-inhibitory properties are distinct from those of SSRIs, which exhibit strong serotonin reuptake selectivity (Zohar and j. et al 1999). At low therapeutic doses, venlafaxine inhibit selectively the 5HT uptake while performing in vivo studies. In addition to these, it also inhibits the reuptake of NE and 5HT at higher therapeutic doses (Roseboom & Kalin, 2000). Paroxetine was once the first-choice treatment for SAD, but more recently, venlafaxine XR has gained approval for this condition in the USA etc. The study also aimed to investigate the connection between improvement in social adjustment and anxiety symptoms (Boyer et al.2004).

Escitalopram is a component of the serotonin receptor transporter (SERT), which is liable for reabsorbing serotonin from the brain's serotonergic neurons, which are involved in mood relaxations, sex, sleep, and other crucial processes. Escitalopram supposedly modifies serotonin levels in the brain and controls mood (Schwartz, 2005). According to a study conducted in 2002 by (Culpepper and colleagues), escitalopram, the S-enantiomer of citalopram, is a SSRI commonly used to treat anxiety disorders. SSRIs work by increasing the concentration of serotonin neurotransmitter in the synaptic cleft. This is achieved by preferentially blocking serotonin transporter (SERT) at pre-synaptic neurons. These findings were reported in a study of (Carandang and colleagues in 2011).

When compared to other antidepressants, escitalopram exhibits effectiveness and is a top choice for treating depression and social anxiety disorder (Hoschi et al. 2014). According to research, escitalopram has been found to improve the quality of life and alleviate symptoms of SAD (Stein et al. 2005) Escitalopram has been proven to be a safe and effective medication for treating Social Anxiety Disorder (SAD) at doses of 10-20mg/day (Jonathan and others, 2004). A study using the Hamilton rating scale found it to be both safe and effective for both sexes. However, the recommended dose should not exceed 40mg/day as doses higher than this have been found to be less well tolerated, with 26% of patients unable to take 50mg/day (Crawford et al., 2011). Despite the common side effects of gastrointestinal problems and sexual dysfunction, SSRIs are still the most. The effectiveness of venlafaxine in improving anxiety symptoms is superior to that of SSRIs, according to some studies (Waugh 2003). The aim of this study is compare the effectiveness of both venalfaxine and escitalopram in the treatment of social anxiety disorder (SAD).

2.1 Methodology

2.1.1 Study design and setting

A Prospective, cohort study was conducted in order to treat social anxiety disorder (SAD) patients advised escitalopram and venlafaxine. The research work was performed in department of psychiatry, Mardan Medical Complex (MMC) a medical teaching institution (MTI). The total duration of study was 6 months with three different time frequencies and the anxiety score was measured after every two months. The dose of the medication was 10-20mg for escitalopram and 75-150mg for venlafaxine.

The anxiety score was measured before treatment starts in the first months of therapy. Then after using prescribed drugs the same process repeated in the third and sixth month of the treatment. This procedure basically contain two factors i.e. drugs (venlafaxine and escitalopram) and Time i.e. T1 (month 1), T2 mean (month 3) and T3 mean (months 6).

2.1.2 Sample size

A sample of 240 patients selected based on the convenient random sampling technique, with the aim of achieving a statistical significance level of 0.05. This sample size was selected on the basis that any differences found in the study outcomes would be statistically meaningful. Population of SAD patients was obtained from the hospital management and information system of MMC

for sample size determination.

2.1.3 Instrument Used

A pre validated tool Himilton rating scale (HAM-A) was used for assessment of severity of anxiety in each individual. The questionnaire was also used to find out the effectiveness of the escitalopram and venlafaxine in patient with SAD.

2.1.4 HAM-A

This is a 14-item scale which assesses both somatic anxiety (physical problems associated with anxiety) and psychic anxiety (mental agitation and psychological distress). Each item on the scale is characterized by a symptom. With a total score range of 0-56, each question is rated on a scale from 0 (not present) to 4(severe), with <17denoting mild severity,18-24 denoting mild to moderate severity, and 25 -30 denoting moderate to severe.

2.1.5 SAD Diagnostic criteria (DSM-5)

This is a Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines social anxiety disorder (SAD) as a condition marked by persistent fear of social or performance situations in which the individual is at risk of embarrassment.

2.1.6 Inclusion and exclusion criteria

Patient with social anxiety disorder prescribed by psychiatrists who are taking venlafaxine 75-150mg and escitalopram 10-20mg having the age of 18 to 70. Patient who were addicted, patient with renal or hepatic impairment, patient who uses the same class of drugs were excluded from the study.

2.1.6 Statistical analysis

The numerical data analysis was carried out using SPSS software package version 16 using the paired T test and one way Anova for concluding the results along with standard deviation and means score. Value of significance was taken 0.005.

3. RESULTS:

3.1. Patient's Socio-Demographic Variable

A sociodemographic profile is a report that outlines the social and demographic features of a particular group of individuals, including factors like age, gender, education level, income, occupation, and geographic location. It is an important tool for identifying and addressing disparities and promoting greater equity across different populations. A total of 240 SAD patients assessed in psychiatry department of MMC hospital mardan during the study period.

Table 1: Demographics of SAD patient

Variable	Venlafaxine	escitalopram	Value(n%)
Gender			
Male	55	50	45.83%
Female	65	70	56.25%
Age			62.91%
18-39 year	78	73	37.08%
>40years	42	47	
Occupation			
Employed Un Employed	65	55	50%
	55	65	50%
Marital status	45	55	41.6%
Single Married	75	65	58.3%
Smoking	24	35	24.5%
Current smoker Ex	36	30	27.5%
smoker Never smoker	60	55	47.91%
Education	48	55	48.22%
Educated Uneducated	72	65	57.08%
Location	55	55	45.83%
Rural Urban	75	65	58.3%
Family income status	20	30	20.83%
Poor class Middle class	40	45	35.41%
Upper class	60	45	43.75%

Table 2: ADR frequency distribution for venlafaxine SR

Sample size : (n=120)

Observed ADR	Female(n)	Male(n)	Total (n)	Percentage (%)
Weight gain	15	6	21	17.5%
ED	0	12	12	10%
Blood pressure	4	5	9	7.5%
Constipation	6	7	13	10.8%
Diarrhea	9	8	17	14.1%
Dry mouth	4	6	10	8.3%
Dizziness	8	7	15	12.5%
Nausea	5	6	11	9.1%
Insomnia	4	5	9	7.5%
Sweating	4	4	8	6.6%

Table 3: ADR frequency distribution for escitalopram

Sample size : (n=120)

Observed ADR	Female(n)	Male(n)	Total (n)	Percentage (%)
Weight gain	15	5	20	16.6%
ED	0	5	5	4.1%
Blood pressure	3	3	6	5.0%
Constipation	5	6	11	9.1%
Diarrhea	7	7	14	11.6%
Dry mouth	4	7	11	9.1%
Dizziness	6	6	12	10.0%
Nausea	3	3	6	5.0%
Insomnia	3	3	6	5.0%
Sweating	3	2	4	4.1%

The Above table shows the side effects which normally occurring with the usage of venlafaxine and escitalopram. Weight gain, diarrhea and dizziness are common with venlafaxine. But increase in blood pressure is also noted in various patients. Weight gain is more common with SSRIs.

Table 4: Compliances and noncompliance show by venlafaxine and escitalopram

Gender	Compliance	%age	Non Compliance	%age
Male	80	33.3%	25	10.4%
Female	100	41.6%	35	14.5%
Total	180/240	75%	60	25%

The above table 4 represent the adherence and non- adherence of the patient while taking the medicines. In this table the greater percentage of non-adherence was observed in female patients because of so many reasons like weight gain etc.

Table 5: Effect of treatment across escitalopram and venlafaxine over time between subjects (mean standard deviation)

Variables	1st month	3rd month	6rd month	p- value
HAM-A score				
Escitalopram	23± (3.3)	21± (3.2)	18± (3.2)	0.002
Venlafaxine	24± (2.9)	20± (2.7)	16± (3.0)	0.001

Table 5 shows that the value of anxiety were measured at different interval of treatment by using HAM-A scale

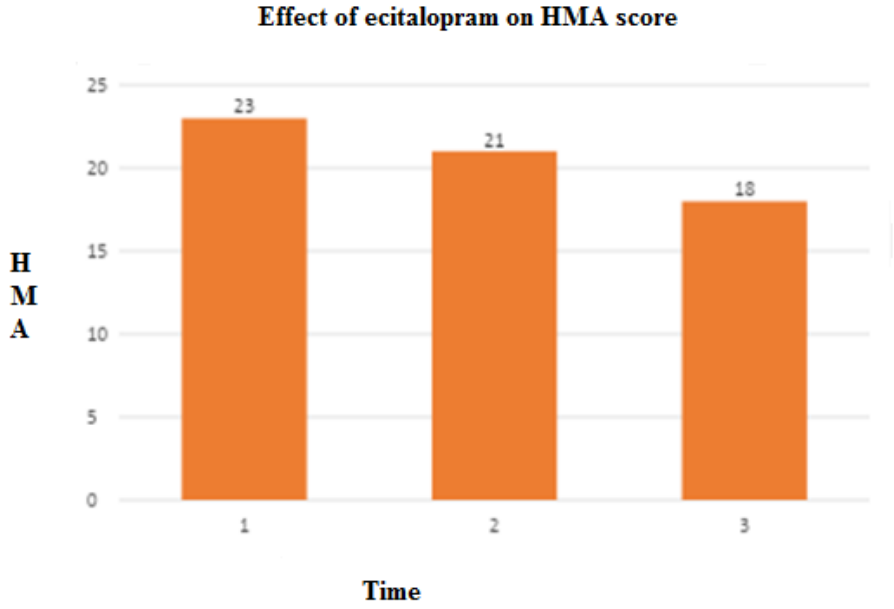

Figure 1. Graph for average value of escitalopram across treatment in month

Figure 1 represents the average of six month results of treatment by decreasing the anxiety score while taking the medication. 1st bar graph represent the average of 1st month with mean of 23±(2.9) , 2nd bar graph represents the average of three months with mean of 21±(2.7) and 3rd represent the average of six months result with mean of 18±(3.0).

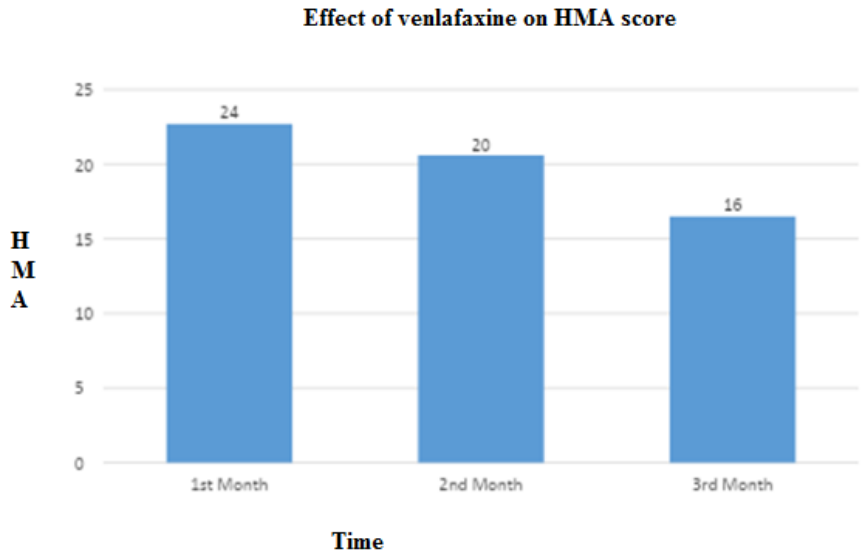

Figure 2: Graph for average value of venlafaxine across treatment in month.

This graph represent that the average of six month results .it is found that HAM-A score has been decreasing continuously with the passage of time. 1st bar graph represent the average of 1st month with mean of 24±(3.3) , 2nd bar graph represent the average of third month with mean

of 20±(3.2) and 3rd represent the average of six month result with mean of 16±(3.2).

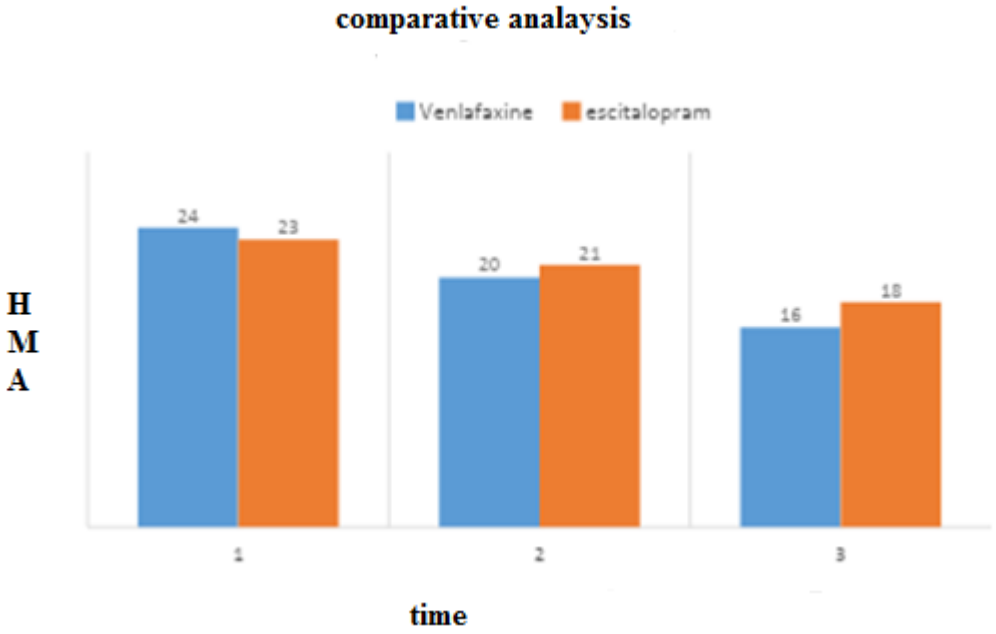

Figure 3: Comparative graph for two drugs across treatment in month

This graph shows the comparison between Escitalopram and Venlafaxine across. It is observed that when the treatment is started the anxiety level was decreasing gradually with time. The measurement of the level of anxiety has been done using HAM-A scale for different months. As it shows that the venlafaxine drops the anxiety level more than the escitalopram as shown in Figure 3.

Discussion:

It is a comparative study in which the effect of two drugs on SAD was observed. The data showed that venlafaxine reduced the anxiety level more as a comparative to escitalopram. Similar findings were reported by Stephen M. Stahl et al (2002), who noted that SNRIs such as venlafaxine offer superior efficacy and safety compared to SSRIs like escitalopram. Additionally, David Smith et al. (2002) also found venlafaxine to be more effective than SSRIs, including escitalopram. To support of this, Stefan Weinmann et al. (2008) reported that venlafaxine was effective in reducing anxiety symptoms. Venlafaxine is safe, well tolerated and efficacious in the treatment of social anxiety disorder and generalized anxiety disorder (Michael R Liebowitz et al.2005). similar findings were also reported where SNRIs like venlafaxine are shown to be efficacious in treating the anxiety disorder like SAD (Stephen M stahl et al.2005). Another analysis compares the efficacy and tolerability of venlafaxine to selective serotonin reuptake inhibitors (SSRIs) for treating social anxiety disorder. It finds that venlafaxine is slightly more effective than SSRIs in reducing symptoms but is associated with more side effects. The study concludes that venlafaxine's therapeutic advantages are offset by concerns about its tolerability (de sila et al 2012). Hence from this study and also proved from the above discussion that it was concluded that venlafaxine SR were found to be more effective in the treatment of social anxiety disorder however there are some ADRs associated with the use of venlafaxine which the clinician must considered while prescribing this drug.

CONCLUSION

According to the study's findings, the two clinically proven antidepressants, venlafaxine and escitalopram greatly improve quality of life and

cause social anxiety symptoms to go away, making them the first choice for treating social anxiety disorder (SAD). While selective serotonin reuptake inhibitors (SSRIs) are frequently used in the treatment of anxiety disorders, serotonin-norepinephrine reuptake inhibitors (SNRIs), such as Venlafaxine, have recently received regulatory approval and are receiving more attention, suggesting a significant change in the way SAD is managed. This study also showed that Venlafaxine demonstrates more effectiveness, providing valuable treatment options for people with anxiety symptoms and highlighting the significance of customized approaches to SAD management.

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