

COMPARISON OF THE EFFICACY OF SERTRALINE AND MIRTAZAPINE FOR TREATING THE DEPRESSION IN PATIENT WITH HEPATITIS C: RANDOMIZED CONTROL TRAIL

Dr. Aneela Jabeen^{*1}, Dr. Faiza Ather², Dr. Altaf Qadir Khan³, Hira Fatima⁴, Dr. Muhammad Zaeem Khalid⁵, Dr. Farhana Ashraf⁶

^{*1}MBBS, DCH, MD Psychiatry Senior Registrar, APWMO, Lahore General Hospital

⁴MS Clinical Psychology, Clinical Supervisor of MS Students (University of the Punjab & Riphah International University), Clinical Psychologist at Lahore General Hospital

^{,2}Associate Professor, MBBS, DPM, MCPS, FCPS (Psych), HOD of Department of Psychiatry and Behavioral Sciences

Lahore General Hospital

⁵MBBS, BSc, Department of Paediatric Surgery, Shaikh Zayed Hospital, Lahore ³Professor of Psychiatry, MBBS, DPM, FCPS (Psych), Consultant Psychiatrist at National Hospital, Lahore. ⁶MBBS, MD Psychiatry Senior Registrar, SWMO, Lahore General Hospital Lahore

DOI: <u>https://doi.org/10.5281/zenodo.15515798</u>

Abstract

Keywords

Sertraline, Mirtazapine, Depression, Efficacy.

Article History

Received on 17 April 2025 Accepted on 17 May 2025 Published on 26 May 2025

Copyright @Author Corresponding Author: * Dr. Aneela Jabeen **Background** Hepatitis C virus (HCV) is the most common blood-borne pathogen and a leading cause of morbidity and mortality. Infection with HCV is a major public health problem worldwide. Depression is a common mental illness; it is one of the leading causes of disability worldwide. Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. Very few studies are available to see the efficacy of antidepressant therapy in hepatitis C population, so this study was planned.

Objective: To compare the efficacy of Sertraline and Mirtazapine for treating the depression in patient with Hepatitis C.

Material & Method: This randomized control trial was carried out at hepatic clinic, Lahore General Hospital Lahore and Jinnah hospital Lahore. The study duration was 12 months after approval of synopsis. After meeting the inclusion and exclusion criteria and demographic detail were noted. The depression was diagnosed based on DSM-V and severity was evaluated by using HAM-D at the base line, with regular follow up at 4th, 8th, and 12th treatment weeks. Patients were divided into groups; drugs were allocated randomly and efficacy of drugs was assessed by using HAM-D.

Results: The mean age of the patients was 41.69 ± 10.61 years, 43(44.79%) patients were male and 53(55.21%) patients were females. In sertraline group the mean change in HAM-D score of the patients was 13.54 ± 1.56 while in mirtazapine group the mean HAM-D score of the patients was

17.27±1.28 (p-value=<0.001).

Conclusion: This randomized control trial concluded that mirtazapine is significantly more efficacious as compared to sertraline for treating the depression in patient with Hepatitis C.

INTRODUCTION

Depression is a common mental illness; it is one of the leading causes of disability worldwide (World Health Organization). Hepatitis C is a major public health problem all over the world, it is a viral infection with varying degree of severity. It is transmitted through blood or blood born products, intravenous drug use, occupational exposure, longterm hemodialysis and children born to women who are HCV positive, 65% to 70% cases are reported to be Intravenous drug users. (1) Hepatitis C is one of main cause of chronic liver disease. It is estimated that 170 million people are being affected by hepatitis C worldwide. (2) (3)

Approximately 85% patients of acute hepatitis C develop chronic HCV infection administration. However not much studies focused on the use of SSRI and other antidepressants in hepatitis C positive patients, majority of research is done on the treatment or the prevention of depression with interferon therapy (8) Very few studies are available to see the efficacy of antidepressant therapy in hepatitis C population. (9)

Rationale

The rationale of study was to compare the efficacy of Sertraline (SSRI) and Mirtazapine for treating the depression in patients with hepatitis C. Sertraline and Mirtazapine have minimal cytochrome P450 enzyme activity, very few drug-drug interactions, pharmacokinetic is linear and there is no known hepatic toxicity.

AIMS AND OBJECTIVES

AIMS: To do the comparison of efficacy of antidepressants for treating depression in patient with hepatitis C.

OBJECTIVES: The current study was designed to compare the efficacy of Sertraline and Mirtazapine for treating the depression in patient with Hepatitis C.

Operational Definitions:

DEPRESSION: Diagnostic and Statistical Manual (DSM-5) was used to diagnose depression. The Hamilton Depression Rating Scale (HAM-D) was



ISSN: (e) 3007-1607 (p) 3007-1593

used to determine the severity of depression. Cut off value for HAM-D was considered above 18. (10)

EFFICACY:

Resolution of number of symptoms of depression and reduction in the severity of symptoms on the Likert scale was used to assess the efficacy of medications.

HEPATITIS C:

Qualitative HCV RNA in serum by Polymerase Chain Reaction (PCR)assay was used to diagnose HCV infection. Cut off value of HCV RNA in serum or plasma with a lower limit of detection was less than or equal to 15 IU/ml was recommended (EASL recommendation 2020).

MATERIAL AND METHOD

This study was done with two parallel treatment groups that are under Randomized Control Trial. All the patients are recruited and their screening was done in Hepatic clinic, Lahore General Hospital Lahore and Jinnah Hospital, Lahore.

Inclusion Criteria:

1.All patients newly diagnosed with Hepatitis C RNA (PCR Qualitative) positive in the last three months, not taking any kind of antiviral medication 2.Patient with Depression meeting the DSM-5 criteria and cutoff value of HAM-D would be considered above 18

3.Patients of both sexes.

4.Age range between 18-60 years.

Exclusion Criteria:

1.Use of psychotropic medication during last three months.

2.Diagnosis of psychiatric disorder in the last six months

3.Substance and/or alcohol abuse in the last six months.

4. Presence of hepatocellular carcinoma

5.Decompensated chronic liver disease

Non probability purposive sampling technique is used and patients with depression were selected through Randomization and drugs were allocated

with simple Randomization. DSM-V and Hamilton Rating Scale for Depression (HAM-D) is used for assessment measures. HAM-D is 24- item version. Rating was completed by the examiner based on the patient interview and observation. The administration took 15 to 20 minutes.

Patients according to the sample size fulfilling the selection criteria were selected in the study who visited the Hepatitis Clinic, Lahore General Hospital, Lahore and Jinnah Hospital, Lahore. Written informed consent was taken. Demographic details (name, age, sex, education, marital status and occupation, etc.) were taken by using questionnaire. The depression was diagnosed based on DSM-V and severity was evaluated by using HAM-D at the base line, with regular follow up at 4th, 8th, and 12th treatment weeks. Severity scores of depression were assessed as mild, moderate and severe. Patients were divided into groups, drugs were allocated randomly and efficacy of drugs was assessed by using HAM-D. The most recent (3 months) Hepatitis C RNA, PCR (Qualitative) done at Hepatitis clinic was recorded in the questionnaire.

The sample size 96 (48 in each group) was calculated by the following formula keeping the power of study equal to 90% and level of significance equal to 5%.



ISSN: (e) 3007-1607 (p) 3007-1593

$$n = \frac{\left(Z_{1-\beta} + Z_{1-\frac{\alpha}{2}}\right) (\delta_1^2 + \delta_2^2)}{(\mu_1 - \mu_2)^2}$$

Where $Z_{1-\beta}$ is the Desired Power of study that is 90% and its value is 1.96 and $Z1-\underline{\alpha}$ is desired 2 level of significance that is equal to 5% and its value is 1.28. While μ 1 is Anticipated mean of HAMD score level in Sertraline group and its value is 12.62 and μ 2 is Anticipated mean of HAMD score level in Mirtazapine group and its value is 14.12 (11) σ 1 is the Standard Deviation of HAMD score level in Sertraline group whose value is 1.72. While σ 2 is Standard Deviation of HAMD score level in Mirtazapine group and its value is 2.72. N is the calculated sample size in each group that is 48.

The collected data was entered and analyzed using SPSS 20. Mean and standard deviation was calculated for quantitative data. Frequency Percentage was calculated for categorical data like gender, marital status, education, occupation, religion. Paired sample t- test was used to see the statistically significant difference in depressive scores at baseline and post intervention. P – Value

< 0.05 was considered as significant.

rable 1. The and 1.0st Comparison of Ham D beore between beddy Oroups						
Ham-D Score	Study Group	N	Mean n	Standard Deviation	P-Value	
				n		
Pre	Sertraline	48	22.92	1.18	0.725	
	Mirtazapine	48	23.00	1.13		
Post	Sertraline	48	9.37	0.91	<0.001	
	Mirtazapine	48	5.73	0.96		

 Table 1: Pre and Post Comparison of Ham-D Score between Study Groups

At pre-evaluation: in sertraline group the mean HAM-D score of the patients was 22.92 ± 1.18 while in mirtazapine group the mean HAM-D score of the patients was 23.00 ± 1.13 (p-value=0.725). At post

evaluation: in sertraline group the mean HAM-D score of the patients was 9.37±0.91 while in mirtazapine group the mean HAM-D score of the patients was 5.73±0.96 (p-value=<0.001)..

Table 2: Summary Statistics of Change in Ham-D Score from Pre to Post

Change in HAM-D Score	N	96
	Mean	15.41
	Standard Deviation	2.35
	Minimum	10.00
	Maximum	20.00



ISSN: (e) 3007-1607 (p) 3007-1593

The study results showed that the mean change in HAM-D score of the patients was 15.41±2.35 with

minimum and maximum HAM-D score of 10 & 20 scores respectively.

Table 3: Compar	ison of Chang	e in Ham-D S	Score between	Study Group
-----------------	---------------	--------------	---------------	-------------

		Study Group		P-Value
Change in HAM- D Score		Sertraline	Mirtazapine	
	Ν	48	48	<0.001
	Mean Deviation	13.54	17.27	
		1.56	1.28	

Result indicate that In sertraline group the mean change in HAM-D score of the patients was 13.54±1.56 while in mirtazapine group the mean HAM-D score of the patients was 17.27±1.28. This difference was statistically significant. i.e. p-value=<0.001.

Discussion

A rapid onset of anti-depressant efficacy is clearly desirable in terms of reduced suffering, reduced risk of suicide, decrease need for hospitalization and improved compliance. Major depression is generally diagnosed in people with a persistent and unreactive low mood and loss of all interest and pleasure accompanied by a range of symptoms including appetite loss, insomnia, and fatigue, loss of energy, concentration, psychomotor poor symptoms, inappropriate guilt and morbid thoughts of death. It was the third leading cause of burden among all diseases of humankind, after lower respiratory infections and HIV/AIDS, in the year 2002 and accounted for 4.5% of total human suffering. (11)

H1: There is a likely to be a significant difference between pre and post sertraline and Mirtazapine treatment of depression patients with Hepatitis C.

In sertraline group the mean change in HAM-D score of the patients was 13.54 ± 1.56 while in mirtazapine group the mean HAM-D score of the patients was 17.27 ± 1.28 . This difference was statistically significant. i.e., p-value=<0.001. At post evaluation: in sertraline group the mean HAM-D score of the patients was 9.37 ± 0.91 while in mirtazapine group the mean HAM-D score of the patients was 5.73 ± 0.96 (p-value=<0.001). Some of the studies are discussed below showing their results as.

Very few studies are available to see the efficacy of antidepressant therapy in hepatitis C population. (9)

Onset of antidepressant action is also relevant to pharmacokinetics. Sertraline appears to have a longer plasma clearance time in the elderly and is suggested to take up to 2-3 weeks to reach a steady- state level whereas for mirtazapine this may be achieved in around 6 days. (12) (13)

Sertraline is a selective serotonin reuptake inhibitor (SSRI) used to treat anxiety and depression. In patients with PBC, sertraline may reduce pruritus and improve overall well-being. An initial dose of 50– 100mg of sertraline is typically used for this indication.54 A study followed 40 PBC patients over an average of 7.5 years. Of the 40 patients, 7 experienced pruritus and were prescribed sertraline; 6 of 7 patients reported significantly less or no pruritus after taking a stable dose of sertraline for over 6 months. (Browning et al., 2003)

H2: There is a likely to be a significant difference between sertraline group of treatment and Mirtazapine group of treatment depression patients with Hepatitis C

A study by Dahal S et al (11) documented in their study that Mirtazapine was well tolerated and was equally effective as sertraline in reducing depressive symptoms. However, mirtazapine was significantly more effective than sertraline after 2 and 4 weeks of treatment.

Tasuku Hashimoto (14) concluded in their study that the mirtazapine as the first-choice antidepressant for current depressive episodes may reduce benzodiazepine use in patients with major depressive disorder.

Sixty-five patients prescribed benzodiazepines from prescription day 1 were analyzed for the primary outcome. The percentage of benzodiazepine users was significantly lower in the mirtazapine than in the SSRIs group at weeks 6, 12, and 24 (21.4 vs. 81.8 %; 11.1 vs. 85.7 %, both



ISSN: (e) 3007-1607 (p) 3007-1593

P < 0.001; and 12.5 vs. 81.8%, P = 0.0011, respectively). (14)

Clinical studies also suggest that the therapeutic effect of mirtazapine is achieved earlier. A metaanalysis of adults with major depression indicated remission was more likely to occur within the first two weeks when treated with mirtazapine compared to an SSRI. (15) A similar result was found in a study comparing sertraline tablets with the Oro-dispersible tablet form of mirtazapine. (16)

On the other hand, a meta-analysis study of mirtazapine versus other antidepressants including SSRIs showed equal efficacy. Additionally, the mirtazapine group improved more than the paroxetine group did in the change in Sheehan Disability Scale scores. (17)

As contrary findings exist between our results and few of the previously published studies, so it is suggested that in future further studies should be done with larger sample size to evaluate the findings of our study. It is further suggested that in future studies should be done in community setting to have better idea in our local population.

Conclusion

This randomized control trial concluded that mirtazapine is significantly more efficacious as compared to Sertraline for treating the depression in patient with Hepatitis C.

REFERENCES

- 1.-Biggins SW&T5. Treatment of recurrent hepatitis C after liver transplantation in liver disease. 9th ed.; 2005.
- 2.-Liver. Clinical Practice Guidelines: management of hepatitis C virus infection. Journal of hepatology. 2011; 55(245-264).
- 3.-Schaefer MCLFADQCRGNSFGRKAFD&PCM. Hepatitis C infection, antiviral treatment and mental health: a European expert consensus statement. Journal of heptology. 2012.
- 4.-Musselman LLHGFMAKPSGRSGKNCB&M. Paroxetine for the prevention of depression induced by high-dose interferon alfa. New England Journal of Medicine. 2001; 344.

- 5. Yates WR&G. Hepatitis C and depression. Depression and anxiety. ; 7.
- 6.-Rowan PJ. What psychiatric screening and monitoring might be needed with the new generation of hepatitis C treatments. World journal of virology. 2015; 4 (13).
- 7.-Egmond E, Mariño Z, Navines R, Oriolo G, Pla A, Bartres C, et al. Incidence of depression in patients with hepatitis C treated with direct-acting antivirals. Brazilian Journal of Psychiatry. 2019; 42(72-76).
- 8.-Schramm TM, Lawford BR, Cooksley WG&MGA. Sertraline treatment of interferon-alfa- induced depressive disorder. Medical Journal of Australia. 2000; 173(359-361).
- 9.-Gleason OC, Yates WR, Isbell MD&PMA. An open-label trial of citalopram for major depression in patients with hepatitis C. Journal of Clinical Psychiatr. 2002; 63(194-198).
- 10.-Rockville M. National Institute of Mental Health. 1976;(179-192).
- 11.-Dahal S, Ojha S, Chapagain M&TP. Efficacy and tolerability of mirtazapine versus sertraline: an open, randomized study in acute treatment in patients with major depressive disorder.
- Journal of Psychiatrists' Association of Nepal. 2014; 3.
- 12.-Muijsers RB, Plosker GL&NS. Sertraline. Drugs & aging. 2002; 19.
- 13.-Anttila SA&LEV. A review of the pharmacological and clinical profile of mirtazapine. CNS drug reviews. 2001;
- 14.-Hashimoto T, Shiina A, Hasegawa T, Kimura H, Oda Y, Niitsu T, et al. Effect of mirtazapine versus selective serotonin reuptake inhibitors on benzodiazepine use in patients with major depressive disorder: a pragmatic, multicenter, openlabel,randomized, active- controlled, 24week trial. Annals of general psychiatry. 2016; 15.



ISSN: (e) 3007-1607 (p) 3007-1593

- 15.-Thase ME, Nierenberg AA, Vrijland P, van Oers HJ, Schutte AJ&SJH. Remission with mirtazapine and selective serotonin reuptake inhibitors: a meta-analysis of individual patient data from 15 controlled trials of acute phase treatment of major depression. International clinical psychopharmacology. 2010; 25.
- 16.-Behnke K, Søgaard J, Martin S, Bäuml J, Ravindran AV, Ågren. Mirtazapine orally disintegrating tablet versus sertraline: a prospective onset of action study. Journal of clinical psychopharmacology. 2003;(23).
- 17.-Watanabe N, Omari I, Nakagawa A, Cipriani A, Barbai C&MH. Multiple metaanalysis of new generation antidepressants (MANGA) Study Group. Mirtazapine versus other antidepressants in the acute-phase treatment of adults with major depression: systematic review and meta-analysis. The Journal of Clinical Psychiatry. 2008; 69.