INTERFERON AND RIBAVARIN ASSOCIATED DEPRESSION IN HCV PATIENTS AND ROLE OF SELECTIVE SEROTONIN REUPTAKE INHIBITORS

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ABSTRACT

Objective: To determine the frequency and severity of depression associated with antiviral therapy of Hepatitis C Virus (HCV) infection and effect of selective serotonin reuptake Inhibitors (SSRIs) to treat these depressive symptoms.

Type of Study: Observational Analytical study.

Place of Study and Duration: The study was conducted at Psychiatry, Medicine and Pathology department of Combined Military Hospital Sialkot Pakistan from February 2009 to July 2010.

Subjects and Methods: All the patients in this study were suffering from HCV infection and were managed with Interferon (3 m.i.u. s/c thrice weekly) and Cap Ribavirin (400 mg bid) for six months. Patients were assessed by Hospital Anxiety and Depression Scale (HADS) - Urdu Version and Beck's Depressive Inventory (BDI) Scores after twelve weeks of antiviral therapy. Depressed patients were managed with selective serotonin reuptake inhibitors (SSRIs) for six weeks and again evaluated on HADS & BDI Scores. Response to SSRIs was defined as complete response, partial response and no response.

Results: A total of 105 patients were studied out of which 75 were male and 30 were female with mean age 29.4 years. Out of these 54 (51.43%) patients developed depression and this tendency to develop depression was not related with the age and sex of the patients. The mean HADS and BDI scores before and after treatments with SSRIs were compared for significance and it was quite significant. There was not a single patient who did not show response to SSRIs.

Conclusion: Depression is frequently associated with antiviral therapy of HCV RNA viraemia with interferon and SSRIs have proved an effective and safe remedy in these patients.

Keywords: Depression, Hepatitis C, Interferon, Selective serotonin reuptake inhibitors(SSRIs).

INTRODUCTION

Globally about 340 million people suffer from depression. Similarly Hepatitis C is one of the major health related problems being faced by Pakistan with prevalence as high as 16% in certain localities[1]. The prevalence of depression amongst different communities in Pakistan, varies from 25-57.5% (females) and 10-25.5% (males)[2-8]. Significant depressive symptoms are seen in 36% of medically ill patients and is reported as third most common adverse effect in HCV infection[9]. These depressive symptoms are identified by using Self Rating Scales like Hospital Anxiety and Depression Scale (HADS) and rated on Beck's Depressive Inventory (BDI), and are used worldwide for screening depression[10,11].

The prevalence of depression varies from 35 to 58% in HCV patients[12-14]. However there is conflicting data about the frequencies of interferon/ribavirin therapy associated depression[15-18]. Some studies had shown no association but others had reported a mild and reversible depressive symptoms 10% to 45% of HCV patients[19-21]. The possible reason of depression with antiviral therapy in these patients is the anti-serotonergic effects of interferon and this also explains why these patients' symptoms are profoundly improved with selective serotonin reuptake inhibitors (SSRI)[19].

In modern days medicine, counseling and psychotherapy is an important aspect of overall

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management of any patient even of organic disorders but is more relevant in psychiatric patients. However the role of psychotherapy alone to treat depressive symptoms in HCV patients remains controversial[22]. Various psychotherapy models including supportive psychotherapy, cognitive behavior therapy and psychodynamic psychotherapy models have been used to treat depression alone or as an adjunct to drug treatment but with variable success rates[23,24]. Therefore the mainstay to manage HCV associated depression remains the drug treatment. The possible drugs included monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs) and selective serotinin reuptake inhibitors (SSRIs). As the major benefits of SSRIs are faster onset of action and minimum side effects therefore SSRIs have become the mainstay of therapy for depressive disorders today[25,26].

In Pakistan although there are few studies on the frequency of hepatitis in depression but there is dearth of literature on this aspect of frequency of depression in hepatitis especially associated with treatment of HCV viraemia. Therefore this study was conducted to assess the frequency of depression in HCV patients and the role SSRIs in interferon/ribavirin therapy related depression in our setting.

MATERIAL AND METHODS

This is a non interventional observational study carried out at Psychiatry, Medicine and Pathology department of Combined Military Hospital Sialkot Pakistan from February 2009 to July 2010. All the patients who reported to Combined Military Hospital Sialkot Pakistan for treatment of Hepatitis C viraemia during the study period were included in this study. However the patients who had a past and or family history of psychiatric illness or were using medication for any chronic medical or surgical illness were excluded from the study. The patients were managed with Interferon (3 m.i.u. s/c thrice weekly) and Cap Ribavirin (400 mg bid) for six months. Basic demographic data including age, sex, education, and occupation were recorded. A written or verbal informed consent was obtained from all participants. Hospital Anxiety and Depression Scale (HADS)-Urdu Version and psychiatric interview based on Present State Examination (PSE) were used to establish the diagnosis of depression according to International Classification of Diseases. The HADS consists of 14 items; 7 items of anxiety and 7 for depression. Scores of 0-7 in respective subscales were considered normal, 8-10 as borderline and 11 or above indicated clinical 'caseness'. The severity of depression was assessed by Beck's Depressive Inventory (BDI). It consists of 21 set of "yes" and "no" questions rated from 0 to 3 to obtain a maximum score of 63. A score of 0-13 showed absent or minimal depression, 14-19 indicated mild depression, 20–28 was consistent with moderate depression while 29–63 score was used to label as severe depression.

All the patients in this study were assessed by HADS and BDI Scores after twelve weeks of antiviral therapy. Patients who were found depressed on HADS and BDI Scores were confirmed by psychiatric interview based on present state examination before starting the anti depressant therapy. The depressed patients were managed with Selective Serotonin Reuptake Inhibitors (SSRIs) after informed consent for six weeks and again evaluated on HADS and BDI scores. The response to SSRIs was defined as complete response, partial response and no response as per following criteria:

Complete Response = HADS Score ≤ 10, and BDI Score ≤ 13

Partial Response = Improvement in severity of depression as per BDI score

No Response = No improvement in severity of depression as per BDI Score

The data was entered and analyzed using Special Package for Social Sciences (SPSS) version 10.0 computer software using standard statistical tests for significance.

RESULTS

During the study period a total of 105 patients were registered who had HCV viraemia for antiviral treatment. The mean age and sex distribution of these patients is given in table 1. Out of these 54 (51.43%) patients developed some degree of depression after twelve weeks of treatment with Interferon and Ribavirin. This tendency to develop depression was not related with the age and sex of the patients as mean age and male to female ratio are similar as is evident from table 1. The table 1 also shows the comparison of HADS and BDI scores after anti viral and antidepressants treatment. The mean HADS and BDI scores before and after treatments with SSRIs were compared for significance by ANOVA and there was a significant decrease in HADS score after SSRIs treatment (*p* value 0.013). Similarly the improvement in BDI score both between and within groups was highly significant (*p* values 0.001 and 0.000). Figure shows the response rates in management of depression to SSRIs.

DISCUSSION

During the study period a total of 105 patients were registered with HCV viraemia for antiviral treatment. After twelve weeks of antiviral therapy for HCV RNA viraemia 54 patients were having depression with a frequency of interferon associated depression as 51.43% in this set of population. Our results are comparable with most of the published data on the subject[19-21]. Nerves et al had reported a frequency of depression in HCV patients as 35 to 58%. Although there was a male preponderance in HCV patients (male 1.4 : female 1) but there was no difference in sex as regard the development of depression is concerned as the male to female ratio in depressed patients remained same (1.38:1). Similarly the tendency to develop depression was not related with the age as mean age of total population (29.4 years) and of depressed population (30.7) were comparable. These findings are in consent with most of the international studies and possibly reflect that mechanism of development of depression is more related to presence of interferon in the tissues rather than other confounders.

Table-1: Comparison of basic demographic data, HAD and BDI Scores of Hepatitis C patients who received antiviral therapy and patients who developed depression and managed with SSRIs.

Characteristics		Patients of hepatitis C treated with antiviral therapy (n = 105)	Patients who developed depression with antiviral therapy (n = 54)
Male		75	39
Female		30	15
Male : Female		1:04	1:038
Mean age		29.4 years	30.7 years
HAD Score	Mean	15.96	9.8
	Max	20	17
	Min	11	1
BDI Score	Mean	22.52	16.57
	Max	32	27
	Min	13	2

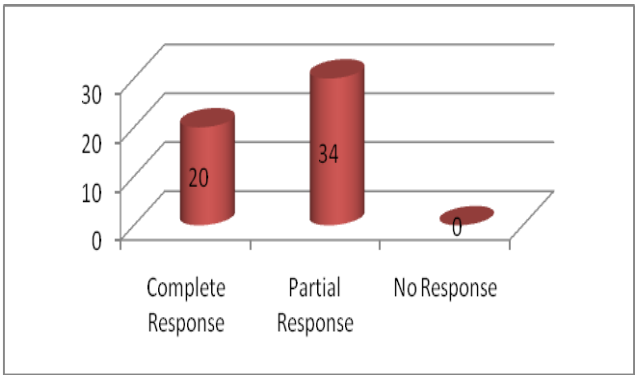

Figure-: Showing response rate to SSRIs (n=54).

In psychiatric practice SSRI's (Citalopram, Fluoxetine, Paroxetine and Sertraline) are the most commonly used drugs to treat depression. The choice among these is usually based on the side-effect profile, or addressing a particular depressive symptom[25]. Patients experiencing fatigue benefit more from activating agents like Fluoxetine and similarly patients with primary sleep disturbance benefit from agents like Paroxetine that promote sleep[26].

All the 54 patients with depression showed some degree of response to SSRIs, as is evident from Fig 1, twenty (37%) patient became completely disease free while 34 (63%) had shown partial response as they had shown improvement in severity of depression. At the start of treatment with SSRIs there were six patients with severe depression but after SSRIs treatment there was not a single patient in this group. This observation is also supported by the statistical analysis of HADS and BDI scores before and after treatment with SSRIs. Mean HADS and BDI Scores improved from 15.96 to 9.81 and from 22.52 to 16.67 respectively. Mean HADS and BDI scores before and after treatments with SSRIs were compared for significance by ANOVA and the values were significant (p value 0.013). Similarly the improvement in BDI score both between and within groups were highly significant (p values 0.001 and 0.000). This response rate observed in our study is in line with the published international data. Weinrieb et al had shown a response rates of 78-88% and because of this excellent response rate SSRIs are being increasingly used as prophylaxis therapy in this group of patients[20]. One drawback of this study is that although counseling sessions were conducted by the physicians at the time of diagnosis but psychotherapy was not included as an arm of therapeutic management.

CONCLUSION

Depression is frequently associated with antiviral therapy of HCV RNA viraemia with interferon. Therefore routine mental health screening and appropriate intervention in these patients is the need of the hour. SSRIs have proved an effective and safe remedy in these patients.

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