ORIGINAL ARTICLE

FREQUENCY OF DEPRESSION AND SOMATIC SYMPTOMS IN PATIENTS ON INTERFERON ALPHA/RIBAVIRIN FOR CHRONIC HEPATITIS C

Abdul Shakoor, Farzana Shafqat*, Tafazzul e Haque Mehmud, Mohammad Akram*, Sarah Riaz†, Zafar Iqbal††, Anwaar A Khan***

Department of Psychiatry, *Gastroenterology, **Rheumatology, †Histopathology, ††Medicine, Shaikh Zayed Hospital, Lahore, Pakistan

Background: Large numbers of patients suffering from Chronic Hepatitis C (HCV) are seeking treatment with interferon alpha (IFN) because of significant advances in overall improvement in the course of HCV and its complications. Objectives were **t**o estimate the frequency of depression and somatic symptoms in patients on interferon alpha/ribavirin treatment for chronic hepatitis C. **Methods:** It was an observational study conducted in the out-patient Department of Gastroenterology Shaikh Zayed Hospital, Lahore during a period of three months, i.e., from September to November 2008. One hundred consecutive patients undergoing interferon alpha/ ribavirin treatment for chronic HCV were included in the study. All patients, irrespective of age, sex or duration of treatment were administered with a check list of common physical complaints and DSM-IV symptoms for Major Depressive Episode. **Results:** Out of a total of 100 subjects 37 were male and 63 were female. In all, 39 (39%) patients fulfilled the diagnostic criteria of DSM-IV for Major Depressive Episode. Major Depression was more common in female 28 (44.4%) as compared to male 11 (28.7%) patients. Somatic symptoms were common in all the patients but they were reported more frequently by patients with Major Depression compared to those without Major Depression. Myalgias, headache, joint pain, nausea/vomiting, abdominal pain and palpitation were the most common physical symptoms. **Conclusion:** Major Depression and somatic complaints are a common consequence of interferon alpha/ribavirin treatment for chronic hepatitis C. All patients receiving this treatment should be periodically assessed for the detection of these side effects to promptly address relevant treatment options.

Keywords: Interferon Alpha, Ribavirin, Hepatitis C, Depression

INTRODUCTION

Hepatitis C is a major health problem worldwide with enormous medical, psychosocial and economic consequences. Large numbers of patients suffering from Chronic Hepatitis C (HCV) are seeking treatment with interferon alpha (IFN-alpha) because of significant advances in overall improvement in the course of HCV and its complications. However, treatment is often hampered by intolerable physical and psychiatric side effects.

Physical complaints like fatigue, generalised aches and pains, headache, abdominal dysfunction, palpitation and dizziness are in common observation and in many cases they are responsible for poor treatment compliance. Emergence of depression during IFN treatment has been associated with reduced viral response.[1] The development of physical complaints such as fatigue and pain associated with disturbance of sleep and appetite strongly predicts the development of full depressive disorder later in the treatment.[2]

Psychiatric complaints including Major Depression have been reported in association with interferon treatment and they are an important cause of treatment discontinuation.[3] This is doubly unfortunate, given evidence that patients who are able to tolerate therapy and achieve a sustained viral response enjoy better physical and emotional health.[4–6] Published reports describing incidence of depression in patient receiving interferon treatment for chronic hepatitis C differ markedly due to use of different criteria for the diagnosis of depression.[7] Best current estimates show that on average, 20–40 percent of patients receiving IFN-alpha in combination with ribavirin will develop clinically significant depression at some point during treatment.[8–10] Infect, suicidal ideation has commonly been identified and completed suicides have also occurred.[11]

Bomaccorso *et al*[12] in their prospective observational study reported that 40.7% of the patients undergoing IFN/Ribavirin treatment for chronic hepatitis C met the diagnostic criteria for Major Depressive Episode of DSM-IV[13].

We aimed to estimate the frequency of depression and somatic complaints in patients undergoing interferon alpha/ribavirin treatment for chronic hepatitis C.

MATERIAL AND METHODS

It was an observational study conducted in the out-patient Department of Gastroenterology in collaboration with the Department of Psychiatry and

Behavioural Medicine Shaikh Zayed Hospital, Lahore during a period of three months, from September 2008 to November 2008. One hundred consecutive patients undergoing interferon alpha/ ribavirin treatment for chronic HCV were included in the study.

All patients, irrespective of age, sex or duration of treatment were administered with a check list of common physical complaints and symptoms of Major Depressive Episode of Diagnostic and Statistical Manual (DSM-IV), (Table-1).

Table-1: DSM-IV criteria of Major Depressive Episode

A-	Five (or more) of the following symptoms have been present during the same two week period and represent a change from previous functioning; at least one of the symptoms is either depressed mood or loss of interest or pleasure. 1. Depressed mood most of the day, particularly in the morning 2. Markedly diminished interest or pleasure in almost all activities nearly every day 3. Significant weight loss or gain 4. Insomnia or hypersomnia 5. Psychomotor agitation or retardation 6. Fatigue or loss of energy 7. Feelings of worthlessness or inappropriate guilt 8. diminished ability to think or concentrate, indecisiveness 9. Recurring thoughts of death or suicide
B-	The symptoms do not meet criteria for a mixed episode
C-	The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
D-	The symptoms are not due to direct physiological effects of a substance or a general medical condition
E-	The symptoms are not better accounted for by bereavement.

RESULTS

Out of a total of 100 subjects, 37 were male and 63 were female patients. There was no significant difference in men and women regarding mean age or duration of interferon alpha/ribavirin treatment.

In all 39 (39%) patients fulfilled the diagnostic criteria of DSM-IV for Major Depressive Episode. The diagnosis of Major Depressive Episode was more common in female 28 (44.4%) as compared to male 11 (28.7%) patients (Table-2). Loss of interest and enjoyment (100%), lack of energy (97%), depressed mood (94%) and poor concentration (92%) were the main symptoms while suicidal ideation was expressed by 12 (30.7%) patients (Table-3).

Although 61 (61%) patients did not meet the diagnostic criteria but frequently had depressive symptoms. Lack of energy (87%), sleep disturbance (24%) and loss of interest or enjoyment (21%) were the most frequent symptoms while one female patient had excessive guilt and no patient in this group expressed suicidal ideation (Table-3).

Physical or somatic symptoms were common across the board but they were more frequently reported by the patients of Major Depressive Episode as compared to those who did not meet the diagnostic criteria of DSM-IV. Common physical symptoms reported by depressed patients were myalgia and headache (90%), joint pain, nausea/vomiting and palpitation (54%) each while the frequency of same complaints by the non depressed group was 70%, 48% and 23% respectively (Table-4).

Table-2: Frequency of Major Depressive Episode (n=100)

		DSM-IV Major Depression n=39 (39%)			No DSM-IV Major Depression n=61 (61%)		
		Male (n=11)	Female (n=28)	Total (n=39)	Male (n=26)	Female (n=35)	Total 61
Age (years)	Range	22–47	25–55	22–55	14–58	13–55	13–58
	Mean	33.69	37.62	35.54	34.88	34.06	34.38
Duration of IFN (weeks)	Range	4-24	4-24	4-24	4-24	4-24	4-24
	Mean	14.38	13.58	13.85	14.70	15.43	14.92

Table-3: Frequency of symptoms of Major Depressive Episode (n=100)

DSM-IV Symptoms of Major Depressive Episode	DSM-IV Major Depressive Episode n=39 (39%)				No DSM-IV Major Depressive Episode n=61 (61%)			
	M	F	Total	%	M	F	Total	%
1- Depressed mood	9	28	37	94	0	1	1	1.6
2- Loss of interest or enjoyment	11	28	39	100	3	10	13	21
3- Sleep disturbance	9	16	25	64	2	13	15	24
4- Weight change	9	13	22	56	2	5	7	14
5- Psychomotor problems	10	22	32	82	2	3	5	08
6- Lack of energy	11	27	38	97	21	32	53	87
7- Poor concentration	10	26	36	92	1	7	8	13
8- Excessive guilt	3	6	9	23	0	1	1	1.6
9- Suicidal ideation	5	7	12	30	0	0	0	00

Table-4: Frequency of Somatic Symptoms (n=100)

Somatic symptoms check list	DSM-IV Major Depressive Episode n=39 (39%)				No DSM-IV Major Depressive Episode n=61(61%)			
	M	F	Total	%	M	F	Total	%
1- Myalgia/Gen. aches and pains	8	27	35	90	14	29	43	70
2- Muscular stiffness (*khachao*)	5	15	20	51	2	10	12	20
3- Headache	10	25	35	90	8	21	29	48
4- Joint pain	5	16	21	54	4	10	14	23
5- Nausea/vomiting	6	11	17	44	5	8	13	21
6- Abdominal pain/distension/Gas	7	14	21	54	3	5	8	13
7- Epigastric burning	5	14	19	49	4	10	14	23
8- Palpitation (*Gabrahat*)	7	14	21	54	1	4	5	8
9- Vertigo/dizziness (*chaker*)	7	13	20	51	1	3	4	7

DISCUSSION

Chronic hepatitis C is a major health problem worldwide.[14] It is increasingly becoming common in Pakistan[15] and is associated with enormous medical, economic and psychosocial consequences. Although treatment with interferon alpha/ribavirin has proved efficacy[9] but overall management is often hampered by troublesome physical and neuropsychiatric side effects. These side effects especially the emergence of depression, are not only associated with an increase in overall burden of disease but also translate into treatment failure or discontinuation of treatment.[3] Depression has also been noted to be associated with a reduced viral response as well.[1,16]

We report an overall 39% incidence of Major Depressive episode of DSM-IV in our sample of 100 patients undergoing interferon alpha/ribavirin treatment for chronic hepatitis C. Moreover, majority of the patients experienced many physical side effects simultaneously with variable frequency ranging from 7–90% and they were reported much more commonly by patients having the diagnosis of Major Depressive Episode. It can be of interest to note that the most commonly reported side effect, i.e., lack of energy or lethargy has not been included in the check list of physical complaints because it constitute one of the nine symptom criteria of Major Depressive Episode in DSM-IV.

In this emerging scenario, the clinicians involved in the treatment of chronic hepatitis C are faced with new challenges regarding decisions like whom to treat, when to stop treatment and most importantly when to seek psychiatric liaison.

A comprehensive strategy needs to be devised to utilize all techniques and resources at our disposal to allow patients tolerate full doses of interferon alpha/ribavirin for an appropriate period while minimizing negative impact on emotional and physical well-being and daily functioning. Mental health services for patients undergoing such treatment can be helpful but are not widely available.[17,18] Thus, much of the responsibility for assessing and treating depression and other neuropsychiatric side effects of INF usually fall to the primary clinical team which is sensitive enough to detect and adequately skilled to properly treat such patients.

Much clinical experience suggests that patients are far more likely to cope with interferon alpha/ribavirin side effects and stay on therapy when they are in an involved, supportive and organized treatment environment. Patient education prior to treatment is essential and should include a clear description of likely side effects and their time course. It is especially important to be sensitive to identify 'at-risk' patients prior to treatment as well as throughout the course of treatment. Majority of the patients with mild to moderate depression can safely and effectively be treated with Selective Serotonin Reuptake Inhibitors while keeping the patients on course of interferon alpha/ ribavirin.[16,19–21] However, for those on the severer side of the spectrum of psychiatric morbidity, a close working relationship with psychiatrists who are familiar with the relevant issues can be quite useful.

CONCLUSION

The incidence of depression in patients on interferon alpha/ribavirin treatment for chronic hepatitis C is comparable to the incidence of depression in similar patients, worldwide. More work needs to be done so that depression may not only be identified at the primary care level but also treated or referred at an early stage to minimise the emotional suffering of the patients. While making National Guideline for treatment of chronic hepatitis C infection, depression as an entity should be included to minimise the emotional suffering of these patients.

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Address for Correspondence:

Dr. Abdul Shakoor, Associate Professor, Department of Psychiatry and Behavioural, Medicine, Shaikh Zayed Hospital, Lahore, Pakistan. **Cell:** +92-322-4430217
Email: ashakoor62@hotmail.com