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ORIGINAL ARTICLE

INTERFERON (IFN α) INDUCED DEPRESSION IN PATIENTS OF HEPATITIS C (HCV)

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ABSTRACT:

HCV is a global problem and the worst affected are the 3rd world countries. In our study of 802 patients 244 male and 161 females were positive for HCV. Majority of the patients were in age group 26-40 Years i-e 56.04% of the study population. Depression an affective disorder was found during screening in 85 (21%) of patients at base line level. This was elevated to 150 (37%) after treatment with IFN-α & ribavirin. Out of these patients 85 (56.6) had mild, 57 patients (38%) had moderate and 8 patient 5.4% had severe depression. We conclude that HCV is associated with depression and its intensity increases with treatment with IFN-α & ribavirin and needs effective control with anti-depressants.

Keywords: Hepatitis C, depression, interferon.

INTRODUCTION

HCV affects 180 million people Worldwide (Schaefer *et al*., 2003). Interferon α (IFN α) was the first effective treatment of this disease, more recently IFN α and Ribavirin has shown good efficacy in treatment of HCV (Hauser *et al*., 2000). Depression is common in hepatitis C, exacerbated by Interferon and is a major reason for discontinuation of therapy (Ondria *et al*., 2007). 20-30 % of patients treated with pegylated interferon and ribavirin report depression during therapy and an indication for decreasing the dose or even discontinuation (Fried *et al*., 2002).

Pathophysiological mechanism that causes the neuropsychiatric side effects particularly depression is unclear although various hypotheses have been suggested a perturbation of serotonin neurotransmitters may be one reason (Valentine *et al*., 1998 and Lincino *et al*., 1998). Early identification of depression by questioning during follow up visits is critical to subsequent management, As there is high prevalence of depression in the general population undiagnosed psychiatric disorder patients receive treatment with IFN α without psychiatric care.

So, a study was conducted to find the prevalence of depression in patients receiving interferon.

MATERIAL AND METHODS

This is a prospective study carried out from 2009-2011. All patients attending the Molecular Biology Lab LUMHS were screened by PCR for HCV RNA and were enrolled according to inclusion criteria. Informed consent was obtained; the study was approved by Ethical Committee. Demographic details were collected on predesigned Proforma. All patients received (IFN α) and ribavirin as advised by physician. The patients were seen by the physician and the researchers weekly during the first 8 weeks and then every fortnight for further 8 weeks and then monthly for further 8 weeks. Blood samples were obtained at patient's medical visits for analysis of CBC and liver transaminases,

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Mental status was monitored and changes diagnosed by Beck Depression Inventory-II criteria, mental health was evaluated before treatment and on each follow up visit.

Development of depression during treatment was diagnosed by using a diagnostic interview according to diagnostic & statistical manual of mental disorders (DSM-IV).

Methodology

Inclusion criteria

1. Age above 18 years and below 60 years
1. Patients of both sexes
2. Detectable HCV infection in PCR
3. ALT > 30 U/L (normal 24 U/L)

Exclusion criteria

1. Presence of other liver disease
2. Coinfection with hepatitis B
3. Cirrhosis
4. Severe cardiac disease
5. Severe neurological disease.

RESULTS AND DISCUSSION

It is a prospective and descriptive study and 802 patients were screened. Out of these 447 were males and 355 females, demographic details are shown in Table-1. Out of these patients HCV RNA was detected in 405 patients (50.4%) Diagram-1, it included 244 males and 161 females Diagram-2, age wise distribution is shown in Table-1. There were 42 males and 19 females in age group 16-25 years, 127 males and 98 females in age group 26-40 years and 64 males and 41 females respectively in age group 41-55 years, 11 males and 3 females in age group of 55 years and above. Maximum number of patients were in age group of 26-40 years that is 127 males and 98 females which is 56.04% of the study population.

Serum ALT levels were elevated in 122 that is 30% of patients at the baseline level; these levels remain elevated until 8 weeks of treatment with IFN-α in 61 patients that is 15 % of the study population, then the levels declined whereas in the rest 15 % the levels remained elevated even at the end of the study period.

Depression was present at the baseline level in 85(21%) of patients Diagram-3 which was then elevated to 150 (37%) of patients after 8 weeks of treatment Diagram-4, out of these 85 patients (56.6%) had mild depression, 57 patients that is (38%) had moderate depression and 8 patients (5.4%) had severe depression. These 8 patients that is (5.4%) also had suicidal ideation. Diagram-4.

HCV infection is a very common infectious disease globally and its prevalence is 1-2% (Kraus *et al*., 2005). It is endemic in Pakistan due to reuse of syringes, inadequate blood screening processes, illiteracy and poor socio-economic conditions.

Medical treatment of HCV is still unsatisfactory because it is expensive and frequently not well tolerated due to somatic side effects and psychological problems. Most important barrier is depression and anxiety and it may induce suicidal ideation (Zidlar *et al*., 2000). Thus the understanding, early recognition of affective treatment of psychiatric side effects is of key importance, as this may increase the probability of successful antiviral therapy.

In our study of 802 patients 21% had depression according to BDI criteria and these patients had minimal depression even at the base line level, this was aggravated to a high degree by interferon and ribavirin therapy to 37% out of these patients who developed depression. 21% had mild depression having a BDI score of 15, 14% had moderate depression BDI score 25 and 2% had severe depression BDI score 55.

Table
Age-wise Distribution of Patient

	<18 years		18-25 Y		26-40 Y		41-55 Y		>55 Y		Total
	M	F	M	F	M	F	M	F	M	F	
HCV RNA +ve	0	0	42	19	127	98	64	41	11	3	405
HCV RNA -ve	3	2	48	44	100	107	47	39	5	2	397

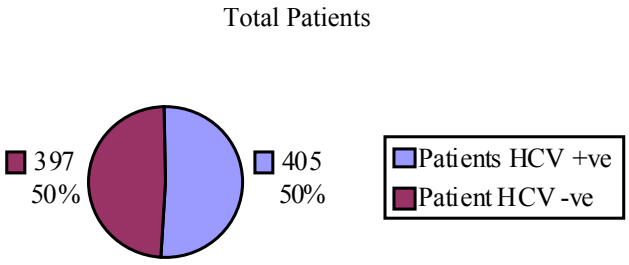

Diagram-1: HCV positive patients after screening

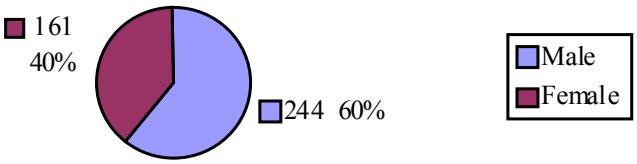

Diagram-2: HCV positive patients after screening

The mechanism of this depression is largely speculative. The proposed reason may be that interferon may induce pro-inflammatory cytokines tumor necrosis factor interleukin 1 and interleukin 6 to promote sickness behavior and may also have effect on Hypothalamic Pituitary adrenal axis (Brown *et al*., 1991). Recent attention has focused on relationship of interferon to alterations in serotonin activity. Serum level of tryptophan is reduced during interferon therapy. There is increase activity of serotonin transporter that

could decrease synaptic serotonin concentration and contribute to depression (Bonaccorso *et al*., 2002).

A *et al* 2003 in which adverse Psychiatric events occurred in 77% of patients in clinical trials with PEG interferon alpha2b and the most common psychiatric effects were

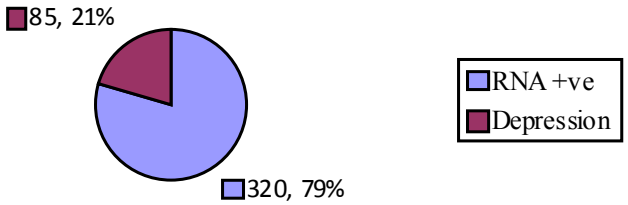

Diagram-3: Depression at Base Line Level

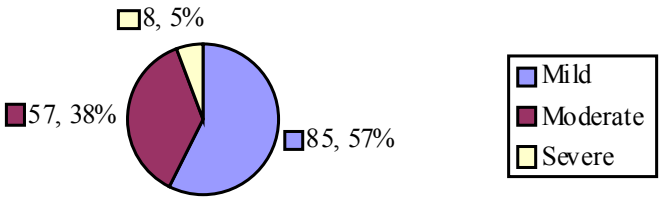

Diagram-4: Status of Depression in patients treated with IFN-α and Ribavirin

In our study Interferon induced depression was seen after 8 weeks of treatment, Fried M.W 2002 reports that depressive events with interferon & ribavirin occurred frequently during the first 24 weeks of therapy than during later period of 48 weeks (Michael 2002). In a study conducted by Miyaoka H *et al*. 1999 depression in hepatitis C is exacerbated by Interferon by 38% after 12 weeks (Miyaoka *et al*., 1999). A very high prevalence was reported by Kraus MR Schafer depression ranging from 25-34%. 3 out of 75 patients developed suicidal ideas (Kraus *et al*., 2003). Peter & Hauser *et al*., 2002 reported depression is common in Hepatitis C and is exacerbated by interferon depression occurred in 38% of patients after 12 weeks (Hauser *et al*., 2002).

Therefore clinical psychiatric examination using standard depression rating scales allows appropriate doses. IFN-α induced major

depression is unlikely to occur within the first 4 weeks of therapy. In a study by McHutchison *et al*. (1998) 36% of patients treated with IFN-α and ribavirin become depressed (McHutchison *et al*., 1998). Whereas Manns *et al*. (2001) reported depression in 31% of patients receiving the drug, our findings are in line with these studies (Manns *et al*., 2001).

SUGGESTIONS

All out efforts should be made to optimize the treatment of HCV, which will include patients compliance and managing the side effects, this will avoid dose reduction and discontinuation of IFN-α, questioning during follow up visits is critical to subsequent management and is a useful research tool. Therefore early recognition and effective treatment of psychiatric side effects of IFN-α and involvement of serotonin pathways favors the use of SSRI. Multidisciplinary management concepts in the future during Hepatitis C therapy is essential to minimize the dropout rate and increase response to treatment with IFN α.

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