

## Hepatitis C and Depression

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Hepatitis C is one of the major health related problem being faced by Pakistan, with prevalence as high as 16% in certain localities.<sup>1</sup> It is estimated that more than 170 million people in world are infected by Hepatitis C Virus (HCV). This represents about 2.5% of world population from which about 32.3 million are in South East Asia.<sup>2,3</sup> Due to unavailability of vaccine the world wide prevalence of HCV infection has not shown a downward trend as seen in hepatitis B. Although both share the same modes of spread, about 3-4 million new cases of HCV infection are reported each year.<sup>2,4</sup> Depression is the third common adverse effect of HCV infection reported in 70% of HCV infected patients, preceded by physical fatigue (86%) and irritability (74%).<sup>5</sup>

The prevalence of depression is reported to be much higher in HCV infected patients (24-70%) as compared to general population (6-10%).<sup>5-7</sup> A recently published systematic review of depression occurring during interferon therapy showed considerable variation in frequency and extent of interferon induced depression from 0% to 82% due to difference in criteria, treatment protocol and cutoff values.<sup>8</sup> But this highlights the importance of recognition of this disorder while managing HCV infection. Not only do the interferon based therapies induce de-Novo depression but it also aggravates the scores of already existing depression.<sup>9,10</sup> Majority of depressive symptoms occur in initial 3-months of therapy.<sup>11</sup> The risk factors for depression during interferon therapy have been identified as presence of depression before commencement of therapy, history of drug abuse, HIV co-infection, older age, organic brain impairment and genetic risk factors in serotonergic system.<sup>10, 12-14</sup> Gender is not identified as a risk for interferon induced depression in contrast to general population where such a risk exists.

The early virological responses (EVR) were significantly lower in patients with depressive symptoms as compared to those without them.<sup>15</sup> The use of antidepressive therapy in such patients significantly improves sustained virological response (SVR).<sup>16</sup> Before initiating treatment for HCV infection, all patients should be screened for evidence of active depression by direct questioning and/or standardized tools such as the CES-D screen questionnaire.<sup>17</sup> Because of the increased risk of poor treatment outcomes, active depression should be treated before therapy for HCV infection is initiated. Citalopram, escitalopram and paroxetine have shown 78-88% improvement in depressive symptoms in HCV infected patients.<sup>18-20</sup> The

antidepressants should be initiated at lower doses to increase adherence to therapy and reduce side effects. While the antidepressant effect usually takes 8-14 days to appear, the side effects usually appear in initial 8 days.<sup>21</sup> It is therefore pertinent to identify and treat depression early in patients of HCV infection as the patient can progress to severe depression even during the therapeutically effective window period after initiation of therapy. SSRI are effective in treating depression in HCV infected patients and can be safely given in patients without cirrhosis and thrombocytopenia but they do increase the risk of bleeding in HCV infected patients.<sup>19, 22, 23</sup> Antidepressants once started should be continued throughout the treatment and for 6 months after treatment cessation.

### REFERENCES

1. Ahmad N, Asgher M, Shafique M. An evidence of high prevalence of Hepatitis C virus in Faisalabad, Pakistan. *Saudi Med J* 2007;28(3):390-5.
2. World Health Organization. Hepatitis C. World Health Organization Fact Sheet No. 164. October 2000 [cited 2008 September 25]; Available from: <http://who.int/mediacentre/factsheets/fs164/en>
3. Alter MJ. Epidemiology of hepatitis C virus infection. *World J Gastroenterol* 2007;13(17):2436-41.
4. Pantazis KD, Elefsiniotis IS, Brokalaki H. New data concerning the epidemiology of Hepatitis B Virus Infection in Greece. *Gastroenterol Res Pract* 2008;2008:580341.
5. Lang CA, Conrad S, Garrett L. Symptom prevalence and clustering of symptoms in people living with chronic hepatitis C infection. *J Pain Symptom Manage* 2006;31(4):335-44.
6. Coughlan B, Sheehan J, Hickey A. Psychological well-being and quality of life in women with an iatrogenic hepatitis C virus infection. *Br J Health Psychol* 2002;7(Pt 1):105-16.
7. World Health Organization. World Health Organization Fact Sheet No. 265. [cited 2008 September 25]; Available from: <http://www.who.int/mediacentre/factsheets/fs265/en/>
8. Schafer A, Wittchen HU, Seufert J. Methodological approaches in the assessment of interferon-alpha-induced depression in patients with chronic hepatitis C - a critical review. *Int J Methods Psychiatr Res* 2007;16(4):186-201.
9. Majer M, Welberg LA, Capuron L, et al. IFN-alpha-induced motor slowing is associated with increased depression and fatigue in patients with

- chronic hepatitis C. *Brain Behav Immun* 2008;22(6):870-80.
10. Martin-Santos R, Diez-Quevedo C, Castellvi P. De novo depression and anxiety disorders and influence on adherence during peginterferon-alpha-2a and ribavirin treatment in patients with hepatitis C. *Aliment Pharmacol Ther* 2008;27(3):257-65.
  11. Schaefer M, Hinzpeter A, Mohmand A. Hepatitis C treatment in "difficult-to-treat" psychiatric patients with pegylated interferon-alpha and ribavirin: response and psychiatric side effects. *Hepatology* 2007;46(4):991-8.
  12. Raison CL, Borisov AS, Broadwell SD. Depression during pegylated interferon-alpha plus ribavirin therapy: prevalence and prediction. *J Clin Psychiatry* 2005;66(1):41-8.
  13. Capuron L, Ravaud A. Prediction of the depressive effects of interferon alfa therapy by the patient's initial affective state. *N Engl J Med* 1999;340(17):1370.
  14. Kraus MR, Al-Taie O, Schafer A. Serotonin-1A receptor gene HTR1A variation predicts interferon-induced depression in chronic hepatitis C. *Gastroenterol* 2007;132(4):1279-86.
  15. Raison CL, Broadwell SD, Borisov AS. Depressive symptoms and viral clearance in patients receiving interferon-alpha and ribavirin for hepatitis C. *Brain Behav Immun* 2005;19(1):23-7.
  16. Loftis JM, Socherman RE, Howell CD. Association of interferon-alpha-induced depression and improved treatment response in patients with hepatitis C. *Neurosci Lett* 2004;365(2):87-91.
  17. Radloff L. The CES-D scale: A self report depression scale for research in the general population. *Applied Psychological Measurement* 1977;1:385-401.
  18. Gleason OC, Yates WR, Philipson MA. Major depressive disorder in hepatitis C: an open-label trial of escitalopram. *Prim Care Companion J Clin Psychiatry* 2005;7(5):225-30.
  19. Schaefer M, Schwaiger M, Garkisch AS. Prevention of interferon-alpha associated depression in psychiatric risk patients with chronic hepatitis C. *J Hepatol* 2005;42(6):793-8.
  20. Kraus MR, Schafer A, Faller H. Paroxetine for the treatment of interferon-alpha-induced depression in chronic hepatitis C. *Aliment Pharmacol Ther* 2002;16(6):1091-9.
  21. Raison CL, Demetrashvili M, Capuron L. Neuropsychiatric adverse effects of interferon-alpha: recognition and management. *CNS Drugs* 2005;19(2):105-23.
  22. Schaefer M, Schmidt F, Folwaczny C. Adherence and mental side effects during hepatitis C treatment with interferon alfa and ribavirin in psychiatric risk groups. *Hepatology* 2003;37(2):443-51.
  23. Weinrieb RM, Auriacombe M, Lynch KG. A critical review of selective serotonin reuptake inhibitor-associated bleeding: balancing the risk of treating hepatitis C-infected patients. *J Clin Psychiatry* 2003;64(12):1502-10.



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