

Hepatitis B and C infections in Pakistan- are we over enthusiastic in treatment?

In Pakistan Hepatitis B Virus (HBV) has high prevalence due to inadequate coverage of the newborn as a result of ignorance and access issues. The chronicity of hepatitis B virus is related almost exclusively to exposure in childhood; therefore vaccination after birth or during childhood is the only way to control and eradicate this disease. Almost 30% children are still not vaccinated against HBV¹. With 4-5 million children born each year² this quantum of HBV infected children will only increase with time.

Once infected, treatment is available to only a select group which is shown in the accompanying review on HBV³. It clearly shows indications for treatment, duration and response rate. In Pakistan lamivudine is the cheapest option, yet beyond the reach of most patients. Its seroconversion rate is around 50% and drug resistance is 6% at 3 years⁴. This is contrary to other reports from the west where many show over 70% resistance at 3-4 years⁵. The possible reason for this disparity is that genotype D is common in Pakistan and has the least drug resistance rate⁶⁻⁹.

Lamivudine has no role if the patient fulfills all criteria but ALT is not raised. It is recommended to wait and watch ALT yearly in these cases and initiate treatment only when ALT is raised persistently to two times the upper limit of normal for over 6 months. A single rise of ALT should not be the motivating factor for initiating treatment. Similarly, carriers and delta positive cases without core or precore mutants are not candidates for therapy. Other oral drugs should be used only when there is drug resistance or no change is seen over 2 years.

Over 10 studies reported from various institutions in Pakistan show that over 80% of HCV infected population have genotype 3¹²⁻¹⁵. Globally this genotype is the most easily treatable virus using conventional interferon 3 million units 3 times a week for 24 weeks, along with 800 mg daily ribavirin (ref). A trial of short-term treatment for 16 weeks using > 2 log fall in RNA levels showed good patient compliance but poor long term results¹⁶. Conventional 24 weeks of therapy ultimately became the gold standard of therapy.

Viral load level has no role in deciding duration or type of therapy since genotype 3 is treated with conventional treatment irrespective of the viral load¹⁷⁻¹⁸. Sustained viral response (SVR) is 60-70%¹² and can be enhanced by careful selection of patients, assurance of good compliance, and properly trained, subcutaneous route of injection. It is recommended to use an insulin syringe, which will ensure subcutaneous, rather than intramuscular injection. Patients should be taught and encouraged to self inject which will reduce chances of accidental needle stick injuries to others¹⁹. Injections are to be used 3 times per week and not on alternate days.

Pegylated interferon is not recommended for type 3 genotype (16 APASL) as conventional alpha interferon is equally effective. It should be limited to non responders and relapsers. Pegylated interferon has only 10-15% better response but is 4-5 times more expensive than standard interferon.

Ribavirin in standard doses may cause hemolysis resulting in fall in hemoglobin levels by 3-4 grams. Treatment should therefore not be started in those with hemoglobin less than 10 g at baseline. Folic acid should be added to help mobilize iron back into the tissues. Use of erythropoietin may be reserved for special cases. Blood transfusion should be avoided.

Non-responders or relapsers²⁰ should be identified either pre- therapy or within the first 3 months of treatment when they fail to show normalization of ALT. Further treatment should not be pressed as they are not likely to respond further. Neither does re-treatment significantly improve the response rate¹⁸. Subsequent treatments with pegylated or other type of interferons are not likely to give added benefit. Supportive care should be given with careful follow up rather than place further financial stress on the patient and family.

Interferon is contraindicated in advanced liver cirrhosis or decompensation as well as during pregnancy and lactation, but may be considered at the end of pregnancy and lactation. Cases with positive HCV RNA and normal ALT should undergo liver biopsy for confirmation and histological evidence of active disease¹⁸ rather than use blind therapy which may be actually harmful.

HCV testing of newborns of HCV positive mothers is not recommended because passively transferred antibodies usually clear within 2 years¹⁸. In children the treatment is not indicated before 10 years age.

Active preventive measures are strongly recommended for control of Hepatitis C as no preventive vaccine is available.

References:

1. Institute of Population Studies (NIPS) and Macro International Inc 2008. WHO/UNICEF Joint Review Report 2006
2. National *Pakistan Demographic and Health Survey 2006-7*. Islamabad, Pakistan: National Institute of Population Studies and Macro International Inc Population.
3. Mumtaz K, Wasim S, Jafri W. Oral treatment of Chronic Hepatitis B. (this issue)
4. Qureshi H, Arif A, Ahmed W, Alam SE. Response to Lamivudine treatment in core and pre core mutants of HBV. (Abstract) PSG 2006 Karachi
5. Lai CL, Dienstag J, Schiff E, Leung NW, Atkins M, Hunt C. Prevalence and clinical correlates of YMDD variants during lamivudine therapy for patients with chronic hepatitis B. *Clin Infect Dis* 2003;36:687-696.
6. Baig S, Siddiqui AA, Ahmed W, Qureshi H, Arif A. The association of complex liver disorders with HBV genotypes prevalent in Pakistan. 2007; 4: 128
7. Alam MM, Zaidi SZ, Shaukat S, Naeem A, Sharif S, Angez M, et al. Molecular epidemiology of Hepatitis B virus genotypes in Pakistan. *BMC Infect Dis*. 2007; 7: 115.
8. M, S, S. Common genotypes of hepatitis B Virus. . Jun 2004; 14(6): 344 - 7.
9. Alam MM, Zaidi SZ, Shaukat S, Sharif S, Angez M, Naeem A et al. Common Genotypes of Hepatitis B virus prevalent in Injecting drug abusers (addicts) of North West Frontier Province of Pakistan. *Virology Journal* 2007; 4: 63
10. Aslam M, Aslam J. Seroprevalence of the antibody to hepatitis C in select groups in the Punjab region of Pakistan. *J Clin Gastroenterol* 2001; 33: 407-11
11. Hamid S, Umar M, Alam A, Siddiqui A, Qureshi H, Butt J, et al. PSG consensus statement on the management of hepatitis C virus infection-2003. *J Pak Med Assoc* 2004; 54: 146-50.
12. Batool U, Qureshi S. Declining sustained virological response in hepatitis C. *J coll Physicians Surg Pak* 2006;16: 187-91
13. Idrees M, Riazuddin S. Frequency distribution of hepatitis C virus genotypes in different geographical regions of Pakistan and their possible routes of transmission. *BMC Infect Dis* 2008;8:69
14. Moatter T, Hussainy AS, Hamid S, Ahmead Z, Siddiqui S. Comparitive analysis of viral titers and histologic features of Pakistani patients infected with hepatitis C virus type 3. *Int J Infect Dis* 2002;6:272-6
15. Shah HA, Jafri W, Malik I, Prescott L, Simmonds P. Hepatitis C virus (HCV) genotypes and chronic liver disease in Pakistan. *J Gastroenterol Hepatol* 1997;12:758-61
16. Zuberi BF, Zuberi FF, Memon SA, Qureshi MH, Ali SZ, Afsar S. Sustained virological response based on rapid virological response in genotype 3 chronic hepatitis C treated with standard interferon in the Pakistani Population. *World J Gastroenterol* 2008;14:2218-21
17. Sarwar S, Butt AK, Alam A, Khan AA, Shafqat F, Malik K, Niazi AK. Value of quantitative HCV RNA in the management of chronic hepatitis C patients with genotype 2 and 3. *Proceed Shaikh Zayed Post Grad Med Inst* 2005;19:55-61
18. Asian Pacific association for the Study of the Liver Consensus Statement on th Diagnosis, Management and Treatment of Hepatitis C Virus Infection. Asian Pacific Association for the study of the liver (APASL) Hepatitis C working party. *J Gastroenterol Hepatol* 2007;22:615-633 Blackwell Publishing
19. Mujeeb SA, KhatriY, Khanani R. Frequency of parenteral exposure and seroprevalence of HBV, HCV and HIV among operation room personnel. *J Hosp Infect* 1998;38:133-7
20. Danish F, Yasmin S. Current Standards in the Pharmacotherapy of Chronic Hepatitis C and Local Practices. (this issue)

Huma Qureshi,

Hepatologist,

Medilink Clinics and OMI Hospital,

Karachi.