Hepatitis C in India – Unanswered questions

After the belated rejection of western guidelines for the treatment of Hepatitis B in Asian countries, buoyed as it was by the findings of the REVEAL study among others, it seems reasonable to look critically at the guidelines for the treatment of Hepatitis C in India in a similar fashion. As most of the work that has been done in the field of hepatitis has been carried out in the West, we unsurprisingly tend to accept and quote from those sources. In the case of Hepatitis B, the timing of infection (neonatal versus adult), the large body of evidence from Chinese patients and the lack of good cohort studies to predict prognosis in the West was enough to make the case for an Asian review. Do we have such imperatives with regard to Hepatitis C?

The epidemiology of the HCV virus is probably as varied in this country as in many countries all over the world. Although the predominant genotypes in North, Central, and East India is, mercifully, the more responsive genotype 3, in the south it is predominantly genotype 1. There is scanty evidence which suggests that the response to treatment may be different here but, clearly, larger studies are needed to make these findings generally applicable. The few studies on the biology of the virus seem to indicate a conservation of structure and behaviour. So, in essence there is as yet no evidence to suggest that we need to change therapeutic guidelines in any major way from that which has been prescribed for the West. Yet that is not the last word on the subject.

There is enough reason, to my mind, to do larger and more meticulous studies to try and look at different strategies of prevention, diagnosis and treatment of HCV. However, this is not driven by the biology of the virus or the host but by the resource poor settings in India.

First, there is a major role for prevention. The scare regarding HIV has changed the rules about blood banking practices and the use of disposable needles and syringes. The slowing of the AIDS epidemic, if the official figures are reliable, can be a surrogate indicator that HCV transmission may also be on a plateau. This needs good epidemiological confirmation because there are indicators that the opposite is true. One recent urban study has shown that young people of the third decade are more frequently infected than those of older age groups which suggests that drug use or even greater use of modern dental care, common among the young, are not given the dangerous connotations that they deserve. Another study also from an urban area has raised the possibility that seemingly innocuous behaviour such as visits to the local barber can be the cause of HCV transmission. This means that if we are interested in managing the disease in India we need more rigorous guidelines to prevent person-to-person transmission.

Again, there are special groups that need intensive attention. The most conspicuous is the growing population of patients with chronic renal failure who do not have the capacity to produce antibodies and at the same time harbour the virus in large amounts. The resource crunch in government institutions makes it necessary to plan strategies to divert patients into sequestered groups so that cross transmission across groups is minimized if not abolished. One wise nephrologist whom I know uses peritoneal dialysis only after patients are properly tested by molecular methods to ensure that they do not have the hepatitis viruses lurking within them. Perhaps, in future, efforts should be made to try and produce effective dialysis systems that do not cause transmission. Research in this area is lacking or inadequate and the separation of the various disciplines of science into watertight compartments has not allowed progress in this area.

This leads us to issues about the expenses and reliability of diagnostic testing. In general serological testing for HCV antibody should suffice except, as mentioned above, in patients with renal failure. To reduce expenses in serological testing, serum pooling may be an answer. This may reduce the number of tests and consequently the expenses especially of impoverished blood banks. Again, this needs both monitoring and strict supervision for maintaining quality. Quantitative tests are very expensive and way beyond the reach of common people although they are the backbone of therapy. Furthermore, there is a woeful lack of standardization in both collection of samples and modes of molecular testing. The latter particularly needs urgent redressal as laboratory results are often not comparable. How does one decrease the costs to the common man and especially in those hospitals which run on very tight budgets? Again pooling of sera may have some success but this applies more to virus detection in situations such as in chronic renal failure. A test detecting core antigen has been found to be very specific but not highly sensitive and may work with a combination of simple tests to replace quantitative real time PCR which is presently the acceptable test.

Finally, there needs to be changes in strategies of treatment. Early diagnosis might facilitate better responses. Therefore, widespread testing of healthcare personnel and others who are at risk as well as random members of the general public may present cases detected early enough to be amenable to therapy. Once infected people are identified, to whom would the scarce resources be allocated amongst whose who cannot afford treatment. This leads to many unanswered questions. Should treatment be withheld from those who have no necroinflammatory change or only mild disease on liver biopsy? Would follow up in these individuals by periodic estimations of liver enzymes predict progressive liver damage. This must be seen in the light of the information that transaminases and imaging can be quite off the mark in predicting histological damage. Is the degree of fibrosis more important than the level of active inflammation? These questions can only be answered within the setting of the Indian milieu. Once a decision is taken that the individual qualifies for treatment, a variety of cheap but effective strategies may be possible but these have not been tested. Will daily injections of the less expensive regular...
interferon be as effective as PEG interferon? The study by Hazari et al has demonstrated enhanced efficacy with daily injections. Finally the response will need to be measured by the fall in the viral load - at 4 weeks or 12 weeks. Then there are the usual pitfalls of sustaining a good viral response. Does an unsustained response spell histological disaster? Again, can Interferon be used to reduce the chances of hepatocellular carcinoma?

So it looks like there are more questions than answers. From the little evidence we have, the virus probably behaves here as elsewhere but we need to tailor our coat (and our investigations!) according to the cloth we have.

REFERENCES

George Kurian  
Professor  
Dept. of Gastrointestinal Sciences  
Christian Medical College  
Vellore