Hemodialysis patients with hepatitis C. Should they be considered for therapy to renal transplant?

Sir,

I read with interest the paper by Dr. Hatem Mansy and his colleagues, entitled hemodialysis patients with hepatitis C: should they be considered for renal transplant,\(^1\) for which I submit respectfully the following comments.

The title of the paper (Should They be Considered for Renal Transplant?) remains by and large unanswered with no data in the paper attempting to answer this very important question. It remains a very descriptive paper, highlighting the clinical, laboratory and pathologic findings in a small number of hemodialysis patients with hepatitis C virus (HCV). With unsubstantiated data the authors conclude that hemodialysis patients with HCV should be regarded as those with hepatitis B, although hepatitis B and C are caused by two completely different viruses, with different natural history, particularly in the transplant setting. Therefore, drawing the same conclusion for both diseases in excluding patients with “chronic active hepatitis” may be misleading. In addition, the authors stated at the end of their paper, and I quote, “We plan close follow-up of 10 of our 13 patients eligible for renal transplant on these criteria, to assess how the HCV infection is affected by immunosuppressive therapy after their transplant.” It seems to me that the authors did not consider antiviral therapy with interferon for their patients\(^!\), rather, they have decided to monitor the progress of their HCV infected patients after renal transplantation to see the effect of immunosuppressive therapy.

Although interferon therapy is not highly effective and the recommendations for this clinical problem remain controversial, I believe the better action is to consider treating these patients prior to transplantation, hoping to eradicate the virus in this setting which can be very advantageous and rewarding, if achieved. Huraib et al have shown a prevalence rate of HCV antibody positivity in up to 95% among hemodialysis patients in Saudi Arabia\(^2\) which we believe is probably related to lack of strict adherence to universal precautions during dialysis, among other factors.\(^3\) Therefore, if antiviral therapy is contemplated in some of these patients, it should be done prior to transplantation, since HCV infection is the main cause of liver dysfunction in kidney graft recipients.\(^4\) Furthermore, low level of viremia and short duration of illness are present in many hemodialysis patients which are both good response predictors for interferon therapy.\(^5\) The therapy should only be attempted if the following criteria are fulfilled: (a) documentation of HCV-RNA in the serum, (b) liver biopsy showing chronic hepatitis C. (c) strict adherence to universal precautions while being maintained on hemodialysis to prevent re-infection while on therapy, and (d) generous empathy and support to these chronic patients while taking interferon. All these requirements must be present if therapy is at all to be completed and be successful. After transplantation HCV is difficult, if not impossible, to treat with interferon in the setting of immunosuppressive therapy for several reasons, which includes (1) a lower response rate in transplant patients,\(^6\) (2) the fact that interferon can up-regulate the expression of HLA class I and II antigens, and may increase the risk of allograft rejection,\(^6\) particularly if baseline immunosuppression has been reduced, (3) the transplanted kidney, at least theoretically, is vulnerable to HCV associated glomerulonephritis, which was recently reported from many countries, including Saudi Arabia.\(^7\) After treatment, if the patient responds to therapy, well and good, if not, and he/she is not cirrhotic with good synthetic function with no other contraindications, I think there should be no reason for the time-being why he/she cannot be transplanted even if there is chronic hepatitis. For those with cirrhosis, they should be considered for combined liver and kidney transplantation if both organs are in end stage disease.

As far as the diagnosis of “chronic active hepatitis,” “chronic persistent hepatitis” or “chronic lobular hepatitis,” I believe all these terminologies are considered inappropriate for the interpretation of liver biopsies in 1996. These terms are considered obsolete by the current recommendations.\(^8\) Scoring these biopsies with Knodell’s Hepatic Activity Index\(^9\) would be more helpful and advantageous as it assesses the activity of the biopsy and stages the disease. Furthermore, this system has the advantage of scoring the disease objectively and the ability to compare biopsies to each other with little or no inter or intra-observer variability. In addition, biopsies from the same patients are subject to sampling errors and may show minimal inflammation, i.e., “chronic persistent hepatitis” or marked inflammation in certain areas, i.e.,
"chronic active hepatitis," these biopsies can be different at different times, i.e., a biopsy can be "chronic persistent hepatitis" that can progress to "chronic active hepatitis," or visa versa, and hence excluding these patients based on the descriptive term of "chronic active hepatitis" may not be appropriate.

I would agree with the authors regarding the lack of correlation in the transaminases in HCV infected hemodialysis patients, as we have shown in our previous published study that transaminases are normal in 85% of HCV infected hemodialysis patients. Furthermore, we have shown that HCV-RNA can be intermittently positive in these patients and that the viremia is usually low while the patients are on hemodialysis, perhaps because of filtration of the virus during dialysis.11

Since we have no other therapeutic alternatives currently available to us, I believe it is worthwhile treating these patients for the time-being. This way we can compare the influence of treated and untreated HCV in hemodialysis patients and on the natural history of the subsequent kidney transplant. All in all, I believe HCV infected hemodialysis patients should be considered for interferon treatment once a genuine infection is documented prior to transplantation to avoid potential problems encountered after renal transplantation which may result in large morbidity and mortality. We have a good opportunity in our hands to provide this therapy as part of a well designed multicenter study in this country where we are unfortunately blessed with epidemic proportions of HCV among hemodialysis patients. This way we can collectively provide meaningful data to the literature regarding this difficult problem and try to keep it under control, especially if other preventive measures are implemented in hemodialysis units in the Kingdom.

Finally, I thank the authors for their published study.

References


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Sir,

In response to Dr. I Altraif's comment on our paper “Hemodialysis patients with hepatitis C - should they be considered for renal transplantation.” There is no doubt that he raised many relevant points, some of them were beyond the scope of this paper. It has been generally accepted that patients with hepatitis B with either high index hepatic activity, early or established liver cirrhosis are excluded from renal transplant, and similar patients with chronic hepatitis C are excluded in a similar way, although we are aware that both are two different viruses with different natural history. In line with the current national policy in this country, as well as in many countries worldwide, this supports the need for liver biopsy in these patients as we demonstrated in our paper since transaminase is no guide to liver histology, and also because of the limited availability of HCV/RNA as measured by PCR test.

In USA most (96%) of the leading transplant centers perform renal transplant in anti-HCV positive recipients, approximately 40% use the absence of abnormal liver function test and chronic active hepatitis in liver biopsy as important criteria. Ten patients in our study had liver biopsy showing chronic persistent hepatitis/chronic interlobular hepatitis without high index of activity to justify treatment with interferon. However, patients with chronic active hepatitis were treated with interferon, a drug which is only effective in 50% of cases with high relapse rate. However, it is the only therapeutic option available to us.

We would like to point out that the paper was submitted for publication late 1995, before the new terminology and scoring biopsies with Knodell's Hepatic Activity Index had been widely introduced and generally accepted. Dr. Altraif has shown that HCV/RNA can be intermittently positive in these patients and that viremia is usually low while the patient is on hemodialysis. However, he postulated that because of the filtration of the virus during dialysis, perhaps it would be worth stressing that recent work by R Hugman et al (1995), showed by PCR test that no HCV/RNA (cells or cell particles) pass through the dialysis membrane, and they could exclude the dialysis machine or dialysis fluid as a transmission route. At the present time, along with various hospitals in the Kingdom, we are following the criteria and guidelines issued by the Saudi Center for Organ Transplantation, that hemodialysis patients with chronic hepatitis C should not be transplanted if they show evidence of cirrhosis or chronic active hepatitis by liver biopsy. This is in line with the recommendations set in our published paper, and in most renal units treatment of chronic hepatitis C is indicated in patients with twofold increase in transaminase, chronicity of the disease for over six months, or if their liver biopsy showed high index hepatic activity (chronic active hepatitis); and in a study of 24 patients who had a follow-up liver biopsy after a mean interval of five years there was a tendency of deterioration of the liver histology in the majority of patients re-biopsied, being more obvious in those who showed chronic active hepatitis in the first biopsy.

For those patients with liver cirrhosis and end stage renal failure on dialysis they should be considered for combined liver and kidney transplantation.

Most nephrologists would disagree with Dr. Altraif’s statement that all hepatitis C infected hemodialysis patients should be considered for interferon treatment once a genuine infection is documented, without documenting evidence of either biochemical or histological evidence of activity. Finally, one of the alarming concerns for the nephrologists is the current increase in the incidence of hepatitis C infection in the dialysis units in spite of dialyzing hepatitis C patients in separate dedicated areas, allocation of particular hemodialysis machines to those infected patients, and applying strict universal precautions while being dialysed. However, these universal precautions are perhaps not applied at the same strict level as applied for patients infected with hepatitis B and the lack of specific vaccine makes more patients vulnerable to infection.

We would like to thank Dr Altraif for his interest and comment on our paper.

References


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