

# Treatment of hepatitis C virus infection and renal disease

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Renal diseases occur frequently in patients chronically infected by hepatitis C virus (HCV). These may be causes or consequences of HCV infection. The prevalence of HCV infection in patients receiving hemodialysis is 6.7% to 10.2% in some centers in Mexico.<sup>1,2</sup> However, the problem may be greater than these percentages suggest because the prevalence of HCV infection is as high as 50% in some countries.<sup>3</sup> HCV infection frequently results in kidney damage. Membranoproliferative glomerulonephritis with or without cryoglobulinemia is the most significant renal disease associated with hepatitis C, followed by membranous nephropathy and hepatorenal syndrome.<sup>4</sup> Treatment of renal disease patients for HCV infection improves several parameters of renal function, particularly in patients with membranoproliferative glomerulonephritis and cryoglobulinemia.<sup>5,6</sup>

The mortality rate of HCV patients with liver cirrhosis is high.<sup>7</sup> HCV infection is considered a risk factor independent from the death (RR = 1.57; 95% CI = 1.2–2).<sup>8</sup> These results are almost identical to those of a recent meta-analysis of 2,341 patients.<sup>9</sup> Because morbidity and liver transplant rejection rates are high in patients with renal disease,<sup>10</sup> it is important to treat HCV infection prior to transplantation.<sup>11</sup>

## Patients receiving dialysis

Interferon monotherapy is commonly used to treat HCV infections in patients receiving dialysis. However, most of the data in support of interferon monotherapy have been derived from small clinical trials whose outcomes are inconsistent. Recently, two meta-analyses provided evidence for the efficacy and safety of subcutaneous administration of 3 million units of interferon three times per week for 24 weeks to patients receiving dialysis. Fabrizi et al.<sup>12</sup> reported that the sustained viral response (SVR) to interferon treatment of patients receiving dialysis is 37% (CI 95% 28–48,  $p < 0.0006$ ), which is much greater than that of patients with normal renal func-

tion (17%–22%), particularly when high doses of interferon are used.<sup>13</sup> Because patients with renal failure are infected with genotype 1 HCV, the success of treatment is low (SVR = 30.6%, 95% CI = 20.9–48). Similarly, Russo et al.<sup>14</sup> reported an SVR of 33% (95% CI = 21–51). Mild to high doses of interferon (6 million units intramuscularly three times per week for 24 weeks) may increase the response rate to 53%, but there are no data to justify this practice. In the study of Fabrizi,<sup>12</sup> genotype affected the response to treatment (SVRs of 26 and 31 for genotype 1 and genotypes other than 1, respectively).

These two meta-analyses also showed that the discontinuation rate for patients receiving dialysis is 17%–29.6%, which is higher than the rate for nonuremic patients.<sup>15</sup> The main side effects are flu-like symptoms, leucopenia, depression, neurological disorders (confusion and seizure), and gastrointestinal disorders. Because of the cost of interferon and its side effects, it is not advisable to use it for patients with low life expectancies or those with comorbidities such as diabetes mellitus, congestive heart failure or malnutrition.<sup>7</sup>

In the past decade, combined therapy with interferon and ribavirin has improved virological and biochemical response rates.<sup>16</sup> Because the conventional dose of ribavirin causes hemolytic anemia in patients with renal failure, a reduced dose of ribavirin (200 mg three times per week) and a high dose of erythropoietin (20,000–30,000 IU/week) are recommended. Combined therapy increases the HCV SVR of dialysis patients to 55%–65%.<sup>17</sup>

The addition of a polyethylene glycol moiety to interferon facilitates slow release of interferon. The mean half-life of pegylated interferon in HCV patients with renal failure (58 h) is similar to that of patients without renal failure (52 h).<sup>18</sup> Therefore, the standard dose of pegylated interferon is considered safe for HCV patients receiving hemodialysis (180 µg/week for 48 weeks). There are few clinical studies on the use of pegylated interferon for HCV patients receiving dialysis. One study claimed that it results in a significant increase in SVR of dialysis patients with HCV,<sup>19</sup> but this finding was refuted by another report.<sup>20</sup> Similarly, one report stated that liver transplant patients with relapsed HCV infection are intolerant of treatment with pegylated interferon,<sup>21</sup> and another reported that the pegylated interferon is well tolerated by transplant patients and that SVR rate is improved without serious side effects.<sup>22</sup>

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## Renal transplant patients

The treatment of chronic HCV patients who are prospects for renal transplantation deserves special attention because of the high morbidity and mortality associated with renal transplantation. Furthermore, the progression of hepatitis C is accelerated by transplantation.<sup>23,24</sup> A small follow-up study of 29 patients showed that patients with renal failure and HCV infection who have no contraindications benefit significantly from interferon treatment, particularly in respect of survival and rejection rates.<sup>3</sup> Therefore, efforts should be made to optimize treatment.

## Patients with cryoglobulinemia

The treatment of cryoglobulinemia is a controversial topic as some studies have demonstrated that it is improved by treatment of liver disease.<sup>25</sup> However, the evidence in support of treatment of these patients was derived from small clinical studies. Recently, a cohort study of 25 patients<sup>5</sup> showed that treatment with interferon and ribavirin or pegylated interferon increased the SVR, reduced the degree of cryoglobulinemia, and improved proteinuria.

## Conclusion

Treatment of chronic HCV infection in subjects with renal failure requires further study.

## Recommendations of the consensus panel

Should patients with renal disease and HCV infection be treated?

The panel of consensus unanimously recommends antiviral treatment of these patients. Consequently, all patients should be evaluated to determine their eligibility for treatment.

## Evidence quality: 2

What is the treatment of choice for patients with renal disease?

Most of the panel members (58%) considered pegylated interferon monotherapy to be the treatment of choice. One-third (33%) considered standard interferon monotherapy to be the treatment of choice.

## Evidence quality: 2

Is the simultaneous use of erythropoietin and HCV medication recommended?

Most members of the panel considered the use of erythropoietin to be justified but 47% of the panelists were in favor of only using it when antiviral treatment is combined with ribavirin.

## Evidence quality: 2

How should renal disease patients with HCV–HIV or HCV–HBV coinfection be treated?

There is insufficient evidence to make recommendations on first line therapy for this complex group of patients.

## Evidence quality: 3

Should liver biopsies be performed on hemodialysis patients with chronic liver failure and HCV infection?

The consensus panel recommended performing liver biopsies on renal failure patients who are receiving hemodialysis, are prospects for renal transplantation, and have no evidence of liver cirrhosis.

## Evidence quality: 3

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