**Chronic Hepatitis C (CHC) Treatment in Two Cystic Fibrosis (CF) Patients**

Marianna Passiu*, Ilaria Meneghelli and Baroukh Maurice Assael  
Cystic Fibrosis Center, Azienda Ospedaliera Universitaria Integrata di Verona, P.le Stefani, Italy  
*Corresponding author: Marianna Passiu, Cystic Fibrosis Center, Azienda Ospedaliera Universitaria Integrata di Verona, P.le Stefani 1, 37126, Italy, Tel +39 045 812 2370; Fax +39 045 812 2042; E-mail: marianna.passiu@ospedaleuniverona.it

**Abstract**

Chronic Hepatitis C (CHC) is a contraindication for Lung Transplantation (LT). Infected patients may not be accepted in waiting lists.

The standard treatment of viral hepatitis C infection (HCV) is pegylated interferon in association with ribavirin, which may lead to a sustained response but is not devoid of side effects. In Cystic Fibrosis (CF) patients this treatment could increase respiratory infections with subsequent pulmonary function deterioration.

Here we present two CF adult patients who developed HCV infection. We decided to treat them in order to eradicate the virus and to allow future LT.

Virological response was sustained and mild side effects were successfully managed, so we recommend treatment with interferon plus ribavirin for HCV infected CF patients.

**Keywords:** Cystic Fibrosis; HCV; Lung Transplantation; Pegylated Interferon; Ribavirin; Side effects

**Introduction**

CF is a multi-organ inherited condition characterized by chronic pulmonary infection that causes progressive airways disease with an inexorable decline in lung function. LT remains the only available therapy for patients with end-stage disease. CF is the most common indication for LT in children and the third most common in adults [1,2].

Patients are usually considered for transplantation when they have a predicted life expectancy of 2 years or less. Patients listed for LT are scored on a number of prognostic factors in order to direct organs to those who have the poorest predicted survival without transplant and the best predicted post-transplant survival [3].

Most CF patients gain a net survival benefit after LT. For example, Titman et al. [4] found that 91% of the patients survived beyond the crossover point when their risk of death fell below that associated with remaining on the list, although this view has been challenged as regards paediatric patients [5]. While it is not within the scope of this paper to discuss the appropriate timing for transplant or to quantify potential benefits in general, we wish here to focus on LT candidates affected by Hepatitis C (HCV).

Cotler et al. in their survey of practices on HCV and LT found that almost one third of the approved lung transplant programs in the US did not accept candidates with Hepatitis C [6]. Hepatitis C is still included as a relative contraindication in e.g. the UK Transplant criteria for listing for lung transplantation of December 2008 [4] and liver disease may prevent transplantation as per the International Guidelines for the Selection of Lung Transplant Candidates [7].

Current standard therapy for HCV includes combination treatment with pegylated interferon (PEG-INF) and ribavirin (RBV) [8]. On the other hand, these drugs are feared to increase the risk of infection, including respiratory, in the pre-LT phase [9,10] and to increase the risk of rejection in the post-LT phase [11].

Two CF adult patients under our care developed Hepatitis C infection while their respiratory function was still preserved (FEV1 higher than 30% predicted). We decided to treat them in order to eradicate HCV and to allow future LT should it become necessary. Treatment was successful and we wish here to report these two cases.

**Methods**

We conducted a retrospective analysis of the electronic records of two patients. Reports were reviewed and approved by the local Ethic Committee and written informed consent was obtained.

**Case 1**

In 1996 one of our patients, a 40 year old, male, affected by CF with pancreatic insufficiency and moderate respiratory impairment (FEV1 56% and FVC 81% predicted), presented with signs of hepatitis (ALT 186 IU/L and AST 75 IU/L). HCV genotype 2A/2C was detected with HCV-RNA at 1,100,000 IU/mL.

In January 2007, while in-hospital for general medical assessment, FEV1 was as low as 34% predicted, FVC 53%, arterial blood oxygen saturation (SO2) was 96%, indicating severe lung dysfunction.

Laboratory tests were: ALT 34 IU/L, AST 36 IU/L, GGT 23 IU/L, in Cystic Fibrosis (CF) patients this treatment could increase respiratory infections with subsequent pulmonary function deterioration. Laboratory tests were: ALT 34 IU/L, AST 36 IU/L, GGT 23 IU/L, HCV genotype 2A/2C was detected at a viremia level of 1,100,000 IU/mL. A 24-week treatment with peginterferon alpha-2a (Pegasys® Roche, 180 mcg s.c. weekly) and ribavirin (Copegus® Roche 400 mg p.o. bid) was started.

HCV-RNA decreased to 2,500 IU/mL after the first administration and it was undetectable after 4 weeks.

Moderate thrombocytopenia was found after the second administration (145,000/mL down from 177,000/mL pre-treatment) with moderate fever at 38°C for 5 days. The patient was then discharged scheduling in-hospital visits every 12 weeks thereafter.

At the first such visit, known, mild-to-moderate side effects of treatment were reported: fever, asthenia, anorexia, nausea and weight loss of more than 10 kg. HCV-RNA was undetectable. At the second one, general conditions were improved (decreased asthenia and nausea, no fever, weight gain). Lung function was: FEV1 41%, FVC 64%, predicted. Treatment was suspended.
Case 2

In 2008 another patient, a 42 year old, male, affected by CF with pancreatic insufficiency and moderate respiratory impairment, presented with signs of hepatitis (ALT 132 IU/L). His clinical history included chronic respiratory colonization with S. aureus, diabetes CF-related, Allergic Bronchopulmonary Aspergillosis (ABPA) and chronic hepatitis by HCV genotype 3a. Spirometry was moderately affected (FEV1 64% and FVC 86% predicted) and SO2 was 91.1%. Abdominal ultrasound examination was performed and no pathological findings detected. HCV viremia was 104,000 IU/ml.

A 24-week treatment with peginterferon alpha-2a (Pegasys® Roche, 180 mcg s.c. weekly) and ribavirin (Copegus® Roche 1,000 mg p.o. daily) was started on January 2010. After 10 days, HCV-RNA was still detectable and mild anemia was found.

On March 2010, this patient was re-hospitalized for routine assessment. HCV-RNA was negative. Functional pulmonary parameters were: FEV1 60%, FVC 81% predicted, SO2 96%.

During treatment, the following adverse events were reported: decreased exercise tolerance, irritability, weight loss (6 kg), decreased appetite, arthralgia, dry eye syndrome and dry skin.

On June 2010 treatment with interferon and ribavirin was suspended. On August 2010 HCV-RNA was confirmed negative. Previously reported adverse events disappeared after stopping treatment. Diabetes was well under control.

Discussion

HCV antiviral treatment with interferon plus ribavirin is not always effective. Sustained response rates are roughly 45% with genotype 1 and 80% with genotype 2 or 3 [12]. This therapy is also not devoid of side effects. In CF patients infected with HCV, respiratory complications may worsen with subsequent respiratory function deterioration. On the other hand, if this same therapy is given after LT, it may increase the risk of rejection [11] and LT itself may be considered to be contraindicated unless HCV infection has previously been eradicated, depriving patients with end stage lung disease of the only effective therapy.

Doucette et al. [13], noting that HCV treatment in renal transplant candidates, before transplantation, improves post-transplant outcome, have treated 5 HCV non CF potential LT candidates without unexpected side effects.

Recently, a case was presented of one male adult CF patient with HCV that was successfully treated with interferon plus ribavirin. In spite of lung infections and respiratory function worsening, he managed to complete treatment with sustained virological response (HCV-RNA undetectable) and could be wait-listed for LT [10].

There is solid evidence that patients who present a sustained virological response, defined as undetectable HCV-RNA 24 weeks after completing therapy, will remain virus-free during long-term follow-up, with a risk of late HCV recurrence of less than 2% [14].

Here we described two CF patients who were treated for HCV, both of whom showed a sustained virological response. Side effects, including transient deterioration of lung function due to intercurrent infections, were successfully managed. In these patients HCV was eradicated before reaching end stage lung disease. Since patients must be HCV free to undergo LT, we recommend treatment with interferon plus ribavirin for HCV infected CF patients.

Conflict of Interest Statement

The authors declare no conflict of interest in respect of the content of the article as well as no funding sources and acknowledgements.

References