

A Model for Treating HCV Hepatitis in Patients Receiving Methadone Maintenance Therapy

Stephen Malnick, MA(Oxon) MSc MBBS(Lond),¹ Victoria Sheidvasser, MD,² Alon Basevitz, MD,¹ and Shabtai Levit, PhD³

¹ Kaplan Medical Center, Rehovot, Israel

² Methadone Treatment Center, Ashdod, Israel

³ Ex-director of Jerusalem & Ashdod MMT and adjunct Lecturer in School of Social Work and Social Welfare, The Hebrew University of Jerusalem and Ariel University Center of Samaria, Israel

ABSTRACT

Introduction: Although hepatitis C virus (HCV) is associated with substance abuse, treatment of addicts is problematic. We report the results of a pilot scheme for treatment of HCV-infected substance abusers in a methadone maintenance center (MMC).

Methods: The treatment program was carried out at a single MMC. Patients were not using illicit drugs or alcohol and received regular treatment with methadone. The program consisted of 5 stages:

1. An explanatory lecture concerning HCV (50/114 attended).
2. 25 of the 50 presented for examination including HCV RNA, genotype and viral load.
3. HCV treatment with pegylated alfa-interferon-1b and ribavirin.
4. The MMC physician and staff aided the clients' medical compliance.
5. A hepatologist (SM) volunteered his services on the basis of one 3 hourly session every 4-6 weeks, in addition to open access telephone consultation with the MMC staff physician.

Results: 50 of 114 HCV seropositive clients attended the initial meeting, 25 (50%) were candidates for treatment, of whom 20 were treated. 10 had genotype 3 infection, 9 genotype 1 and 1 genotype 2. The sustained virological response (SVR) on an intention-to-treat basis was 8/20 (40%).

Discussion: We present a model for the successful treatment of chronic HCV hepatitis in patients receiving methadone.

INTRODUCTION

Chronic hepatitis C virus (HCV) infection is estimated to be present in 170 million people worldwide (1). Since the discovery of the virus and the use of ELISA testing and subsequently nucleic acid testing of blood products, the main route of new infection is via injection drug use (IDU) (2).

Despite the fact that IDU is a major source of HCV infection, prior to 2002 this group of patients was not evaluated for treatment of chronic HCV hepatitis. A 1997 NIH consensus conference recommended a period of 6-12 months of abstinence from illicit drug use prior to HCV treatment (3). A subsequent NIH consensus panel in 2002 stated that patients with active injection drug use could be considered for HCV treatment (4).

There is limited experience in the successful treatment of current intravenous drug users and persons receiving drug dependency treatment in both the U.S.A. and Europe. Several groups have reported outcomes with an SVR between 29% to 50%, although these studies used non-pegylated interferon and in some cases interferon monotherapy only (5-10). Despite this only a small minority of intravenous drug users receive treatment.

Hepatitis C is classified into several genotypes, from type 1 to type 6. The common forms in the U.S.A., Europe and Israel are type 1, 2 and 3. The standard of care of chronic HCV hepatitis at the time of the study consisted of pegylated interferon and ribavirin. Genotype 1 causes a more severe disease, responds less to treatment and requires 48 weeks of treatment. Genotypes 2 and 3 cause a less severe disease and require only 24 weeks of treatment. Therapeutic decisions including stopping rules are based on changes in viral load at predetermined time points (11).

Address for Correspondence: ✉ Dr. Stephen Malnick, Department of Internal Medicine C, Kaplan Medical Center, Rehovot 76100, Israel.

✉ Stephen@malnick.net

In Israel all citizens are eligible for treatment of illnesses within a basket of services, at minimal cost. This basket includes treatment of HCV hepatitis. There is a 50% prevalence of HCV hepatitis in recipients of methadone maintenance treatment (12). We, therefore, decided to implement a scheme for effectively treating clients of a MMC who had chronic HCV hepatitis. We report the results of this trial.

METHODS

The treatment program was carried out at a single methadone maintenance center in Ashdod in central Israel. Clients attending these centers are routinely tested for HBV, HCV and HIV infection. The clients are required to attend the methadone maintenance center on a weekly basis in order to receive their weekly dose of methadone. At this time they are also tested for the use of illicit drugs or alcohol. This mandatory visit was utilized as an opportunity for the client to be reviewed by the staff physician of the methadone maintenance center regarding problems with the treatment, both medical and social, and in addition on certain occasions to be examined by a hepatologist.

THE PROGRAM CONSISTED OF 5 STAGES:

1. An initial explanatory lecture concerning HCV with a question-and-answer session made available to all HCV seropositive clients (50/114 attended).
2. 25 of the 50 presented for a standard HCV hepatitis work-up including routine biochemical tests, auto-antibody screen, serum ferritin, ceruloplasmin, TSH, HCV RNA, genotype and viral load.
3. HCV treatment with pegylated alfa-interferon-1b and ribavirin on a standard weight-based regimen.
4. The methadone maintenance center physician and staff aided the clients' medical compliance and advised regarding side-effects of the treatment including depression, weakness and issues related to problems with employment due to absences related to the side-effects of the medication.
5. A hepatologist volunteered his services on a regular basis at the methadone maintenance center for 2 hourly sessions, and was available on an open access basis to the physician from the methadone maintenance center in order to advise on any problems that arose. The hepatologist worked in conjunction with all the major health funds (HMOs) in Israel which reduced bureaucratic obstacles.

Indications for treatment of HCV hepatitis included elevated liver enzymes, fibrosis of at least F2 grade and HCV RNA positivity in the blood. Contraindications for the program included HIV positivity, evidence for HBV infection, autoimmune disease, active angina pectoris, retinopathy of any kind, newly diagnosed thyroid disease and recent or active depression.

A sustained viral response (SVR) which is equivalent to cure was defined as the absence of HCV RNA in the serum on a sensitive assay 24 weeks after the end of treatment.

This study was approved by the Institutional Review Board of Kaplan Medical Center.

RESULTS

Of 114 clients with HCV seropositivity by standard ELISA testing, 50 attended an initial group meeting. Of these 50, 25 were judged to be candidates for treatment and 20 of these received treatment; 5 declined treatment for social reasons. The other 25 candidates were not suitable for treatment for several reasons – lack of HCV RNA in the serum (8), normal liver transaminases (5), depression (2), employment issues (9), planning pregnancy in the near future (1).

Of the 20 clients who received treatment 9 (45%) were genotype 1, 1 (5%) was genotype 2 and 10 (50%) were genotype 3. The vast majority of the clients were of male gender, 19 (95%).

Treatment was stopped in 4 patients for social reasons – three had problems with performing their jobs and one was imprisoned and his treatment was discontinued, despite this not being permitted. In 2 patients the treatment was stopped due to depression.

An SVR was achieved in 8 of the 20 treated patients (40% on an intention to treat basis), 1 patient was a viral relapser. The SVR in the patients who completed treatment was 8 of 13 (61.5%).

DISCUSSION

In this report we describe a model for treating patients with HCV hepatitis acquired by IDU who are receiving methadone maintenance. This model is based on close cooperation between a volunteering hepatologist and the methadone maintenance center staff, especially the physician from the methadone maintenance center and the center's director who is a registered social worker. The results obtained are similar to those achieved in real world treatment situations in patients with chronic HCV hepatitis who are not substance abusers (4).

Despite IDUs being a major risk group for past and current HCV infection, physicians often exclude IDUs from therapy of HCV hepatitis due to concerns about compliance, psychiatric comorbidity and the risk of HCV reinfection. Initial studies by Sylvestre (5) and Backmund et al. (6) showed a SVR among IDU patients similar to that observed in trials of HCV treatment. Following this the NIH issued revised guidelines in 2002 stating that HCV treatment should be linked to drug treatment programs and to consider active IDUs on a case-to-case basis (4).

Despite this treatment uptake among IDUs is only about 1% annually (13). More than 80% of IDUs have reported a willingness to receive treatment (13) and also in our study 44% (50/114) of those who attended a single explanatory lecture were willing to consider therapy. This suggests that in Israel IDUs are interested in receiving treatment for HCV hepatitis.

In our model of treatment, the care of the HCV-infected patient is carried out at the methadone maintenance center. The clients are required to attend the methadone maintenance center on a weekly basis as a condition for receiving their methadone therapy. The methadone maintenance center has a well developed support system including a physician and social worker. The physician from the methadone maintenance center acted as an intermediary between the medical requirements (laboratory tests for therapeutic decisions, such as stopping rules) and the sometimes burdensome medical bureaucracy. In addition, the methadone maintenance center clients found it difficult to attend clinics for blood tests to be taken and having a familiar physician on-site increased their compliance. This support system is able to identify those patients who are interested in receiving treatment for HCV hepatitis and provide a support system for dealing with the side-effects of treatment. The provision of volunteer services by a hepatologist in our model enabled the use of the existing medical services with no additional expenses. The hepatologist was also available for telephone consultations regarding issues associated with the treatment, specifically treatment-related side-effects such as anemia, neutropenia and depression, in addition to decisions regarding cessation of treatment based on stopping rules. The greater part of the cost of the treatment (both therapeutic and diagnostic) is covered by the basket of services to which Israeli citizens are entitled.

Furthermore, during the treatment it became apparent that treatment-related mood changes were a problem for many of the clients and their partners and an evening meeting with all the staff, the clients and the hepatologist

was arranged in which all these issues were addressed. This may explain the 80% rate of adherence to treatment in our patients.

The health system in Israel requires a maximum copayment by patients of approximately \$70 per month. The copayment for methadone is an additional charge and the total cost may approach 40% of the client's total monthly income received from National Insurance. Financial support, if available, would greatly increase the ability of clients to receive treatment.

The treatment of HCV hepatitis is prolonged with many potential side-effects. In addition there is a marked similarity between the physiological symptoms induced by treatment and the withdrawal syndrome. For this reason an effective support system is very important, both prior to the start of treatment to increase the client's awareness of this possibility and also during treatment to help them deal with such situations should they arise. The clients participate in the methadone treatment program in order to avoid the withdrawal symptoms and find themselves having such symptoms as a result of treatment.

Half of our patients had genotype 3 which has a high rate of response to treatment, requires only 24 weeks of treatment and if there is a rapid viral response (HCV RNA negative after 4 weeks of treatment) may be eligible for only 12 weeks of treatment (14). This shortened period of treatment may improve compliance.

Recently the protease inhibitors boceprevir and telaprevir have been approved for treatment of genotype 1 HCV hepatitis in both naïve and treatment-experienced patients (15). These treatment protocols are more complicated than the previous standard of care, have a higher rate of success for both naïve and treatment-experienced patients and also have drug interactions with methadone. Our model for treatment can be applied to these new treatment regimens. The incorporation of telemedicine may be useful, too, especially since treatment with telaprevir has a high incidence of rashes and severe cutaneous reactions including Stevens-Johnson syndrome.

In summary, we present a successful model, utilizing existing infrastructure, for diagnosing and treating chronic HCV hepatitis in a methadone maintenance center. This model could be applied nationally and also adapted for use in prisons which also have a large number of inmates with HCV hepatitis.

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