Treatment of chronic hepatitis C in Canadian prison inmates

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PURPOSE: To assess sustained viral response rate and adherence to standard interferon alpha-2b and ribavirin therapy in inmates with chronic hepatitis C (HCV) in Canadian penitentiaries in the Pacific region.

METHODS: A retrospective chart review of all inmates with chronic HCV who were treated with standard interferon alpha-2b and ribavirin therapy between March 2001 and October 2002.

RESULTS: A total of 90 male inmates were treated. The mean age at time of treatment was 40 years. There were 49 inmates with HCV genotype 1, 11 with HCV genotype 2 and 30 with HCV genotype 3. Eight inmates discontinued treatment because of intolerance to side effects. Nine inmates were stopped by the physician because of non-response at an average of 27 weeks. All inmates achieved at least 80% adherence of interferon and ribavirin therapy. The overall sustained virological response (SVR) was 55.9%. SVR was 31.6% for genotype 1, 100% for genotype 2 and 71.4% for genotype 3.

CONCLUSION: There was excellent SVR and adherence to treatment with interferon and ribavirin. This experience highlights an important opportunity to treat a population with a high prevalence of HCV-positive persons who may otherwise not seek treatment.

Key Words: *Hepatitis C; Incarcerated; Inmates; Interferon; Prison; Ribavirin; Therapy*

Le traitement de l'hépatite C chronique chez des détenus de prisons canadiennes

OBJECTIF : Évaluer le taux de réponse virale soutenue et le respect du traitement standard à l'interféron alpha-2b et à la ribavirine chez des détenus atteints d'hépatite C (VHC) chronique de pénitenciers canadiens de la région du Pacifique.

MÉTHODOLOGIE : Analyse rétrospective des dossiers de tous les détenus atteints du VHC chronique ayant reçu un traitement standard à l'interféron alpha-2b et à la ribavirine entre mars 2001 et octobre 2002.

RÉSULTATS : Un total de 90 hommes a été traité. L'âge moyen au moment du traitement était de 40 ans. Quarante-neuf patients souffraient du génotype 1 du VHC, 11 du génotype 2 du VHC, et 30, du génotype 3 du VHC. Huit patients ont arrêté leur traitement en raison d'une intolérance aux effets secondaires. Neuf patients ont dû y mettre un terme sous les conseils de leur médecin en raison de non-réponse, au bout d'une moyenne de 27 semaines. Tous les patients ont affiché une adhésion d'au moins 80 % au traitement à l'interféron et à la ribavirine. La réponse virologique soutenue (RVS) globale s'élevait à 55,9 %. La RVS atteignait 31,6 % pour le génotype 1, 100 % pour le génotype 2 et 71,4 % pour le génotype 3.

CONCLUSION : La RVS et l'adhésion au traitement à l'interféron et à la ribavirine étaient excellentes. Cette expérience démontre une importante possibilité de soigner une population présentant une forte prévalence de personnes positives au VHC qui ne se feraient peut-être pas traiter autrement.

Although prison populations carry a larger burden of illness than the population at large, public health systems have tended to overlook this issue. In one study (1), 70% of those incarcerated were identified to need treatment for substance abuse. Furthermore, they were 10 times more likely to have HIV, 40% more likely to receive treatment for diabetes and 68% more likely to be treated for heart conditions. In addition, chronic hepatitis from hepatitis C (HCV) has emerged as a substantial public health concern over the past decade.

Chronic HCV affects an estimated 300 million people worldwide, and within Canada the prevalence is estimated to be between 0.75% and 1.0% of the general population (2). In contrast, the prevalence within the Canadian prison system is disproportionately high, with estimates ranging from 28% to 40% (1). Unfortunately, despite the fact that the incarcerated have such a high prevalence of HCV, it is a group that has been overlooked for treatment. In 2000, only 91 inmates across all of Canada were started on treatment for HCV, and in 2001, only 123 inmates were started on treatment (1). A number of factors may be perceived as deterrents for treating inmates. These include a history of psychiatric illness precluding treatment, the likely poor adherence to treatment regimens, intolerance to side effects and the risk of reinfection with HCV. Treatment of HCV with interferon alpha-2b and ribavirin therapy has been shown to be effective for many years now, with 41% to 47% of inmates achieving a sustained virological response (SVR) (3-5). With newer pegylated interferons, overall SVR rates are now estimated to be 54% (6,7).

If successful, treating HCV in prison may have health economic benefits because HCV is a leading cause of chronic liver disease and the most common indication for liver transplantation (5). Two American studies (8,9) have shown that treating

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TABLE 1
Baseline characteristics of treated inmates

Characteristic	N=90
Mean age, years	40
Male sex, n (%)	90 (100)
Psychiatric history	
Depression, n (%)	5 (5.4)
Substance abuse history, n (%)	
Intravenous drugs	70 (77)
Alcohol	40 (43)
Hepatitis C genotype, n (%)	
1	49 (54)
2	11 (12)
3	30 (33)
Fibrosis score, n (%)*	
0	6 (9.5)
1	21 (33)
2	23 (36.5)
3	9 (14)
4	4 (6)

**Sixty-three of the 90 inmates underwent liver biopsies*

HCV in the prison population can be highly effective, but this issue has never been addressed in the Canadian prison population. We report on the clinical experience in the evaluation and treatment of 90 inmates in British Columbia (BC) between March 2001 and October 2002.

METHODS

A retrospective chart review of all inmates who were treated with interferon alpha-2b and ribavirin combination therapy (Rebetron, Schering Canada), for chronic HCV between March 2001 and October 2002 in eight different penitentiaries in BC across three different security levels was undertaken. There were two minimum security prisons – Elbow Lake Institution (Harrison Mills, BC) and Ferndale Institution (Mission, BC); three medium security prisons – Matsqui Institution (Abbotsford, BC), Mission Institution (Mission, BC) and William Head Institution (Victoria, BC); one maximum security prison – Kent Institution (Agassiz, BC); and one multilevel prison – Regional Health Centre (Abbotsford, BC). All treatment was supervised by a Correctional Service Canada Medical Infectious Diseases Consultant. Ongoing care was delivered by the nursing staff within the correctional institutions. The chart review specifically included the end points of SVR to therapy, adherence to therapy and recorded adverse effects of treatment.

The present study was approved by the University of British Columbia Clinical Research Ethics Board.

Statistical analysis

Both descriptive and analytic statistics were used in the present study. For analytic statistics, a χ^2 test was used for categorical variables. The alpha level of significance for a two-tailed test was set at 0.05 (ie, $P<0.05$). A Web-based χ^2 calculator was used to perform the analytic statistics (10).

HCV surveillance

Testing for HCV in the Correctional Service Canada penitentiaries is voluntary. At intake, all inmates are offered testing. Testing may also be undertaken at the request of the inmate, because of perceived risks, elevated aminotransferase levels during routine health care testing or the evaluation of symptoms. Potential candidates for HCV treatment were screened for a history of depression and other psychiatric diseases. Standard liver biochemistry, hematology profiles, HCV-RNA with genotyping and, in the majority of cases, liver biopsy were performed before initiation of treatment.

Treatment

Treatment consisted of standard interferon alpha-2b (3 MU) administered subcutaneously three times a week along with ribavirin at the recommended dose of 1000 mg/day to 1200 mg/day depending on weight greater than or less than 75 kg. HCV-RNA was measured at 12, 24, 36 and 48 weeks of treatment, as well as six months post-treatment. For genotype 1, if the serum HCV-RNA was detectable at week 24, treatment was stopped as per treatment protocol. Funding for treatment was provided by Correctional Service Canada. Inmate teaching and administration of therapy was directly supervised by a registered nurse in the correctional services health care facility.

RESULTS

Between March 2001 and October 2002, 214 inmates were evaluated and found to be HCV-seropositive. Of these, 90 inmates were considered to be eligible for treatment. The remaining 124 inmates were not treated because of undetectable serum HCV-RNA (19%), serum aminotransferase levels that were within normal limits during incarceration follow-up (8%), or inmate preference not to be treated including those awaiting future therapies (8%), psychiatric disease (3%), comorbid medical conditions (1.6%) and normal liver biopsy (0.8%). Five inmates (4%) were released from prison before they were to start treatment. No specified reason for nontreatment was recorded for 65 inmates (52%) although on review, it was thought that the most likely reason was because of unremarkable serum liver enzymes.

Table 1 shows the baseline characteristics of those treated. The correctional institutions studied only incarcerated males. The majority of inmates had a history of substance abuse, of which 70 (77%) had a history of injection drug use. Of the 90 inmates who underwent treatment, HCV genotype 1 was predominant, with just over one-half of the cohort infected with this strain (54%). One-third of the cohort was infected with genotype 3 and the remainder with genotype 2. Sixty-three inmates (70%) underwent liver biopsy, with the majority having a fibrosis score of 1 or 2 (11).

Thirteen inmates were lost to follow-up. Of these, 10 inmates had undetectable HCV at end of treatment. On an intention to treat (ITT) basis, the overall SVR rate was 47.7%. Analysis on a per protocol (PP) basis (ie, those who had a six-month post-treatment HCV-RNA) revealed an SVR rate of 55.9%. SVR for genotype 1 (n=49) was 24.5% (ITT) and 31.6% (PP), genotype 2 (n=11) was 100% (both ITT and PP), and genotype 3 (n=30) was 66.7% (ITT) and 71.4% (PP). Because of the movement of inmates between institutions, it was not possible to exactly determine effect of security level on treatment outcome or adherence. However, this did not appear to be at all related.

The most common adverse effects reported were insomnia and mood disorders (31%). Sixteen inmates (18%) had an antidepressant added to their medication regimen. Twenty-four

inmates (26.6%) were started on a benzodiazepines, while two (2.2%) were started on an antipsychotic agent. Other common adverse effects included headaches, rash, fatigue, nausea and decreased appetite. There were no reported suicide attempts. Eight inmates stopped treatment because of intolerance to side effects at an average of 19 weeks (range nine to 31 weeks). All inmates who stopped treatment were HCV genotype 1. None were discontinued treatment for psychiatric reasons. Five inmates required a reduction in the dose of interferon. All inmates who completed treatment achieved at least 80% adherence of the doses and duration of interferon and ribavirin therapy.

DISCUSSION

The present study was the first to assess the effectiveness of treatment of HCV within the Canadian prison system. Although the efficacy of antiviral agents is well known, the effectiveness of therapy, a concept that includes feasibility of treatment in a clinical setting such as the Canadian correctional system, has not been studied. Our experience demonstrates that the treatment of HCV within prisons is clinically feasible and that the SVR rates obtained in this incarcerated population are comparable, if not superior, to rates achieved in the community. The present study also suggests that concerns about treatment in this setting, including the need for a significant commitment from the inmate, anticipated poor adherence, prior history of psychiatric illness, substance abuse and risk of reinfection, may not be valid. A significant reason for reluctance with regard to treatment of HCV in Canadian prisoners is the concern that the incarcerated individual with HCV may not be able to make the commitment needed to complete 24 to 48 weeks of interferon-based therapy in combination with ribavirin, given that this is a very difficult regimen to tolerate. In the present study, we noted that an overall adherence rate of 80% to dose and duration of therapy was achieved, despite over 60% of inmates experiencing some adverse effects. We note that only 9% of inmates withdrew from treatment because of intolerable adverse reactions, a rate that is comparable with the withdrawal rates observed when treating the general population. Reichard et al (12) reported a 7% withdrawal rate and McHutchison et al (5) found a 6% withdrawal rate. Furthermore, although 5% of the inmates treated in the present study had a previous history of depression, no inmates stopped treatment because of psychiatric side effects. Sixteen of the 90 inmates (17%) were started on an antidepressant, but there were no reports of attempted suicide during the treatment period. We believe that our experience shows that treating HCV in the prison population is no less likely to fail than treating this disease in the community at large, and that the closer monitoring of psychiatric side effects in the prison setting allows interferon to be safely administered even in inmates with a previous history of psychiatric illness. Moreover, we noted a high proportion of genotypes 2 and 3, which are associated with a high a priori likelihood of treatment success with a shorter duration compared with genotype 1 (6,7); this may be additional motivation to consider therapy.

Since a 1995 Canadian survey (13) reported that 11% of inmates continue to inject drugs while in prison, a belief that there are high rates of injection drug use and subsequently risk of reinfection with HCV within the prison system may also be a reason for reluctance regarding treatment. Although injection drug use has become the major mode of transmission of HCV since routine screening for HCV in the blood supply started in 1990, accounting for nearly 60% of newly acquired infections with an estimated 50% to 80% of needle-sharers expected to become infected with HCV after one year of drug use, and although almost all become infected after eight years of use, to date, there is no clear consensus on what the HCV reinfection rates are in Canadian inmates (14). In the present study, 77% of the prisoners treated had a previous history of injection drug use, and it is possible that a proportion of these individuals continued to use drugs while in prison. Nonetheless, most of our study population were adherent to therapy, and 56% achieved an SVR at one year. The specific issue of possibility of reinfection was beyond the scope of the current study; however, we speculate that those prison inmates who commit to a prolonged course of antiviral therapy are less likely to risk reinfection, especially if counselling is included as part of an anti-HCV therapy program.

It may be argued that treatment of HCV-infected incarcerated individuals should be deferred on the basis of cost. A health economic analysis was beyond the scope of the current study, but the material pharmaceutical costs as well as laboratory monitoring, etc, must be balanced against the costs of treating chronic liver failure, its complications and the potential for further spread of HCV in the community at large. As previously noted, the prevalence of HCV within prisons in Canada is estimated to be between 28% and 40%. Given that the majority of inmates enter the Canadian federal system between 30 and 50 years of age and are released within six years, treating inmates and initiating harm reduction strategies while in prison has great potential in curbing the spread of HCV. This may be especially important because access to adequate primary health care in regard to HCV may be uncertain once the incarcerated individual leaves the correctional facility.

Our experience suggests that treating HCV in the Canadian correctional services setting is effective both in terms of administration of treatment and antiviral efficacy. Our experience highlights a unique opportunity to treat a population with a high prevalence of HCV, especially because most can be expected to return to the community within a few years. To maximize the global effectiveness, we believe that the treatment of HCV should include pharmacological therapy, counselling programs and provision of mental health support, in addition to drug addiction programs.

DISCLOSURES: This work was presented as poster presentation at Digestive Diseases Week, New Orleans, Louisiana, USA in May 2004.

DISCLAIMER: Any opinions expressed in this paper reflect those of the authors only and may not be reflective of the opinions or policy of Correctional Service Canada or the Government of Canada.

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