Indications for interferon/ribavirin therapy in hepatitis C patients: Findings from a survey of Canadian hepatologists

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OBJECTIVE: To survey practising hepatologists about their attitudes and practices regarding interferon and ribavirin combination therapy for hepatitis C (HCV) patients in Canada.

METHODS: A nonanonymous fax and mail survey in Canada. The questionnaire consisted of two sets of questions: the likelihood (in percentage) of treating a patient with certain clinical characteristics; and opinions (Yes/No) regarding how his/her treatment decision is influenced by other factors (ie, patient age, genotype). Thirty-eight of 44 eligible participants responded to the survey with a response rate of 86.4%.

RESULTS: Most participants indicated that they were likely to treat patients with "moderate/severe hepatitis with fibrosis" (median 80.0%), and compensated cirrhosis (median 75%). However, the participants were less willing to treat patients with coexisting conditions (median 25.0%) or mild hepatitis (median 13.8%).

CONCLUSIONS: The findings from the present study indicate that there is a substantial variation in opinion among Canadian hepatologists towards treating HCV patients. The present study, however, suggests that the survey respondents appear, in general, to adhere to the HCV treatment guidelines by the Canadian Association for the Study of the Liver.

Key Words: Hepatitis C; Interferon; Practice guidelines; Practice patterns; Survey; Therapy

Infection with hepatitis C (HCV) is one of the most common causes of liver disease, affecting approximately 1% of the Canadian population (1,2), and is the single most common reason for liver transplantation (3). In the past several years, the management of chronic HCV infection has evolved rapidly and antiviral treatment has become an important aspect of care for people infected with HCV. A number of recent, large clinical trials have shown that in comparison with interferon monotherapy, interferon/ribavirin combination treatment has significantly increased the sustained response rates in patients with chronic HCV (3,4). Thus, interferon/ribavirin treatment has become a mainstream clinical modality in treating chronic HCV patients. However, little is known regarding how Canadian hepatologists prescribe the combination to their HCV patients and how various disease-related (eg, disease stage) and patient-related factors (eg, age and comorbidity) influence hepatologists’ clinical decision-making. Little is known also about clinicians’ adherence to guidelines regarding antiviral therapy, such as the newly developed chronic HCV treatment guidelines by the Canadian Association for Study of the Liver (CASL) (5).

Canadian liver specialists were surveyed to gain knowledge of the current clinical practice regarding interferon and ribavirin treatment in hepatitis C patients.
avirin combination therapy for HCV patients in Canada, and to provide insights regarding adherence to published guidelines.

METHODS

Fifty-four clinicians with special expertise in liver diseases (hepatology) were identified through two steps. First, the latest version of the Canadian Medical Directory (CMD) on CD-Rom (6), which contains information regarding 58,621 currently practicing Canadian physicians, was used for a comprehensive search. Based on their practices, physicians were grouped into their corresponding main specialties (one or more). Although CMD allows searches by 60 specialties (eg, cardiology and rheumatology) and 45 subspecialties (eg, diabetes, pain management), hepatology was not indexed as a main or subspecialty. Thus, a systematic search was conducted in the specialties of gastroenterology, infectious diseases, endocrinology and pediatrics, searching for text with any mention of hepatology. In total, 43 potential hepatologists were identified from the CMD. Of this group, 79% were identified as liver specialists (with or without an additional descriptor; eg, gastroenterologist), 13% were identified as gastroenterologists and 8% were identified as internists.

As another independent source, two of the present coauthors (LS and JH) were asked to provide names of active hepatologists based on their knowledge of colleagues across the country. An additional 11 active hepatologists, who were all listed as gastroenterologists in the CMD, were identified. A one-page questionnaire along with a cover letter outlining the study objectives was sent to all eligible hepatologists across 10 provinces between November 2001 and January 2002 via fax (85%), or by mail (15%) when fax numbers were not available. The survey requested information regarding current practice patterns using interferon/ribavirin combination therapy. Participants were also asked to take into account any changes that they would make based on the availability of pegylated interferon in the near future. The questionnaire consisted of two sets of questions:

- Opinions (Yes/No) regarding how his/her treatment decision is influenced by other factors (ie, patient age, genotype).

All questionnaires were anonymous and no personal characteristics (ie, age, sex and years in practice) were asked in the survey. Demographic characteristics were obtained from the CMD. A reminder letter along with a stamped return envelope and the original questionnaire was sent to all nonresponders four weeks after the initial contact.

ANALYSES

Simple descriptive statistics were used to describe central tendency (mean, median) and range for each survey item. The 95% CI for means were calculated using the conventional normal distribution method. Because there is no available statistical formula to directly calculate the 95% CI for medians, a bootstrap approach was employed (7,8). This technique involved dividing the total participants into subgroups (replicates), from which a random sample is taken with replacement and a new median was calculated each time. A fer a large number of such experiments, the lower and upper 95% CI were determined from the values at 2.5% and 97.5% percentiles. All the calculations were performed using SAS 8.0 (SAS, USA) (9).

RESULTS

Of the 54 potential participants, 10 were ineligible and excluded because they had retired (1), moved (4), were no longer treating HCV patients (3) or lacked correct contact information (2). In total, 38 participants responded, resulting in a response rate of 86.4%. The mean length of clinical practice (based on the year of graduation) for the 38 eligible participants was 21.5 years with a SD of 10.3 years. Nineteen per cent were women and 82.4% reported liver disease as the major component of their practice.

Table 1 provides summary estimates of the likelihood that a hepatologist in Canada would prescribe interferon/ribavirin therapy to a HCV patient at various stages. The results show a substantial variation in most questions. Most clinicians indi-
Patients with more severe fibrosis or compensated cirrhosis are normally considered to be treatment candidates, and decompen-sated liver disease is regarded as an absolute contraindica-
tion. However, there is less clarity as to whether and which
severity of liver disease is regarded as an absolute contraindi-
cation and treatment is not recommended (5). The guidelines
indicate that patient and liver biopsy in treatment decisions. Although
clinicians adhere to the CASL guidelines with respect to
treatment of patients with normal enzymes (6% versus 12%) and mild hepatitis (29% versus 32%) would be treated. The results also
demonstrated less variability among clinicians was observed for these
tients (range 0% to 100%) and future guidelines should
address this question specifically.

Survey respondents appeared to be aware of the importance
of genotype and liver biopsy in treatment decisions. Although
The present study has limitations. We considered a limited
number of factors, and did not exhaustively explore the role of
all potential disease-related and patient-related factors. The
role of human immunodeficiency virus, geographical, demo-
raphic and economic barriers to treatment, such as varying provincial reimbursement policies for antiviral therapy, were not considered. We could not evaluate the extent to which physician disagreement with published guidelines accounted for practice that deviated from that suggested by guidelines. Survey responses often differ from actual prescribing practice. Nonetheless, given the completeness of the sample and the relatively high response rate for a physician survey, we believe that the present survey presents an accurate, if brief, snapshot of the factors used by Canadian liver specialists in allocating antiviral treatment for HCV patients. It also demonstrates that hepatologists in general do adhere to the CASL guidelines on treatment. Finally, heterogeneity in practice patterns in certain groups (eg, patients with mild to moderate fibrosis) suggests that future iterations of treatment guidelines may benefit from a greater degree of specificity, so as to allow patients to be offered consistent treatment recommendations based directly on evidence.

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REFERENCES
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