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Access to care of patients with chronic hepatitis C virus infection in a university hospital: Is opioid dependence a limiting condition?

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ABSTRACT

Background: We aimed to examine access to care of opioid-dependent patients with chronic hepatitis C.
Methods: A standardized form was used to conduct a retrospective survey from 1999 to 2003 in a French university hospital. All HCV RNA positive in- or outpatients who had not had a liver biopsy or anti-HCV treatment were included. Opioid-dependence was defined as active opioid drug use or being on opioid substitution treatment.
Results: The survey included 580 patients; 137 (23.6%) were opioid-dependent. Fewer patients with than without current opioid dependence had had genotyping (40.1% versus 67.7%, $p < 0.001$), liver biopsy (51.8% versus 62.8%, $p = 0.022$), and anti-HCV treatment (8.8% versus 18.3%, $p = 0.008$). Genotyping was independently, negatively, associated with: (1) current opioid-dependence (OR = 0.3, 95%CI = 0.2–0.5), (2) former opioid-dependence (OR = 0.5, 95%CI = 0.3–0.9), (3) unemployment (OR = 0.5, 95%CI = 0.3–0.7), and (4) HCV infection discovered by screening (OR = 0.5, 95%CI = 0.3–0.7). Access to liver biopsy was independently, negatively associated with current opioid-dependence (OR = 0.6, 95%CI = 0.4–0.9), but positively associated with alcohol consumption (OR = 2.0, 95%CI = 1.2–3.4) and abnormal ALT level (OR = 2.2, 95%CI = 1.5–3.2). Access to anti-HCV treatment was independently, negatively associated with HCV infection discovered by screening (OR = 0.5, 95%CI = 0.3–0.9), but positively associated with moderate hepatitis (OR = 6.8, 95%CI = 2.8–16.8), extensive fibrosis or cirrhosis (OR = 12.3, 95%CI = 5.5–27.5), abnormal ALT level (OR = 2.1, 95%CI = 1.3–3.6) and age (40–64 years) (OR = 1.9, 95%CI = 1.0–3.4).
Conclusions: Genotyping and liver biopsies were performed less frequently on current opioid dependent patients. Absence of genotyping was also independently associated with unemployment and former opioid-dependence. Alcohol consumption or abnormal ALT levels favored access to biopsy. Histological grade strongly conditioned access to anti-HCV treatment.

1. Introduction

Approximately 2% of the world population (Shepard et al., 2005) is infected with hepatitis C virus (HCV). The infection rate in France is 0.84% (95%CI: 0.65–1.10) (Meffre et al., 2006). In Western countries, 30–98% of intravenous drug users (IVDUs) are infected with HCV (Roy et al., 2002) and, since the 1990s, they have been a major source of new HCV infections (Williams, 1999). Severe liver complications (e.g. cirrhosis, hepatocellular carcinoma) occur in more than 20% of patients with chronic HCV infection (Roudot-Thoraval et al., 1997). The prognosis for IVDUs with HCV infection is often poorer than for other patients because of other factors (e.g. hepatitis B virus [HBV], human immunodeficiency virus [HIV] or excessive alcohol consumption) (Seeff and Hoofnagle, 2002). Therefore, screening and treating HCV infection in IVDUs is essential for public health and economic reasons (Sheerin et al., 2003). However, until 2002, no guidelines recommended anti-HCV treatment for current illicit drug users, because of suspected poor compliance with the treatment and a higher risk of re-infection (Anonymous, 1997; Anonymous, 1999). Only recently have studies shown that IVDUs can be effectively treated for HCV infection (Robaeys and Buntinx, 2005; Van Thiel et al., 2003). A French Consensus Conference (Seeff and Hoofnagle, 2002) recommended that IVDUs receive anti-HCV treatment, managed by a multidisciplinary

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team. Despite guidelines recommending anti-HIV treatment for IVDUs, previous studies (Carrieri et al., 1999; Hu et al., 1995) found that it was more difficult for these patients to receive anti-viral HIV treatment because physicians did not regard their psychological, sociological and economic conditions as optimal. This is the first study to consider specifically the access to care of opioid-dependent patients with and without chronic HCV infection (with or without HIV coinfection), in a university hospital.

We hypothesized that current opioid-dependent patients (i.e., on opioid substitution treatment [OST] or active opioid drug users) with HCV infection, would be confronted with difficulties relating to diagnosis and treatment similar to those encountered by HIV-infected IVDUs.

The aim of our study was, therefore, to examine whether current opioid-dependence were less likely to have access to genotyping, liver biopsy or anti-HCV treatment than other patients.

2. Methods

2.1. Study design

We conducted a retrospective study from January 1st, 1999 to April 30th, 2003 using a structured form filled out by physicians in charge of patients with chronic hepatitis C.

2.2. Setting

The survey was performed at Cochin Hospital, a Paris university hospital belonging to the *Assistance Publique – Hôpitaux de Paris* (the Paris Public Hospital network (41 hospitals)). This hospital (1376 short-stay beds in two different locations) provides all major medical and surgical services, except nephrology, neurosurgery and cardiovascular surgery.

2.3. Study population

All in- or outpatients, aged 18 years or over, were included in the study from January 1st, 1999 to April 30th, 2003. These patients tested positive for HCV RNA (polymerase chain reaction (PCR) on serum samples), and never had a liver biopsy or received anti-HCV treatment (i.e., naive patients). We excluded patients with unknown transaminase levels (ALT and AST), biopsy dates or periods of treatment. Informed consent was obtained from patients for inclusion in the study, and data collection was approved by the CNIL (*Commission Nationale de l'Informatique et des Libertés*; the French Data Protection Agency).

2.4. Data collection

Data were collected during the survey period by the physician in charge of the patient. Information was recorded at the patient's first visit and once yearly thereafter, regardless of the number of follow-up visits. Physicians filled out a structured form during the patient's visit (interview, examination, biological data). Forty-one senior physicians belonging to a medical unit agreed to participate in the study and included patients. A clinical research technician was responsible for imputing the missing data on incomplete forms. Information collected included: self-reported sociodemographic characteristics, current drug or alcohol consumption, presence or absence of OST, modes of transmission, date of first exposure to transmission risk factors, circumstances of diagnosis, known HIV or HBs serostatus, other associated severe diseases, biological data, HCV genotype, and dates of biopsy and of anti-HCV treatment.

2.5. Definitions of variables

We compared active drug users (32 patients) and patients on OST (105 patients) and found no differences in sociodemographic characteristics, alcohol consumption, biological data, genotyping, access to biopsy and anti-HCV treatment (data not shown). This led us to create a variable "current opioid-dependent patients", pooling those patients who reported active opioid drug use or OST (methadone or buprenorphine) at the time of their medical visits. For multivariate analyses, we analyzed opioid dependence in three categories: "current opioid-dependent patients", "former opioid-dependent patients" and "never opioid-dependent patients". The former opioid-dependent patients were those declaring HCV transmission through intravenous drug use but not actively using drugs or on OST during the study period. The duration of infection was estimated from the period between first exposure to transmission risk factors (reported by the patient) and the time of inclusion in the study. Alcohol consumption, assessed by physicians during the patient's interview, was classified as 0–29 g/day or ≥30 g/day. ALT and AST levels were classified according to threshold values: 90 IU/ml (≥2N) was considered abnormal. HCV genotypes were categorized as genotype 1, genotypes 2 or 3, and others. Liver histological lesions were categorized on the basis of Metavir score as: "no or minimal hepatitis" (A ≤ 1 and F ≤ 1), "extensive fibrosis or cirrhosis" (F3 and F4) and "other lesions" (Bedossa and Poynard, 1996). If several results were obtained for a given variable, at different follow-up visits during the study period, only the most severe result was considered for analysis. Access to liver biopsy was defined as: liver biopsy planned or performed. Access to anti-HCV treatment was defined as the prescription of anti-HCV treatment. Other associated severe diseases (other than HIV or HBV infections) were: certain infectious and parasitic diseases; neoplasms; hematological diseases and certain disorders involving the immune mechanism; endocrine, nutritional and metabolic diseases; mental and behavioral disorders; diseases of the nervous system; diseases of the circulatory system; diseases of the respiratory system; diseases of the digestive system; and diseases of the skin and subcutaneous tissue.

2.6. Statistical analysis

Data were analyzed using standard descriptive statistics as appropriate (frequency, mean, standard deviation [SD]). Bivariate analyses were performed, using (^{2}-tests to compare opioid-dependent patients and others. For multivariate analyses, we used logistic regression models to assess associations between access to care (i.e., genotyping, liver biopsy planned or performed or anti-HCV treatment prescribed) and sociodemographic, clinical and biological parameters. Those variables showing differences in access to care with a p-value ≤0.20 in univariate analysis were eligible for inclusion in the multivariate model. A stepwise inclusion procedure was used. Infection duration, alcohol consumption and histological grade were included in the regression models after multiple imputations of missing values. Five imputations, (using fully conditional specification for missing data (i.e., iterative Monte Carlo Markov Chain simulations)) were used to produce a pooled output, estimating the missing values in the original dataset. The final model included only factors making a significant contribution to outcome. Associations were expressed as odd ratio (OR) with 95% confidence intervals (95%CI). Statistical significance was set at the 0.05 level. SPSS Software for Windows™ version 17.0 was used for statistical analysis.

3. Results

3.1. Patient characteristics and methods of hepatitis care

The characteristics of the 580 naive HCV-positive patients included in the study are presented in Table 1; 68.6% were men, with a mean age of 43.7 years (SD: 12.9), and a median age of 41 years (range: 18–92), 41.4% were unemployed and 9.1% retired. HIV positive serostatus was reported for 22.1% of patients with known HIV serostatus. Among patients with known alcohol consumption, 72.8% drank less than 30 g a day; among those genotyped, 56.1% had genotype 1, and among those with a biopsy, 140 had moderate hepatitis or extensive fibrosis or cirrhosis. The opioid-dependent group included 137 patients (23.6%): 19 (13.6%) were both active opioid drug users and on OST; 13 (9.3%) reported only current active opioid drug use without OST; and 105 (75.0%) were on OST without current active opioid drug use. Two hundred sixty-six patients (45.9%) had access to liver biopsy without receiving anti-HCV treatment; 83 (14.3%) had access to liver biopsy and to anti-HCV treatment, and 10 (1.7%) received anti-HCV treatment without previous liver biopsy.

3.2. Comparison between current opioid-dependent HCV patients and others

Current opioid-dependent HCV patients were more likely to be male, younger and unemployed than other patients (Table 1). They had a higher rate of alcohol consumption, more frequent known HIV positive serostatus, but suffered less from another associated severe diseases. One third of the other patients had been exposed to hepatitis C through intravenous drug use. No difference was found between current opioid-dependent patients and others for ALT and AST levels, genotype groups or histological grades. Liver biopsy and genotyping (performed or planned) were less frequent for current opioid-dependent patients, who were also less frequently prescribed anti-HCV treatment