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ORIGINAL ARTICLE

Management of psychiatric disorders and addictive behaviors in patients with viral hepatitis C in France

Prise en charge des troubles psychiatriques et des conduites addictives chez les patients atteints d'hépatite C en France

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Summary

Introduction. – Guidelines concerning the management of psychiatric disorders and addictive behaviors in patients with chronic hepatitis C and the conditions of collaboration between hepatogastroenterologists, infectiologists, psychiatrists and psychologists have not been published. This has a negative influence on optimal therapeutic management of chronic hepatitis C virus (HCV) infection. The aim of this study was to describe the current clinical practices for ambulatory management of psychiatric disorders and addictions, and the influence of a possible psychiatric and/or psychological collaboration.

Patients and methods. – A retrospective survey was conducted among 101 clinicians treating patients with chronic hepatitis C. Data were collected from personal interviews with the managing clinicians and from the files of patients with chronic hepatitis C patients who presented psychiatric disorders.

Results. – Analysis of the 101 interviews and 598 patient files showed that 19% of patients had not received an optimal treatment for their HCV infection because of a psychiatric problem, and that less than 50% of the managing clinicians were working in collaboration with a psychiatrist or a psychologist. In conclusion, lack of collaboration between hepatogastroenterologists

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and psychiatrists could be deleterious for the optimal treatment of HCV infected patients. Improvement is required.

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Résumé

Introduction. – Les recommandations concernant la prise en charge des troubles psychiatriques et des conduites addictives, chez les patients atteints d'hépatite chronique C, et les modalités de collaboration entre médecins somaticiens, psychiatres et psychologues sont peu formalisées. Ces carences influencent négativement la prise en charge thérapeutique. Le but de cette étude était de décrire les pratiques actuelles de prise en charge ambulatoire des troubles psychiatriques et des addictions par les médecins somaticiens et l'influence d'une collaboration psychiatrique et/ou psychologique éventuelle.

Matériel et méthode. – Il s'agit d'une enquête rétrospective menée auprès de 101 médecins somaticiens à partir d'entretiens individuels et d'une analyse de dossiers de patients atteints d'hépatite chronique C ayant une problématique psychiatrique.

Résultats. – L'analyse des 101 questionnaires et des 598 dossiers a montré que 19% des patients ne bénéficiaient pas d'un traitement optimal pour raisons psychiatriques et que moins de 50% des médecins travaillaient avec un psychiatre et/ou un psychologue. En conclusion, le manque de relations entre les médecins hépatologues et les psychiatres pourrait être délétère pour la prise en charge thérapeutique des malades et ces relations nécessitent donc d'être améliorées.

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Introduction

In the general population in France, the estimated prevalence of chronic hepatitis C virus (HCV) infection is 0.9% [1]. In psychiatric and penitentiary populations, it is thought to be much higher, to the order of 6 to 7% [2,3]. In addition, 16 to 40% of alcoholic patients and 60% of drug users are infected by the HCV [4,5].

At the present time, the standard treatment for chronic HCV infection is a 24–48 week regimen, depending on the HCV genotype, combining pegylated interferon in a weekly dose plus ribavirin taken daily. Globally this treatment is expected to achieve definitive eradication of the HCV in 60% of patients [6–8].

It is known however that only 50% of patients have a single virus infection (HCV alone) and about 40% of patients with human immunodeficiency virus (HIV) co-infection are treated. HCV infection is one of the main causes of death in patients with HIV/HCV co-infection [9,10].

Psychiatric disorders and addictive behaviors are commonly observed in patients with HCV infection, greatly hindering efficient care [9–12]. These problems are probably the main reasons why antiviral treatment is either not started or if started later discontinued, with the known consequences of diminished quality of life [11–23].

Although many studies have demonstrated that appropriate support for psychiatric and addictive problems improves patient adherence and sustained virological response to levels comparable with the general population [11,18,21–23], and despite recommendations for extended therapeutic indications in patients with these problems [8,19], many are still not receiving optimal antiviral treatment.

The purpose of this study was to learn more about current clinical practices for the management of psychiatric disorders and addictive behaviors in patients with chronic HCV infection. Secondary objectives were to determine whether psychiatric disorders and addictive behaviors hinder

initiation of antiviral treatment or favor its discontinuation, to analyze the impact and frequency of collaboration between managing clinicians and psychiatrists and/or psychologists, to describe how managing clinicians assess psychiatric disorders and addictive behaviors, and to ascertain the nature and modalities of practices employed when psychiatric disorders develop during antiviral treatment.

Patients and methods

This was a survey of current practices conducted in May and June 2007 among French clinicians, hepatogastroenterologists and/or infectiologists, specialized in the management of patients with HCV infection. The participating clinicians were selected at random among the 400 clinicians in France managing more than 10 patients with HCV infection per year. The random sample took into account the national distribution by specialty (80% hepatogastroenterology and 20% infectiology) as well as the type of practice (75% hospital physicians, 25% private practitioners).

Fifty-one hospital hepatogastroenterologists (29 in teaching hospitals and 22 in general hospitals) and 22 private practitioners, as well as 28 hospital infectiologists (19 in teaching hospitals and nine in general hospitals) agreed to participate in the survey. The survey involved 29 university hospital centers and 22 general hospitals throughout France.

Data were collected during individual interviews with the clinicians, at their site of practice. The interviews were conducted by a trained professional who collected two types of information:

- data concerning patients currently managed by the specialist. A four-part questionnaire had 30 items on management practices for psychiatric disorders and addictive behaviors (diagnosis, assessment, treatment) before or during the antiviral treatment among patients who consulted during the preceding month. Collaboration or not with a psychiatrist or psychologist and the modalities of such collaboration as well as the clinician's expectations for treatment guidelines was noted;
- data were also collected from the files of the last six patients consulting the clinician for HCV infection whose psychiatric disorders before or during the antiviral treatment had contraindicated the

Table 1 Managing clinician's (hepatogastroenterologists and infectiologists) opinion concerning the importance of having an opinion from a corresponding psychiatrist or a psychologist.

		Very important (%)	Rather important (%)	Not very important (%)
Before treatment	Clinician who has a corresponding psychiatrist and/psychologist	55	41	4
	Clinician who does not have a corresponding psychiatrist and/psychologist	19	62	19
After treatment	Clinician who has a corresponding psychiatrist and/psychologist	7	51	2
	Clinician who does not have a corresponding psychiatrist and/psychologist	19	69	12

treatment, led to early discontinuation, or warranted referral for psychiatric management. This part of the survey involved 39 items. Clinicians were asked to furnish information from the files of at least two patients who had not received antiviral treatment for their HCV infection because of a psychiatric disorder.

The statistical analysis was performed with SPSS software. The Chi² test was used to compare qualitative variables and analysis of variance for quantitative variables. The threshold of statistical significance was 5%. Test results between 5% and 10% were noted for information. This survey was conducted by a professional agency, Stethos, with the support of Roche laboratories under the leadership of the C-Psy scientific committee.

Results

One hundred and one clinicians participated in the interviews and data were collected from 598 patient files: 215 files of patients who had not been treated because of a psychiatric problem (including 194 patients who had never received an antiviral treatment), 92 files of patients whose treatment was discontinued because of a psychiatric problem, and 291 files of patients presenting undesirable psychiatric effects during their antiviral treatment.

Currently managed patients

Among all patients managed by the participating clinicians during the month preceding the survey, 37.1% had HCV infection. Globally, 17.4% of patients followed by the clinician were treated for their HCV infection (i.e. less than 50%

of the patients currently managed by the clinician); 4.4% were not treated for their HCV infection (12.3% of current patients) and 2.3% had interrupted their antiviral treatment because of a psychiatric problem (6.4% of current patients).

Frequency and impact of collaboration with psychiatrists and/or psychologists

Less than 50% of the managing clinicians had an established collaboration scheme with a psychiatrist or a psychologist: 25% with a psychiatrist alone, 10% with a psychologist alone, and 14% with both. Clinicians who reported collaboration with a psychiatrist or a psychologist were more aware of the need for a specialist's opinion, particularly before starting an antiviral treatment. A psychiatrist's opinion was considered as "important" or "very important" by many clinicians, hepatogastroenterologists and/or infectiologists, before and during the antiviral treatment (Table 1). There was no difference in collaboration practices as a function of type of practice (hospital, teaching or general hospital, private practice) (Table 2).

Assessment of psychiatric disorders and addictive behaviors

For 78% of the managing clinicians, a psychiatric assessment was obtained "always" or "often". Ninety percent of the clinicians performed this assessment themselves, without using a standardized diagnostic tool. Before starting

Table 2 Established collaboration with a psychiatrist and/or psychologist by type of practice.

Type of clinician	Collaboration	No collaboration	<i>p</i> ^a
Hospital hepatogastroenterologist (<i>n</i> = 51)	25 (50%)	26 (50%)	NS
Infectiologist (<i>n</i> = 28)	14 (50%)	14 (50%)	
Private practice hepatogastroenterologist (<i>n</i> = 22)	10 (45%)	12 (55%)	
Total (<i>n</i> = 101)	49	52	

NS: not significant.

^a Chi² *p* = 0.95.

an antiviral treatment, 40% of the clinicians "always" or "often" requested the opinion of a psychiatrist and 20% "always" initiated a psychiatric follow-up for patients they considered at risk of developing a psychiatric disorder.

The clinicians searched for the following signs of psychiatric disorders: personal history of depression (75%), attempted suicide (31%), personal history of psychiatric and/or psychological disorders (22%), anxiety (19%), known psychosis (14%), bipolar disorders (6%). Conversely, few clinicians stated they searched for a family history of psychiatric disorders: depression (44%), attempted suicide (15%), bipolar disorders (7%).

Search for alcohol and opiate abuse was systematic for 83% and 59% of clinicians respectively, and 50% and 49% respectively searched for use of cannabis and tobacco. This assessment was performed generally by the managing clinician, without a standardized evaluation tool for 90%.

The managing clinicians who worked in collaboration with psychiatrists or psychologists considered psychiatric disorders, particularly bipolar disorders, to be of particular importance. Those who did not have access to this type of collaboration focused more on addictive behaviors (especially alcohol abuse) and, in the event of psychiatric disorders, on past history of depression or attempted suicide.

Reasons for not starting or interrupting antiviral treatment

The decision to interrupt an antiviral treatment because of a psychiatric disorder was made by the managing clinician alone in 23% of the cases. When another opinion was necessary before stopping the antiviral treatment, it was requested from a psychiatrist for 75% of the cases and from a psychologist for 2%. Psychiatric disorders and addictive behaviors which led to exclusion from antiviral treatment are summarized in Table 3. The decision to not treat was significantly less frequent among clinicians who had access to collaboration with a psychiatrist and/or a psychologist (Table 4).

Table 3 Psychiatric states leading to exclusion from antiviral treatment.

<i>Current state of depression (%)</i>	
Systematic exclusion	46
Common exclusion	43
<i>Personal history of a psychotic episode (%)</i>	
Systematic exclusion	24
Common exclusion	53
<i>Opiate addiction (%)</i>	
Systematic exclusion	19
Common exclusion	42
<i>Alcohol addiction (%)</i>	
Systematic exclusion	17
Common exclusion	53
<i>Signs of hypomania (%)</i>	
Systematic exclusion	17
Common exclusion	55

Management practices for psychiatric disorders and prescription of psychotropic drugs

Hepatogastroenterologists and/or infectiologists often prescribed psychotropic drugs themselves. Before treatment, these clinicians prescribed anxiolytics (75%), hypnotics (53%), and antidepressants (51%).

For clinicians with access to a collaborating psychiatrist, more than half (59%) referred the patient to the psychiatrist for prescription of antidepressants.

Expectations of the managing clinicians

For 70% of the hepatogastroenterologists and infectiologists managing patients with HCV infection, the contraindications for antiviral treatment are not well defined. Thus,

Table 4 Influence of collaboration with psychiatrists or psychologists on psychiatric assessment, decision, or prescription of psychotropic drugs.

Clinician's statement of management practices (n = 101)	Without collaboration (%) (n = 49)	With collaboration (%) (n = 52)	P ^a
Systematic referral for psychiatric opinion before antiviral treatment	50	63	NS
Intention to abstain from treatment in the event of hypomania	63	47	NS
Intention to abstain from treatment if there is a history of depression or anxiety disorders	25	4	0.01
Intention to stop antiviral treatment early if depressive symptoms or anxiety disorders develop	31	14	0.07
Prescription of antidepressants by the clinician	31	12	0.04

NS: not significant.

^a Chi²

Table 5 Characteristics of the patients in the study cohort.

	Never treated for hepatitis C (<i>n</i> = 215)	Not treated after discontinuation of a prior antiviral treatment (<i>n</i> = 92)	Ongoing antiviral treatment (<i>n</i> = 291)	<i>p</i>
Male (%)	63	64	62	NS ^a
Mean age (yrs)	42.2 ± 10.1	43.3 ± 11.5	44.2 ± 9.3	NS ^b
HIV co-infection (%)	26	32	21	0.08 ^a
Contamination drug abuse (%)	62	60	50	0.02 ^a
Genotype 1 (%)	62	71	44	< 0.001 ^a
Genotype 3 (%)	17	17	22	NS ^a

NS: not significant.

^a Chi².

^b Analysis of variance.

97% stated they wanted more precise definitions for the type of psychiatric disorders which contraindicated antiviral treatment as well as the reasons for referring patients to a specialist for the prescription of psychotropic drugs. Similarly, 78% of the practitioners wanted to have a clear definition of the contraindications for antiviral treatment among patients exhibiting addictive behaviors.

The characteristics of the patients included are given in Table 5.

Patients not given antiviral treatment because of psychiatric disorders (*n* = 215)

The decision not to treat was made by the managing clinician alone for 18% of the patients. Many clinical features were determinant for non-treatment: depression (58%), anxiety (42%), history of anxiety and depression (45%), history of addiction (33%). Eight-two percent of the patients were referred to a psychiatrist and/or a psychologist who decided not to treat (33% of patients) or to delay treatment onset (56% of patients).

Patients who had a prior antiviral treatment that was discontinued because of psychiatric disorders (*n* = 92)

The decision to discontinue antiviral treatment was made by the managing hepatogastroenterologist or infectiologist alone for 29% of the cases of interrupted treatment. The psychiatric disorders which led to treatment withdrawal were: suicidal ideation (48%), anxiety disorders (40%), impulsive aggressive behavior (29%), insomnia (29%), poor control of addictive behavior (15%), maniac crisis (12%), suicide attempt (10%).

For 20% of these patients, no therapeutic intervention was initiated before interrupting the antiviral treatment; 68% of the patients were referred for a psychiatric opinion. Psychotropic drugs were started, as a preventive measure for 27% and as a curative measure for 84%. In general, hypnotics and antidepressants were prescribed by the managing clinician as a preventive measure; curative antidepressants or antipsychotics were prescribed by the psychiatrist.

Patients receiving treatment and presenting psychiatric disorders (*n* = 291)

The main psychiatric disorders observed during the antiviral treatment were: anxiety (78%), insomnia (63%), impulsive

aggressive behavior (43%), signs of hypomania (12%), suicidal ideation (10%), maniacal behavior (8%). Uncontrolled addictive behavior was observed in 17%.

Half of the patients (51%) were referred to a psychiatrist and 25% to a psychologist; 35% of the patients were not referred to either specialist.

Psychotropic drugs were not generally prescribed for prevention (27%). Conversely, their use for curative purposes (85%) was much more common, generally with hypnotics, anxiolytics, and antidepressants. For the psychiatrists, the prescription of antidepressants was a preventive measure for 29% of the patients and a curative measure for 54%. Antipsychotic drugs were rarely used.

Discussion

The main limitations of this survey were the retrospective and declarative nature of the data collection. The specific opinion of the psychiatrist or psychologist was not recorded in this part of the survey but is the object of an ongoing analysis.

This survey demonstrated a major discordance between the clinical practices of physicians specialized in the treatment of viral hepatitis and current guidelines which recommend a multidisciplinary approach to patient management. A lack of a formally identified management scheme was also noted.

The results illustrate the importance of elaborating clearly defined procedures for determining contraindications for treatment due to psychiatric disorders or addictive behavior. They also highlight the need for a defined protocol for managing such disorders before, during, and even after antiviral treatment.

Although the managing clinicians stated that a psychiatric opinion is essential before and during antiviral treatment, only 39% of them had an established collaboration with a psychiatrist. When the managing physician considers that a psychiatric opinion was necessary for a patient at risk of a psychiatric disorder, it was effectively requested for only 20%. When a patient presented a psychiatric disorder during treatment, a psychiatric opinion was requested for 51%. If the antiviral treatment was discontinued, 71% of the patients were referred to a psychiatrist. These findings show that collaboration between hepatitis C specialists and psychiatrists is currently insufficient, despite the fact

that a clearly defined team approach has a demonstrated beneficial effect in terms of optimal care, adherence, and therapeutic efficacy, comparable to that observed in the general population [11–16,18].

This insufficient collaboration is probably related to insufficient implication of psychiatrists regarding this specific clinical situation, to the difficulty certain medical specialties have in working together, and the absence of clearly established guidelines. In addition, the current demographics of the psychiatric specialty in France and the lack of specific financial support for the development of such cooperative efforts are certainly involved.

In patients with HCV infection, psychiatric disorders greatly influence the decision to either not initiate antiviral treatment (12.3% of patients) or to interrupt it (6.4% of patients). In this survey, 18.7% of patients were not given an optimal treatment because they had a psychiatric problem. This situation arises because hepatogastroenterologists and infectiologists have to make difficult management decisions without the guidance of a standard method for assessing psychiatric disorders and their impact on the efficacy or tolerance of the antiviral treatment. Practitioners search for many different types of disorders, but with no particular hierarchy, and with a rarely formalized data collection system. Ninety percent of the clinicians in this survey searched for such disorders without the help of a standardized diagnostic or assessment tool, notably for assessing mood disorders or alcohol abuse, which are nonetheless essential elements to be identified. A few searched for essential elements such as a familial psychiatric history of bipolar disorders or suicide and isolated or apparently unmotivated events (an episode of depression or use of a psychoactive agent), often cited as the contraindications for treatment.

While psychiatric care could be expected to stabilize the patient's psychic state and enable sustained antiviral treatment, the only therapeutic intervention proposed for 20% of the patients was to interrupt treatment. Specialized care was instituted for only 65% of these patients and, even after the opinion of a psychiatrist had been requested, 33% of the patients who received psychiatric care were still not treated and 68% had their treatment discontinued. Considering these observations, it can be concluded that the awareness of psychiatrists concerning this specific problematics is insufficient.

For patients with HCV infection, current practices in France constitute a loss of chance. To change these practices, coordinated care schemes should be promoted. Practitioners should be given specific training for the management of psychiatric disorders in patients with chronic hepatitis C. In addition, guidelines concerning care practices before, during and after treatment should be published. These changes would also benefit other patients for whom, as has been suggested by certain reports, the impact of the secondary psychiatric effects of the antiviral treatment would be decreased [18,21–24].

The recommendations of the AFSSAPS, particularly those concerning the use of the *Mini International Neuropsychiatric Interview* (MINI) to assess psychiatric disorders, or the use of a user-friendly self-administered questionnaire such as AUDIT to assess addiction to alcohol, should be helpful in favoring the needed changes in management practices [17].

The main psychiatric symptoms observed during antiviral treatment cover the entire spectrum of mood disorders. Associated symptoms are often specific and related to manic or hypomanic behavior (irritability, aggressiveness, impulsiveness) or depression. A specialized assessment is required, both because of the complexity of the diagnosis and because of the implications for therapeutic decision-making [24,25]. In this context, hepatogastroenterologists and/or infectiologists frequently prescribe antidepressants (for prevention or cure) without having assessed the possible existence of bipolar disorders. The prescription of an antidepressant for a predisposed patient or a patient with a mixed set of symptoms can lead to manic or hypomanic transformation, serious behavioral disorders, interruption of care, or a modification of the cycle of the bipolar disorder [12,24]. Being overly "ready" to prescribe an antidepressant without carefully assessing the underlying psychopathological background can have prejudicial consequences, while less frequently prescribed antipsychotics might be indicated for certain patients with this type of symptom. The recent statement by the AFSSAPS should be helpful in establishing an appropriate therapeutic orientation [17].

While hepatogastroenterologists and infectiologists appear to appreciate having an expert opinion from a psychiatrist, indispensable for diagnosis, drug prescription, and the decision for hospitalization, it is also important to emphasize the major complementary and beneficial role of psychologists. These specialists contribute specific competencies in terms of identifying and assessing psychiatric disorders and in the practical implementation of individual or group psychotherapy. Thus, in order to optimize therapeutic management of patients with HCV infection, it is important to carefully define the expected contribution of each specialty and organize a well-coordinated management scheme.

Therapeutic decision-making should be based on a clinical assessment of patient needs rather than on resource availability. Each reference center should have an identified expert psychiatrist to coordinate care for patients with chronic HCV infection. This clinician could contribute expertise, facilitate care organization, orient management decisions, and create a link with colleagues in the psychiatrics department. This post might be funded within the framework of a general interest project or a psychiatric liaison activity.

Psychiatric disorders and addictive behaviors have a negative impact on access to care and optimal management of patients with chronic HCV infection. For these patients, the absence of an adapted, formally defined psychiatric management scheme and the lack of precise guidelines constitute a loss of chance for cure.

The development of multidisciplinary management schemes should be favored so that hepatogastroenterologists, infectiologists, psychiatrists and psychologists can coordinate their interventions within the framework of a well-coordinated network where each specialty has a defined mission. The designation of an expert psychiatrist for each referral center would be an important step in this direction.

This reorganization and the elaboration of management guidelines are the necessary prerequisites for efficient care

of patients with HCV infection who also present psychiatric disorders or use psychoactive substances [11,18,21,22,26].

These steps must also be taken in order to enable the research projects needed to determine more precisely the risk factors for the development of psychiatric disorders during antiviral treatment, the nosography of these disorders, the appropriate tools for their assessment and detection, and the most adapted treatments.

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