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The influence of antiviral therapy on psychiatric symptoms among patients with hepatitis C and schizophrenia

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Abstract

Background—Antiviral therapy for chronic infection with HCV is associated with significant neuropsychiatric side effects. Research indicates that patients with mental illness are less likely to receive antiviral therapy, despite limited data regarding the influence of antiviral therapy on psychiatric symptoms in patients with specific psychiatric disorders. The aim of this study was to determine whether antiviral therapy is associated with higher rates of psychiatric symptoms in patients with schizophrenia (SCHZ).

Methods—A regional Veterans Healthcare Administration database was used to identify veterans meeting criteria for this retrospective chart review. Patients confirmed to have SCHZ and to have received antiviral therapy for HCV between 1998 and 2006 ($n=30$) were compared with a control group of demographically matched (age, race and gender) patients with SCHZ who did not receive antiviral therapy ($n=30$). Clinicians blinded to antiviral therapy status used chart notes to evaluate whether patients exhibited prominent symptoms of SCHZ, depression or mania during a 6 month pre-treatment period, the treatment period and a 6 month post-treatment period (or during equivalent periods for the control group).

Results—Groups did not significantly differ in rates of symptoms of SCHZ, depression or mania during any study period. During the treatment period, groups did not significantly differ in rates of emergency room visits or inpatient hospitalizations.

Conclusions—Our retrospective chart review suggests that patients with SCHZ experience similar rates of psychiatric symptoms on and off antiviral therapy. Despite limitations and

constraints of the methods, our data suggest that SCHZ is not a contraindication to antiviral therapy for HCV.

Introduction

Within the US, chronic HCV infects approximately 1.8% of adults and 5.4% of veterans [1,2]. Individuals who suffer from schizophrenia or schizoaffective disorder (SCHZ) are at significantly higher risk for contracting HCV; for example, our group conducted a study utilizing a Veterans Healthcare Administration (VHA) medical record database and found that, of those tested for HCV, 9.9% (219/2,207) of veterans with SCHZ and no documented history of substance use disorder (SUD) were confirmed to have HCV compared with 31.1% (943/3,029) of veterans with comorbid SCHZ and SUD and only 5.3% (3,888/73,687) of veterans with no history of SCHZ or SUD [3]. Despite the disproportionately high prevalence of HCV among seriously mentally ill adults, many providers are reluctant to treat psychiatric patients who have HCV because of concerns that antiviral therapy might exacerbate psychiatric symptoms or that patients with psychiatric illness might be less compliant with antiviral therapy [4]. Our retrospective VHA database study found that patients with comorbid SCHZ and SUD were significantly less likely to receive antiviral therapy for HCV relative to controls without SCHZ or SUD [3]. Another VHA database study demonstrated that SUD, major depression, mild depression, bipolar disorder and SCHZ were each independently predictive of non-treatment for HCV [5].

Although psychiatric comorbidities are common among patients with HCV, few studies have examined HCV treatment outcomes within psychiatric populations. One study of 33 HCV-infected veterans treated with antiviral therapy for 6 months found that, despite similar virological response rates, 32% of patients with psychiatric comorbidities developed severe neuropsychiatric side effects that led to antiviral therapy discontinuation, compared with only 14% of patients without psychiatric comorbidities [6]. A larger retrospective chart review study revealed that patients with psychiatric disorders and/or SUDs ($n=294$) were as likely as controls without these comorbidities ($n=353$) to complete and respond to antiviral therapy for HCV [7]. Unfortunately, most published studies group all psychiatric diagnoses together and do not clarify whether specific diagnostic groups are at differential risk for psychiatric side effects, non-compliance or poor response.

To our knowledge, the only published study specific to patients with SCHZ is our retrospective chart review comparing antiviral therapy completion and response rates among 30 HCV-infected patients with SCHZ and a demographically matched control group of HCV-infected patients with no history of SCHZ [8]. In this study, we found that patients with SCHZ were no more likely than patients without SCHZ to prematurely discontinue antiviral therapy for psychiatric symptoms, medical complications or other adverse events. Moreover, patients with SCHZ completed and responded to antiviral therapy at rates comparable to those without SCHZ. The design of this study, however, prevented us from more directly exploring whether antiviral therapy contributes to an exacerbation in symptoms of SCHZ. Therefore, the goal of the present study was to extend our previous findings by comparing rates of psychiatric symptoms in patients with SCHZ who were receiving antiviral therapy for HCV to rates of psychiatric symptoms among patients with SCHZ and HCV who were not receiving antiviral therapy.

Methods

Patient selection and assessment

We conducted a retrospective medical record review of all patients with SCHZ and HCV infection who were receiving antiviral therapy between 1998 and 2006 at VHA facilities

within the Veterans Integrated Service Network 20 (VISN 20), which comprises Washington, Oregon, Alaska and Idaho. By using the VHA CHIPS data warehouse, which extracts data from electronic patient medical records at each facility, we first identified a pool of potential study candidates using three broad search terms: detectable HCV viral load by PCR, prescribed antiviral therapy between 1998 and 2006, and a diagnosis of SCHZ on at least one clinic encounter or their problem list. This search yielded a total of 76 individual records.

Complete electronic medical records were then reviewed to ensure that patients met full eligibility criteria for inclusion in the antiviral therapy group (ANT+): that is, the laboratory record and progress notes confirmed the patient was treated for HCV with antiviral therapy and, across progress notes, qualified providers evidenced reasonable consensus that the patient met criteria for SCHZ. Of the initial 76 cases, 43 (56.6%) were excluded because chart notes revealed that they did not have SCHZ (for example, although SCHZ had been listed on at least one encounter, chart notes indicated that the patient had no history of SCHZ, that the patient had been clearly diagnosed with other psychiatric disorders or SUDs or the diagnosis of SCHZ had been ruled out). Subsequently, a total of 30 individuals were included in the final ANT+ group. In several of these cases ($n=5/30$), the medical record indicated that symptoms of SCHZ were present during the study period and that SCHZ was the most probable working diagnosis throughout the record. In all other cases ($n=25/30$), the medical record indicated that there was a definitive diagnosis of SCHZ during the study period.

The CHIPS data warehouse was then used to randomly identify a demographically case-matched control group of individuals with SCHZ and HCV who had not received antiviral therapy (ANT- group). A thorough medical record review of the resulting sample was then used to confirm that patients met full eligibility criteria for the ANT- control group: that is, across the medical record progress notes, qualified providers evidenced reasonable consensus that the patient met criteria for SCHZ; patients had a detectable HCV viral load by PCR; and laboratory record and progress notes confirmed the patient had not been treated for HCV with antiviral therapy. A total of 31 cases were reviewed, but 1 case was excluded because of spontaneous clearance of HCV. This resulted in a total of 30 control participants matched to the ANT+ cases by age (± 5 years), race and gender.

Complete medical record reviews were conducted using structured data collection forms to collect data on demographic characteristics, mental health history and treatment, psychotropic/antiviral prescriptions, liver biopsy and laboratory results, and emergency room visits/inpatient hospitalizations during the study period. In order to ensure the reliability and validity of our data collection forms and procedures, 11.6% (7/60; 4 ANT+, 3 ANT-) records were each reviewed by two separate reviewers, blind to each other's responses. Average inter-rater agreement on variables of interest (including those listed in Table 1 and Table 2) was 87.6%.

For each patient, all medical record progress notes were then copied electronically into a separate clinical subject file. For those in the ANT+ group, this clinical subject file was divided into three study periods: the pre-treatment period, which included the 6 months prior to antiviral therapy; the treatment period, which varied in length; and the post-treatment period, which included the 6 months following antiviral therapy termination. Medical records for the ANT- group were reviewed using the same dates; therefore, study periods matched the ANT+ group. Next, study personnel carefully reviewed the electronic clinical subject file and removed any information that revealed the patient's identity or whether or not the patient was or had ever been on antiviral therapy. This included removing patient

and physician names and removing all antiviral therapy related text involving the terms 'interferon', 'IFN', 'riba', 'RBV', 'hep', 'treatment', 'Tx' and 'liver'.

Finally, one of two licensed and credentialed mental health providers with expertise in both HCV and serious mental illness, one psychiatrist (MD) and one clinical psychologist (PhD), were asked to review these revised clinical subject files and to complete clinician rating forms while blind to each patient's identity and ANT status. Clinician rating forms included items asking clinicians to evaluate whether or not, based on all available progress notes, each patient exhibited prominent symptoms of SCHZ, depression and/or mania across each of the three study periods. Specifically, patients were rated as having 'unstable SCHZ' if their chart notes indicated they were experiencing prominent positive and/or negative symptoms during the study period, beyond what would be typical for a patient's in-repisode baseline. Patients were rated as having a 'depressive episode' if chart notes indicated they were experiencing prominent depressive symptoms during the study period that most likely met the full criteria for a depressive episode or if chart notes indicated general consensus among qualified providers that the patient was experiencing a full-blown depressive episode. Patients were rated as having 'prominent manic symptoms' if chart notes indicated they were experiencing clinically significant manic symptoms, regardless of whether they met criteria for a manic episode. Criteria were used to evaluate for 'depressive episodes' rather than depressive symptoms because the range of individual depressive symptoms is so broad (for example, weight loss, insomnia, reduced concentration). These individual symptoms can frequently be attributable to non-psychiatric conditions (for example, medical comorbidities); it therefore proved unreliable to assess for the presence of individual depressive symptoms and more clinically meaningful to assess for full blown episodes. By contrast, criteria were used to evaluate for 'prominent manic symptoms' rather than episodes because the presence of manic symptoms was relatively infrequent, yet clear, and because providers did not tend to document adequate information to distinguish between prominent manic symptoms versus an episode. Clinicians were also asked to evaluate whether, relative to the pre-treatment period, a patient's schizophrenic symptoms (including both positive and negative symptoms) were 'worse' during the treatment period and whether, relative to the treatment period, a patient's schizophrenic symptoms were 'worse' during the post-treatment period. To ensure the reliability and validity of the clinician ratings, 13.3% (8/60; 4 ANT+, 3 ANT-) of records were each reviewed by both clinicians who were blind to each other's responses. Average inter-rater agreement on items relating to psychiatric symptoms (Table 3) was 90%.

Definitions

Antiviral therapy included either monotherapy or combination therapy with pegylated or non-pegylated interferon and, in the case of combination therapy, ribavirin. Psychiatric and SUD symptoms, episodes and disorders were based on diagnostic criteria as defined in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) [9]. Alcohol use disorders (AUDs) included abuse as well as dependence. Drug use disorder (DUD) included abuse of or dependence on any substance other than alcohol, nicotine or caffeine. Lifetime history of a disorder was based on evidence of the disorder at any point in the medical record. Active diagnoses were based on diagnoses addressed in patient progress notes within 6 months of antiviral therapy initiation. Alcohol and drug use were based on progress notes and urine drug analysis results. A patient was considered to be receiving alcohol or substance abuse therapy if they were followed by any addictions specialist for individual or group therapy or case management (not just medication management) to specifically address SUD. A patient was considered to be receiving mental health services if they were seen by any mental health specialist (for example, psychiatrist, psychiatric nurse practitioner, psychologist, mental health therapist or psychiatric social worker). A patient

was considered to be receiving psychotropic medications regardless of who prescribed them (for example, primary care provider).

Statistical analysis

For each of the three study periods, characteristics were compared across groups. At times, patient medical records yielded insufficient data to accurately specify or rate certain variables (for example, injection drug use or the presence of specific psychiatric symptoms) in which case patients were excluded from related analyses. For continuous variables, Mann–Whitney U tests were used to account for non-normal distributions. Dichotomous variables were evaluated with χ^2 statistics if all expected cell counts exceeded five; otherwise, Fisher's exact tests were used.

Results

Baseline characteristics for the total sample and for each group are included in Table 1. The total sample ($n=60$) was predominantly male, Caucasian and middle-aged. Because of case-matching, groups did not differ in terms of demographic variables (age, race and gender). The majority of the total sample had a lifetime history of AUD (49/60; 81.7%), but only 14.3% (3/21) of ANT+ patients with a history of AUD were known to be using alcohol within 6 months prior to starting antiviral therapy. Over half of the total sample had a lifetime history of DUD (39/60; 65.0%) and 22.2% (4/18) of ANT+ patients with a history of DUD were known to be using within 6 months prior to beginning antiviral therapy. Although compared with the ANT– group, the ANT+ group had lower rates of lifetime AUDs and SUDs, and higher rates of remission during the pre-treatment period; only the difference in rates of lifetime AUD reach statistical significance.

High rates of active psychiatric disorder other than SCHZ were present across both groups during the pre-treatment period; however, groups did not differ in terms of the rates of any type of active psychiatric disorder and both groups were equally likely to have been prescribed psychotropic medications at baseline. The ANT+ group was hospitalized less frequently for psychiatric reasons within 5 years of the treatment period than the ANT– group, but this difference was not statistically significant.

The ANT+ group was significantly more likely than the ANT– group to have abnormal liver laboratory results and most patients within the ANT+ group evidenced abnormally high alanine aminotransferase (ALT; 67.9%) and aspartate aminotransferase (AST; 75.0%) concentrations at baseline. Liver biopsy results were only available within the ANT+ group, of which 58.8% evidenced advanced fibrosis (stage 3 or 4) and 41.2% evidenced advanced inflammation (grade 3 or 4). Rates of advanced liver disease are high within the treated group probably because, historically, providers have not frequently recommended treatment to patients unless they have presented with clinical indications of advanced liver disease, such as abnormal liver functioning tests. Other factors could include the high rates of AUD among veterans with HCV. Within the total sample, genotype information was available for 55.0%, (33/60) of patients, with 60.6% (20/33) of those infected with either genotypes 1 or 4 and 39.4% (13/33) infected with either genotypes 2 or 3. Within the ANT+ group, all but one patient received combination therapy with ribavirin (96.6%). Most patients were prescribed pegylated interferon- α 2a (53.3%) or pegylated interferon- α 2b (30.3%), but 13.3% were prescribed interferon- α 2b and ribavirin. A detailed discussion of the completion and response rates for the ANT+ group, as well as related factors (for example, reasons for early discontinuation), can be found elsewhere [8].

For each treatment period, rates of psychiatric symptoms were compared across groups (Table 3). No significant differences between the ANT+ and ANT– groups were found

during any treatment period ($P>0.050$) in terms of rates of unstable SCHZ, depressive episodes or prominent manic symptoms. Although compared with the ANT+ group, the ANT- group had higher rates of unstable SCHZ during all treatment periods, these differences did not reach statistical significance. Likewise, although compared with the ANT- group, the ANT+ group had higher rates of depressive episodes during the post-treatment period, this difference did not reach statistical significance.

Groups did not differ in terms of the percentage of individuals whose SCHZ symptoms were rated as worse during the treatment period relative to the pre-treatment period (ANT+ 21.4% versus ANT- 26.1%). Likewise, there were no significant differences between the ANT+ and ANT- groups in terms of the percentage of individuals whose SCLJZ symptoms were rated as worse during the post-treatment period relative to the treatment period (ANT+ 26.9% versus ANT- 17.4%). There were also no significant differences between the ANT+ and ANT- groups in terms of the percentage of individuals whose SCHZ symptoms were rated as better during the treatment versus pre-treatment periods or during the post-treatment versus treatment periods.

Table 2 compares groups in terms of adverse events and psychiatric treatment factors present during the treatment period. Very few patients in either group required emergency room visits or inpatient hospitalizations during the treatment period, with no significant differences between groups. Although rates of alcohol and drug use were lower in the ANT+ group than the ANT- group, these differences did not reach statistical significance.

Within the total sample, despite high rates of lifetime AUD and DUD, only three patients were followed by an addiction specialist during the treatment period, only one of which was in the ANT+ group. However, during the treatment period, 85.0% of all patients received mental health services from a mental health specialist, and 55.0% had psychotropic medication dose adjustments. During the treatment period, the ANT+ group was significantly more likely to have received mental health services from a mental health specialist when compared with the ANT- group. Groups did not significantly differ in terms of rates of psychotropic medication adjustments.

For those in the ANT+ group, a more complete reporting of antiviral completion and response rates as well as reasons for early discontinuation and adverse events can be found elsewhere [8]. In brief, 53.3% (16/30) completed a full course of antiviral therapy as recommended by their provider. Of those who discontinued early, documented reasons for discontinuation included the following: 42.9% (6/14) treatment non-compliance, 42.9% (6/14) medical side effects, 14.3% (2/14) neuropsychiatric side effects, 14.3% (2/14) serious adverse events and 14.3% (2/14) inadequate viral response. Of those patients in the ANT+ group with genotype 1 (for whom standard care is to provide 48 weeks of antiviral therapy), 42.9% (6/14) achieved an end-of-treatment response (ETR; defined as an undetectable HCV viral load upon treatment termination) and 35.7% (5/14) achieved a sustained viral response (SVR; defined as an undetectable HCV viral load at least 6 months after treatment termination). Of those patients with genotypes 2 and 3 (for whom standard care is to provide 24 weeks of antiviral therapy), 100% (13/13) achieved an ETR and 76.9% (10/13) achieved an SVR. Post-hoc Fisher's exact analyses were conducted to determine whether patients within the ANT+ group were more likely to have experienced a depressive episode during the post-treatment period if they achieved an ETR or an SVR. Although those who achieved an ETR had a lower rate of depression (6/18; 33.3%) than those who did not achieve an ETR (4/7; 57.1%), this difference did not reach statistical significance. Differences were statistically significant in that those who achieved an SVR had a significantly lower rate of depression (3/15; 20.0%) than those who did not achieve an SVR (7/10; 70.0%).

Discussion

Our retrospective chart review suggests that patients with SCHZ and HCV infection who do and do not undergo antiviral therapy experience comparable rates of psychiatric symptoms, suggesting that antiviral therapy does not disproportionately exacerbate psychiatric symptoms in individuals with SCHZ. However, our results also indicate that patients with SCHZ who are receiving antiviral therapy for HCV are significantly more likely to be followed by mental health providers over the course of treatment, as compared with patients with SCHZ and HCV who are not receiving antiviral therapy. Although it is unclear to what extent this factor might have helped to reduce any antiviral-induced exacerbations in psychiatric symptoms, importantly, we found no evidence to suggest that a diagnosis of SCHZ uniformly contraindicates antiviral therapy for HCV, especially if such individuals are regularly monitored by mental health providers. Nevertheless, our modest sample size might have limited our power to detect differences across groups, and replication of results using larger samples is necessary to confirm conclusions and further clarify outcomes within this population. Although additional studies are needed, our data combined with studies confirming disproportionately high rates of HCV among patients with SCHZ [3,10,11] suggest that excluding this population from antiviral therapy is not justified. Our findings are consistent with both the National Institutes of Health and the VHA treatment guidelines, which recommend 'establishment of screening tests for all groups at high risk of HCV infection' and the extension of appropriate treatment to special populations infected with HCV, such as those with psychiatric disorders [9,12]. In short, our overall findings support treatment of patients with SCHZ for HCV if they otherwise meet medical criteria for antiviral therapy.

Of note, our study design does not directly explore whether special treatment precautions are necessary to optimize outcomes and safety for patients with SCHZ. However, our group previously found that, in a sample of 60 patients who underwent antiviral therapy for HCV (30 of whom had SCHZ), patients who received mental health services during antiviral therapy had a higher likelihood of achieving an SVR (odds ratio = 12.2; $P=0.035$) [8]. Combined with the results of our present study, these findings suggest that concurrent mental health services are an important factor for psychiatric patients receiving antiviral therapy, one that could both reduce the risk of psychiatric exacerbations and promote successful viral response.

Although empirically validated treatment guidelines do not exist for psychiatric populations, several groups provide HCV treatment recommendations based on their clinical expertise with psychiatrically complex patients [13–15]. In general, these groups recommend that psychiatric patients be offered antiviral therapy for HCV if they are medically eligible, if they are able to attend medical appointments regularly and if they are willing to engage in psychiatric and substance abuse therapy during antiviral therapy. Furthermore, education about disease course, treatment efficacy and side effects is strongly encouraged prior to treatment initiation. For example, the Northwest Hepatitis C Resource Center at the Portland VA Medical Center offers a one-time HCV education group to individuals initially diagnosed with HCV [16]. Mental health and substance abuse screenings are conducted during this education group and prior to treatment initiation. Individuals who screen positive are referred to psychiatric and substance abuse treatment programmes prior to antiviral therapy initiation and for monitoring of symptoms at regular intervals throughout antiviral therapy, a practice that is supported by our findings. In general, because psychiatric medication adjustments and increased support might be required throughout antiviral therapy should symptom exacerbations or relapses arise, an increasing number of programmes have successfully used a multidisciplinary approach to HCV care [13].

Although group differences in rates of psychiatric symptoms did not reach statistical significance during any study period, it is notable that 42.3% of patients with SCHZ who received antiviral therapy experienced a depressive episode during the post-treatment period, whereas only 23.1% experienced a depressive episode during the pre-treatment period and only 24.1% experienced a depressive episode during the treatment period. Post-hoc analyses revealed that patients who did not achieve an SVR were significantly more likely to suffer a depressive episode during the post-treatment period (70.0%) compared with those that did achieve an SVR (20.0%). Although factors influencing this finding remain unclear, these data indicate that patients with SCHZ who do not successfully respond to antiviral therapy are at significant risk for a depressive episode following treatment. This could, in turn, highlight the importance of mental healthcare and monitoring both during antiviral therapy as well as for a period following antiviral therapy termination.

Our study's primary limitations include its relatively small sample size and its reliance on categorical data, which in combination might have limited our power to detect group differences. For example, compared with the ANT- group, the ANT+ group had lower rates of psychiatric hospitalizations in the 5 years prior to initiating treatment, lower lifetime rates of drug use disorders, higher rates of substance use remission during the pre-treatment period and lower rates of unstable SCHZ during the pre-treatment period. However, none of these differences was statistically significant, raising the possibility of type II error. Results should, therefore, be interpreted cautiously, as it remains possible that our ANT+ group was more stable than our ANT- group at baseline. For example, providers might have had a tendency to select certain SCHZ patients for antiviral therapy because they were psychiatrically stable, more likely to attend medical appointments or had stronger psychosocial supports or resources. Prospective studies using larger sample sizes are needed to better explore and more thoroughly illuminate the effects of baseline psychiatric stability on patient selection and psychiatric side effects of antiviral therapy treatment.

An additional primary limitation is that the retrospective chart review design did not allow us to use standardized side effect and symptom rating scales; thus, it remains unclear to what extent providers might have inconsistently documented psychiatric symptoms or adverse events. In cases where there were inadequate chart notes to comment on symptom status for a particular study period (for example, too few visits or too few details within existing notes), patients were removed from the analysis. However, in the absence of standard assessment instruments or protocols, chart notes might not fully or accurately provide data on specific symptoms and the lack of mention in a chart note, for example, does not necessarily mean that a patient does not have a particular symptom. Thus, results should be interpreted cautiously until replicated through a prospective design.

There are several additional limitations to consider. Firstly, because so few patients with SCHZ have received antiviral therapy for HCV, we opted to include all SCHZ patients who received any type of monotherapy or combination therapy with ribavirin, including pegylated and regular interferons. Thus, it remains unknown whether type of antiviral therapy differentially influences psychiatric side effects in individuals with SCHZ, because our small sample size precluded meaningful subanalyses by interferon type. Secondly, we cannot entirely rule out the possibility that patients were receiving concurrent care at non-VA facilities, in which case data from these facilities (for example, hospitalizations) would have been missed. It would be rare, however, for outside care to not at least be noted in a patient's chart and, as all chart notes were reviewed thoroughly, the frequency of such a scenario is likely to have been quite low if at all. Thirdly, although we were able to assess treatment completion rates, our chart review design prevented us from measuring other important markers of treatment adherence, such as percentage of doses taken as prescribed or clinic no-show rates; given its relevance to safety and efficacy, treatment adherence

should be carefully monitored in future prospective studies. Fourthly, although we made every attempt to blind raters to antiviral status, it is impossible to determine whether blinding was completely effective in all cases; thus, it is unclear to what extent this may have influenced ratings.

Despite limitations, our study design has important strengths. To our knowledge, our study represents the only published empirical data on the effect of HCV treatment on psychiatric symptoms in patients with SCHZ. Unlike previous research, our study specifically focuses on patients with SCHZ, rather than combining patients with diverse psychiatric diagnoses together. To ensure validity, we confirmed all diagnoses by thorough medical record review and established high interrater agreement for individual data points, psychiatric symptom ratings and the overall study. Groups were demographically matched in terms of age, gender and race, and clinical raters were blind to antiviral status. Thus, we have eliminated several important factors that could have otherwise differentially effected group outcomes. On the basis of the present findings, and those from our previous study [8], HCV patients with SCHZ should be considered potential candidates for antiviral therapy.

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Table 1

Baseline characteristics of patients with schizophrenia and hepatitis C receiving and not receiving antiviral therapy

Characteristic	Total sample	ANT+ ^a	ANT- ^b	P-value ^c
Total number of patients, <i>N</i>	60	30	30	-
Demographics				
Mean age, years $\pm$ SD	50.0 $\pm$ 5.3	50.2 $\pm$ 5.1	49.7 $\pm$ 5.5	0.694
Male gender	58 (96.7)	29 (96.7)	29 (96.7)	1.000
Caucasian	56 (93.3)	28 (93.3)	28 (93.3)	1.000
Vietnam era veteran	48 (81.4)	26 (86.7)	22 (75.9)	0.287
Substance use history^d				
Lifetime history of:				
Alcohol use disorder	49 (81.7)	21 (70.0)	28 (93.3)	0.020 ⁱ
Other drug use disorder	39 (65.0)	18 (60.0)	21 (70.0)	0.417
Injection drug use, <i>n/N</i> (%)	30/52 (57.7)	15/28 (53.6)	15/24 (62.5)	0.512
During the pre-treatment period ^e :				
Alcohol use, <i>n/N</i> (%) ^f	12/49 (24.5)	3/21 (14.3)	9/28 (32.1)	0.150
Drug use, <i>n/N</i> (%) ^g	12/38 (31.6)	4/18 (22.2)	8/20 (40.0)	0.239
Psychiatric history^d				
Active diagnoses during the pre-treatment period ^{e,h}				
Mood disorders	17 (28.3)	11 (36.7)	6 (20.0)	0.204
PTSD	13 (21.7)	9 (30.0)	4 (13.3)	0.152
Other anxiety disorders	5 (8.3)	2 (6.7)	3 (10.0)	0.666
Personality disorders	6 (10.0)	2 (6.7)	4 (13.3)	0.417
Psychotropic medications during the pre-treatment period	58 (96.7)	29 (96.7)	29 (96.7)	1.000
Mean number of psychiatric hospitalizations 5 years prior to the treatment period $\pm$ SD	2.75 $\pm$ 4.47	1.96 $\pm$ 3.49	3.55 $\pm$ 5.22	-
Medical characteristics				
Mean ALT, U/I $\pm$ SD (<i>n</i>)	79.9 $\pm$ 64.5 (55)	111.6 $\pm$ 75.1 (28)	47.0 $\pm$ 23.8 (27)	0.000 ^j
High ALT, <i>n/N</i> (%)	30/55 (54.5%)	19/28 (67.9%)	11/27 (40.7%)	0.043 ⁱ
High AST, <i>n/N</i> (%)	32/58 (55.2%)	21/28 (75.0%)	11/30 (36.7%)	0.003 ^k

Data expressed as *n* with (%) in terms of *n* over total *N*, unless otherwise indicated.

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

^aThe antiviral therapy (ANT+) group includes patients with schizophrenia and HCV infection who received interferon treatment.

^bThe non-antiviral therapy (ANT-) group includes patients with schizophrenia and HCV who did not receive interferon treatment.

^cP-values reflect differences between the ANT+ and ANT- groups.

^dSubstance use and psychiatric disorders were based on definitions in the DSM-IV-TR.

^eThe pre-treatment period refers to 6 months prior to the start of the treatment period.

^fThe number of patients with medical record documentation of alcohol use during the pre-treatment period out of those with a lifetime history of an alcohol use disorder.

^gThe number of patients with medical record documentation of illicit drug use during the pre-treatment period out of those with a lifetime history of a drug use disorder.

^hDepressive disorders included major depressive disorders, dysthymic disorders, depressive disorder not otherwise specified (NOS), mood disorders owing to medical conditions and mood disorder NOS. Post-traumatic stress disorder (PTSD) was recorded separately from other anxiety disorders. Other anxiety disorders included panic disorder, agoraphobia, specific phobias, social phobias, generalized anxiety disorder, anxiety disorder due to medical conditions, anxiety disorder NOS and adjustment disorders. Personality disorders included all subtypes including personality disorder NOS. A psychiatric diagnosis was considered active if providers documented and therefore addressed the diagnosis in patient progress notes within 6 months of antiviral therapy initiation.

ⁱ<0.050

^j<0.001

^k<0.010

Table 2

Adverse events and psychiatric treatment factors during the treatment period for patients with schizophrenia and hepatitis C receiving and not receiving antiviral therapy

	Total sample	ANT+ ^a	ANT- ^b	P-value ^c
Total number, <i>N</i>	60	30	30	-
Adverse events during the treatment period				
Mean emergency room visits				
Psychiatric, number $\pm$ SD	0.08 $\pm$ 0.28	0.07 $\pm$ 0.25	0.10 $\pm$ 0.31	0.643
Medical, number $\pm$ SD	0.35 $\pm$ 0.78	0.43 $\pm$ 0.90	0.27 $\pm$ 0.64	0.490
Mean inpatient hospitalizations				
Psychiatric, number $\pm$ SD	0.22 $\pm$ 0.86	0.07 $\pm$ 0.26	0.37 $\pm$ 1.16	0.248
Medical, number $\pm$ SD	0.15 $\pm$ 0.48	0.13 $\pm$ 0.35	0.17 $\pm$ 0.59	0.730
Alcohol use, <i>n/N</i> (%) ^d	7/46 (15.2)	1/21 (4.8)	6/25 (24.0)	0.106
Drug use, <i>n/N</i> (%) ^e	11/37 (29.7)	3/18 (16.7)	8/19 (42.1)	0.091
Psychiatric treatment factors present during the treatment period				
Addictions specialist, <i>n/N</i> (%) ^f	3/34 (8.8)	1/13 (7.7)	2/21 (9.5)	1.000
Mental health services ^g	51 (85.0)	29 (96.7)	22 (73.3)	0.026 ⁱ
Psychotropic medication changes ^h	33 (55.0)	20 (66.7)	13 (43.3)	0.069

Data expressed as *n* with (%) in terms of *n* over total *N*, unless otherwise indicated.

^aThe antiviral therapy (ANT+) group includes patients with schizophrenia and hepatitis C virus (HCV) infection who received interferon treatment.

^bThe non-antiviral therapy (ANT-) group includes patients with schizophrenia and HCV who did not receive interferon treatment.

^cP-values reflect differences between the ANT+ and ANT- groups.

^dThe number of patients with medical record documentation of alcohol use during the treatment period out of those with a lifetime history of an alcohol use disorder.

^eThe number of patients with medical record documentation of illicit drug use out of those with a lifetime history of a drug use disorder.

^fAddictions specialist refers to therapy, counselling or case management services (not just medication management) by an addiction specialist for drug or alcohol abuse during the treatment period.

^gMental health services refer to medication management, therapy, counselling or case management by a mental health specialist during the treatment period.

^hPsychotropic medication changes refer to any initiation, discontinuation or dose adjustment to psychotropic medications during the treatment period.

ⁱ<0.050.

Table 3

Percentage of patients with schizophrenia and HCV receiving and not receiving antiviral therapy with prominent psychiatric symptoms

	Total sample	ANT+ ^a	ANT- ^b	P-value ^c
Total number, <i>N</i>	60	30	30	-
Pre-treatment period ^d				
Unstable schizophrenia	23/57 (40.4%)	9/30 (30.0%)	14/27 (51.9%)	0.093
Depressive episode	13/52 (25.0%)	6/26 (23.1%)	7/26 (26.9%)	0.749
Prominent manic symptoms	4/56 (7.1%)	3/28 (10.7%)	1/28 (3.6%)	0.611
Treatment period ^e				
Unstable schizophrenia	17/53 (32.1%)	7/28 (26.0%)	10/25 (40.0%)	0.243
Worse than pre-treatment period	12/51 (23.5%)	6/28 (21.4%)	6/23 (26.1%)	0.696
Better than pre-treatment period	3/51 (5.9%)	2/28 (7.1%)	1/23 (4.3%)	1.000
Depressive episode	12/50 (24.0%)	7/29 (24.1%)	5/21 (23.8%)	0.979
Prominent manic symptoms	4/55 (7.3%)	3/29 (10.3%)	1/26 (3.8%)	0.613
Post-treatment period ^f				
Unstable schizophrenia	16/55 (29.1%)	7/27 (25.9%)	9/28 (32.1%)	0.612
Worse than treatment period	11/49 (22.4%)	7/26 (26.9%)	4/23 (17.4%)	0.425
Better than treatment period	4/49 (8.2%)	2/26 (7.7%)	2/23 (8.7%)	1.000
Depressive episode	18/51 (35.3%)	11/26 (42.3%)	7/25 (28.0%)	0.285
Prominent manic symptoms	3/55 (5.5%)	2/27 (7.4%)	1/28 (3.6%)	0.611

Data expressed as *n* with (%) in terms of *n* over total *N*, unless otherwise indicated. Where expressed as a fraction, *n* is over the total available data points because, in some cases, charts did not yield adequate information with which to make a determination.

^aThe antiviral therapy (ANT+) group includes patients with schizophrenia and HCV infection who received interferon treatment.

^bThe non-antiviral therapy (ANT-) group includes patients with schizophrenia and HCV who did not receive interferon treatment.

^cP-values reflect differences between the ANT+ and ANT- groups.

^dThe pre-treatment period refers to 6 months prior to the start of the treatment period.

^eThe treatment period varied in length for each patient.

^fThe post-treatment period refers to 6 months following the end of the treatment period. Unstable schizophrenia indicates prominent positive and/or negative symptoms during the study period, beyond what would be typical for a patient's interepisode baseline. Depressive episode indicates prominent depressive symptoms during the study period that meet criteria for a depressive episode. Prominent manic symptoms indicate any clinically significant manic symptoms, regardless of whether criteria were met for a manic episode.