

Low rate of HCV treatment among eligible HIV-infected and uninfected IDUs with access to hepatitis care

MS Sulkowski², YM Higgins², SH Mehta¹, GM Lucas^{1,2}, R Montes de Oca¹, M Torbenson², RD Moore^{1,2}, DL Thomas^{1,2}

¹School of Public Health and ²School of Medicine, Johns Hopkins University, Baltimore, MD, USA

Correspondence to: Mark Sulkowski, MD 600 N Wolfe St, 1830 Building, Rm 445 Baltimore, MD 21205 Phone: (410)-614-6089 Email: msulkowski@jhmi.edu

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ABSTRACT (revised)

Background: Most HCV-infected IDUs do not receive HCV treatment. The objective of this study was to determine the proportion of HIV-infected and uninfected IDUs (former and active) who are eligible for and initiate HCV therapy with Peginterferon/Ribavirin (PEG/RBV) in the absence of geographic and financial barriers.

Methods: Between 3/04-3/06, HCV-infected IDUs were enrolled sequentially from the Johns Hopkins Program for Alcoholism and Other Drug Dependencies and the JHU HIV clinic. Each IDU underwent a comprehensive evaluation: medical, psychiatric and drug/alcohol use history, depression screen, physical exam, and laboratory testing. Subjects were deemed ineligible for PEG/RBV therapy if any of the criterion were met: 1) HCV RNA not detected; 2) Pregnant or not willing to use birth control; Life expectancy < 2 years (e.g., advanced AIDS or cancer); 4) Active depression with suicidal ideation; 5) Allergic reaction to PEG/RBV; 6) Severe hematologic abnormality (e.g., Hb < 10.5 g/dL, ANC < 1000/mm³, platelet ct < 50,000/mm³); 7) Renal insufficiency (Cr > 2.5). All treatment-eligible subjects were given the opportunity to take PEG/RBV, available on-site at no cost.

Results: 363 HCV seropositive subjects with HCV RNA testing (HIV/HCV:183; HCV:180) were enrolled. HIV coinfecting IDUs were younger (40 ± 4.5 years) and were more likely to be African-American (90% > 74%) than those with HCV alone. No difference was observed in the prevalence of mental illness, alcohol abuse or interest in receiving HCV treatment (93%). HIV-coinfected IDUs were more likely to have undetectable HCV RNA (HIV/HCV: 21/183, 11%; HCV: 40/143, 22%, P < .001) and, among those with viremia, less likely to be eligible for HCV treatment (HIV/HCV: 89/147, 60%; HCV: 95/140, 74%, P=0.02). The majority of treatment eligible IDUs underwent liver biopsy (93%) and significant fibrosis (Ishak stage > 1) was identified in 33% and 21% of coinfecting and monoinfected IDUs respectively. The most common reasons for ineligibility were: Severe depression; Life expectancy < 2 yrs (e.g., untreated AIDS); hematologic abnormality; renal insufficiency of the treatment-eligible IDUs, ~ 33% initiated HCV therapy, defined as at least PEG injection (HIV/HCV: 30/89, 34%; HCV: 31/95, 33%).

Conclusions: While only 60% of HIV/HCV coinfecting IDUs were ineligible for HCV treatment, most (74%) of HCV monoinfected IDUs were treatment-eligible. Despite the removal of financial and geographic barriers, only one-third of treatment-eligible IDUs initiated HCV treatment. Strategies are needed to increase HCV treatment uptake among IDUs, particularly those with significant liver disease.

BACKGROUND/OBJECTIVE

• Despite published recommendations, few injection drug users (IDUs) with or without HIV coinfection have been treated for hepatitis C (HCV). Low rates of treatment have been attributed to high rates of treatment ineligibility due to medical and psychiatric comorbid conditions as well as limited access to medical care.

• **The primary objective of this study was to determine the proportion of HIV-infected and uninfected IDUs (former and active) who are 1) eligible for, 2) have immediate medical need for, and 3) initiate HCV therapy with peginterferon/ and ribavirin (PEG/RBV) in the absence of geographic and financial barriers.**

Study Subjects:

• Between March 2004 and 2006, 363 HCV seropositive persons reporting IDU were enrolled from two settings: the Johns Hopkins Program for Alcoholism and Other Drug Dependencies (PAODD clinic, HIV seronegative subject) and the Johns Hopkins HIV clinic (HIV seropositive subjects).

Measurements:

• Subjects with HCV were evaluated for HCV treatment eligibility, which included: medical, psychiatric and drug/alcohol use history, CES-D screen, physical exam, and laboratory testing (white blood cell and platelet count, hemoglobin level, serum creatinine, serum chemistries – glucose, alanine and aspartate aminotransferase, total bilirubin, albumin, quantitative hepatitis C RNA level). HIV coinfecting subjects had HIV RNA level and CD4 cell count.

HCV Treatment Eligibility:

- Subjects were ineligible if any of the criterion were met:
 - 1) HCV RNA not detected by PCR; 2) Pregnant or not willing to use birth control; Life expectancy < 2 years (e.g., advanced AIDS, ELSD or cancer); 4) Severe, active depression with suicidal ideation; 5) Allergic reaction to PegIFN/RBV; 6) Severe hematologic abnormality (e.g. hemoglobin < 10.5 g/dL, absolute neutrophil count < 1000/mm³, platelet count < 50,000/mm³); 7) Renal insufficiency (creatinine > 2.5); 8) Miscellaneous conditions (e.g. sarcoidosis, uncontrolled seizure disorders, active autoimmune disease).
 - Subjects were not excluded on the basis of active drug/alcohol use and stable psychiatric disease.

Medical Care:

• Liver biopsy: Treatment-eligible subjects were offered liver biopsy at no cost. Liver biopsy specimens were staged according to the Ishak system to determine the severity of HCV-related liver disease and relative need for HCV treatment. Subjects were informed of their hepatic biopsy stage according to standardized, written scripts. Liver biopsy was not required.
 • HCV treatment: Independent of liver biopsy performance or findings, treatment-eligible subjects were offered HCV treatment consistent with the current standard-of-care, peginterferon alfa-2a (Pegasys™) 180 mcg by subcutaneous injection weekly and weight-based ribavirin (< 75 kg, 1000 mg/day; > 75 kg, 1200 mg/day).

Medical Care (Continued):

- HCV treatment: Subjects were given detailed information regarding the potential benefits/risks of treatment; those accepting treatment provided informed written consent. Treatment was provided in a convenient location at no cost to the subject.
- **Analysis:** The proportion (95% CI) of IDUs ineligible for treatment was measured. Eligible and ineligible persons were compared with respect to HIV status, sociodemographic variables, alcohol and drug use using contingency tables for categorical variables and t-tests and Mann-Whitney test for continuous variables. Eligibility in HIV-infected and uninfected IDUs was compared using a chi-square test of proportions.
- **Medical need:** The proportion (95% CI) of treatment eligible IDUs with significant fibrosis (Ishak Stage > 1) was calculated.
- **Treatment:** Initiation was defined as the administration of at least one injection of peginterferon. Treatment initiation among eligible IDUs was determined.

RESULTS

• The outcome of "case-by case" medical evaluations of 363 HCV seropositive IDUs in whom hepatitis C viremia was assessed is outlined in Figure 1 according to HIV status. HCV RNA was not detected in 21 (11%) and 40 (22%) of IDUs with and without HIV coinfection (RR 1.9, 95% CI 1.19 – 3.15).

• Eligibility evaluations were completed in 92% and 79% of HCV RNA + subjects with and without HIV coinfection, respectively. Among those completing evaluations, HIV/HCV coinfecting IDUs, 90% HIV/HCV coinfecting IDUs and 26% of HCV monoinfected IDUs were ineligible for HCV treatment (RR 1.1, 95% CI 1.1 – 2.1). Among IDUs with HIV infection the most common reasons for ineligibility were advanced, untreated HIV disease (n = 16) and/or hematologic abnormalities (n = 38); whereas, among those monoinfected, severe, poorly controlled depression (n = 11) was the most commonly identified contraindication. Demographic and clinical characteristics of eligible and ineligible subjects are shown in Table 1. IDU intensity was not associated with treatment eligibility whereas, among those with HIV, heavy alcohol use and unstable housing was more common in those ineligible for treatment.

• Liver biopsy was performed in 93% (n = 171) of all treatment eligible subjects. Interestingly, no (stage 0) or minimal portal fibrosis (stage 1) was identified in 67% and 79% of HIV/HCV coinfecting and HCV monoinfected IDUs, respectively (Figure 2, N = 162) with complete staging available. On the other hand, bridging fibrosis or cirrhosis (stage 3-6) was found in 17 – 22% of IDUs.

• The majority (93%) of eligible IDUs indicated interest in receiving HCV treatment. However, while all eligible persons were offered treatment, only one-third of HIV/HCV coinfecting and HCV monoinfected IDUs initiated HCV therapy (defined as taking at least one dose of peginterferon alfa-2a). While HIV coinfecting IDUs were less likely to be treatment eligible, no difference was observed in HCV treatment initiation among coinfecting and monoinfected persons. Overall, the majority of IDUs did not take HCV treatment despite access to therapy in the absence of financial and geographic barriers.

Figure 1. Flow diagram of subjects (n=363)

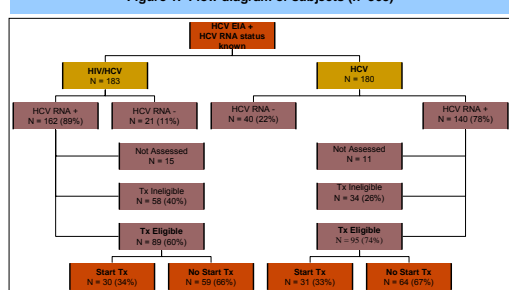


Figure 2. Hepatic Fibrosis Stage by HIV Status (N = 162)

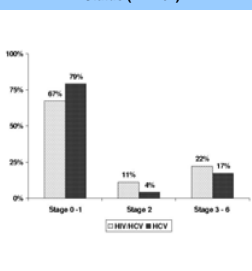


Table 1. HCV treatment eligibility among HIV/HCV coinfecting and HCV monoinfected IDUs with viremia and complete evaluation (n = 235)

	HIV/HCV		HCV		P	
	Ineligible N = 53	Eligible N = 77	Ineligible N = 24	Eligible N = 91		
Male	26 (49.1)	43 (55.8)	0.44	11 (45.8)	41 (50.6)	0.68
Black race	50 (94.3)	68 (88.3)	0.49	19 (79.2)	59 (72.8)	0.36
Age, years	40.0	41.0	0.63	45.5	45.0	0.59
Education > high school	(37/74.0)	(35/45.0)	0.03	(39/51.0)	(39/48.0)	0.00
Manic depression	15 (28.3)	21 (27.6)	0.95	12 (50.0)	23 (28.5)	0.25
Suicide plan < 6 months	6 (11.3)	5 (6.49)	0.35	9 (37.5)	5 (6.17)	0.001
Depression score > 16 (CES-D)	36 (67.92)	42 (54.55)	0.12	14 (58.33)	41 (50.62)	0.50
Alcohol use/day			0.04	16 (62.50)	40 (49.38)	0.49
No alcohol	31 (58.49)	47 (57.14)	0.102	15 (30.41)	34 (41.98)	
Moderate	16 (30.17)	31 (40.26)		7 (28.17)	17 (21.03)	
Heavy	6 (11.32)	2 (2.60)		2 (8.33)	7 (8.64)	
Frequency injection heroin < 6 months	36 (67.92)	57 (74.03)	0.74	14 (58.33)	41 (50.62)	0.23
None	8 (15.09)	9 (11.69)		10 (41.67)	31 (38.27)	
<1/day	9 (16.98)	11 (14.29)		0 (0.00)	9 (11.11)	
>1/day	17 (32.08)	17 (22.08)	0.23	12 (50.00)	40 (49.38)	0.95
Cocaine < 6 months	7 (13.21)	2 (2.60)	0.20	1 (4.17)	5 (6.17)	0.98
Shared needles < 6 months	37 (69.81)	46 (59.74)	0.24	22 (91.67)	73 (90.12)	1.00
Drug treatment < 6 months	10 (18.87)	8 (23.38)	0.81	14 (58.33)	47 (58.02)	0.89
No health insurance	34 (64.15)	57 (74.03)	0.05	14 (58.33)	42 (51.85)	0.66
One Sleeping place < 3 months	12 (14.46)	23 (26.44)	0.01			
Current ART						
CD4 count/mm ³ (N, %)						
<200	31 (59.62)	17 (22.08)	<0.01			
200-350	5 (9.62)	18 (23.38)				
>350	16 (30.17)	42 (54.55)				
HIV RNA < 400 copies/mL	13 (24.53)	35 (45.45)	0.01			
Hemoglobin, g/dL †	10.7	13.0	<0.01	11.7	13.3	0.001
(0.3-12.1)	(11.5-14.2)			(10.3-13.0)	(11.0-14.3)	
WBC/mm ³	3695	4590	0.01	6885	6330	0.26
(2405-5405)	(3450-6120)			(5020-7540)	(5050-7540)	
Platelet count/mm ³ †	173	218	0.03	257	237	0.33
(133-244)	(172-268)			(212-338)	(191-268)	
Albumin, g/dL †	3.7	4.0	0.001	4.0	4.2	0.02
(3.2-4.0)	(3.7-4.3)			(3.8-4.3)	(4.0-4.4)	
Creatinine, mg/dL †	0.9	0.9	0.07	0.9	0.8	0.51
(0.7-1.2)	(0.7-0.9)			(0.6-1.1)	(0.7-0.9)	

† Chi-square or Fisher exact test for frequencies; Wilcoxon for medians' median (interquartile range)

CONCLUSIONS

- 1) **Eligibility for treatment:** Following careful case-by-case assessment of treatment eligibility, we found that ~ 40% of HIV/HCV coinfecting IDUs and ~ 26% of HCV monoinfected IDUs had contraindications to HCV treatment with peginterferon/RBV.

Among coinfecting IDUs, the most prevalent contraindication to HCV therapy was AIDS and its medical consequences (e.g., anemia) whereas for monoinfected IDUs, untreated psychiatric disease was common.

Strategies to improve delivery of care for HIV and mental illness to IDUs are needed to increase rates of HCV treatment eligibility.

- 2) **Medical need for treatment:** While some IDUs had significant fibrosis (> Ishak stage 1) on liver biopsy, many IDUs (79% monoinfected; 67% coinfecting) had no or minimal fibrosis. This finding suggest that disease staging may be an important part of individual treatment decisions; inexpensive, non-invasive tests (e.g., serum markers or FibroScan™) are needed to facilitate this approach.

- 3) **Initiation of HCV treatment:** Despite removal of financial and geographic constraints, only ~ 33% of HIV-infected and uninfected IDUs underwent HCV treatment. These data indicate that the provision of access to treatment is not sufficient to increase HCV treatment rates among IDUs. Additional research is needed to elucidate the barriers to HCV treatment and to develop strategies to deliver HCV care to IDUs with significant liver disease.