Does chronic hepatitis C cause fatigue?

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AIMS

- An association between chronic hepatitis C (CHC) and chronic fatigue is found in numerous studies. But is this association a causal one? Does CHC cause chronic fatigue? Or is the association due to confounders – for example patient awareness of having a chronic infection? The aim of this study was to illuminate that question.

Fatigue: "A sensation of exhaustion during or after usual activities, or a feeling of inadequate energy to begin these activities"

Ref. Chen MK. The epidemiology of self-perceived fatigue among adults. Prev Med 1986,15:74-81

Table 1 Characteristics of the patients

	HCV RNA –	HCV RNA +	All
Males	4/11 (36%)	21/32 (66%)	25/43 (58%)
Mean age at HCV exposure	23.9 years	21.6 years	22.2 years
Mean age at HSCL-25 examination	34.4 years	33.4 years	33.7 years
Mean duration from HCV exposure to HSCL-25 examination	10.5 years	11.8 years	11.5 years

Table 2 Mean scores on assessment of fatigue according to HCV RNA

	HCV RNA –		HCV RNA +	
	Mean score	CI 95%	Mean score	CI 95%
Feeling low in energy	2.9	2.3, 3.5	2.3	1.9, 2.6
Feeling that everything is an effort	3.1	2.5, 3.7	2.2	1.8, 2.6
Combined fatigue score	6.0	4.8, 7.2	4.5	3.9, 5.1

Table 3 Coefficients from linear regression analysis of the Combined fatigue score including the independent variables gender, duration since HCV exposure, age, and HCV RNA

Model	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95,0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
1 (Constant)	4.539	1.626		2.791	.008	1.247	7.831
Gender	.241	.551	.068	.437	.664	-.875	1.357
Duration since HCV exposure	.016	.045	.068	.361	.720	-.076	.108
Age	.033	.049	.128	.673	.505	-.066	.132
HCV RNA	-1.447	.623	-.361	-2.323	.026	-2.707	-.186

a. Dependent Variable: Combined fatigue score Gender: 0 = males, 1 = females; HCV RNA: 0 = negative (not chronic hepatitis C), 1 = positive (chronic hepatitis C)

RESULTS

- The study included 43 anti-HCV positive people who have injected drugs (PWID) (Figure 1)
  - 26% had spontaneous clearance, 74% had CHC
- Mean duration from HCV exposure to mental assessment was 11.5 years (Table 1)
- CHC was significantly associated with lower level of fatigue than exposure to HCV without CHC (Figure 2, Table 2, and Table 3)
- Age, gender, and the duration since HCV exposure did not influence the fatigue scores significantly (Table 3)

Figure 1 Selection of patients - which also illustrates the inclusion criteria for the study

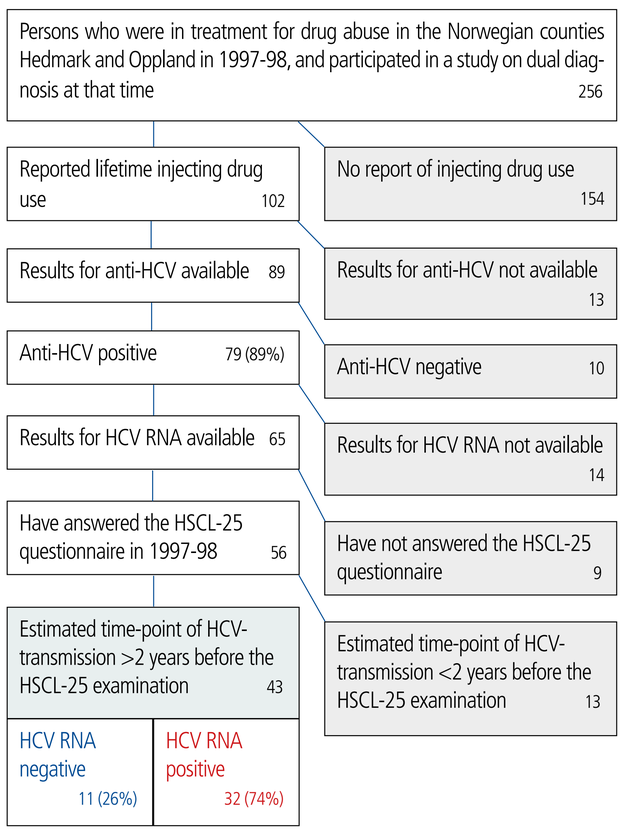
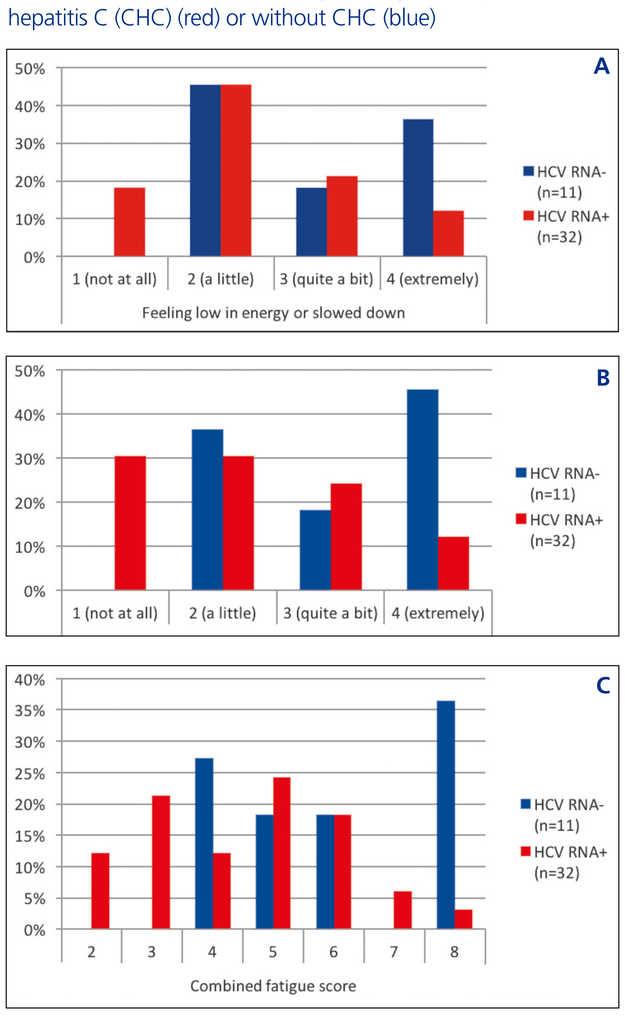


Figure 2 Scores on Feeling low in energy (A), Feeling that everything is an effort (B) and Combined fatigue score (C) among anti-HCV positive people who inject drugs (PWID) with chronic hepatitis C (CHC) (red) or without CHC (blue)



METHODS AND PATIENTS

- In a study conducted in 1997 and 1998 on concurrent substance abuse and mental disorder, a cohort of patients who had been admitted for substance abuse treatment in two counties of Norway underwent a diagnostic assessment on mental disorder and substance abuse. Lifetime injecting drug use (IDU) was reported by 102 patients. Inclusion criteria were conform to the selection of patients presented in Figure 1.
- Information on hepatitis C virus (HCV) was obtained through linkage to the county Department of Microbiology. Patients exposed to HCV with spontaneous clearance (anti-HCV positive/HCV RNA negative) were compared to patients without spontaneous clearance (anti-HCV positive/HCV RNA positive) concerning the level of fatigue
- The assessment in 1997/98 included two items from the self-administrated

Hopkins Symptom Check List (HSCL-25) directly relevant for fatigue:

- Feeling low in energy or slowed down
- Feeling everything is an effort

- HSCL-25 requires answers in 4 grades and is based on the situation the last 14 days: 1. Not at all, 2. A little, 3. Quite a bit, and 4. Extremely

The answers on these items were the dependent variables, supplemented with a *Combined fatigue* score which represented the addition of the scores of the two items.

CONCLUSIONS

- This study on fatigue associated to CHC was based on an assessment conducted in a population of people who inject drugs (PWID) at a time when awareness of hepatitis C was low. Lower level of fatigue among PWID with CHC compared to those who had been exposed and had spontaneous clearance, is surprising. This may be accidental, even if it was statistically significant. A possible explanation is that the positive association between CHC and chronic fatigue found in other studies may be caused by other mechanisms than purely somatic ones. Patient awareness of having CHC is a possible alternative explanation. Theoretically, our finding may also be explained by brain affection in ways that enhance fatigue in patients exposed to HCV also when the viremia is cleared spontaneously.

Even if the association between CHC and chronic fatigue found in many recent studies may be caused by patient awareness, the fatigue should not be neglected. The best treatment may still be antiviral medication – not psychotherapy.

Disclosures: Kielland has given sponsored lectures for MSD and Abbvie. Sandnes and Landheim declare no conflict of interest.

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