Silibinin Prior to Triple Therapy Leads to End of Treatment Success in Difficult to Treat HIV/Hepatitis C Co-Infected Individuals

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Background

Efficacy of current hepatitis C virus (HCV) triple therapy, including a protease inhibitor, is limited in HIV/HCV-coinfected patients with advanced liver fibrosis and non-response to previous pegylated interferon plus ribavirin (peginterferon-ribavirin). These patients experience on-treatment failure during triple therapy in up to 50%, and they cannot wait for availability/ affordable next-generation anti-HCV drugs. In a pilot study, we investigated the efficacy of a lead-in therapy with silibinin before triple therapy in difficult-to-treat patients.

Methods

Inclusion criteria were HIV/HCV coinfection with advanced liver fibrosis and documented failure of previous peginterferon-ribavirin treatment. Intervention was a lead-in therapy with intravenous silibinin 20 mg/kg/day for 14 days. Subsequently, peginterferon-ribavirin combined with telaprevir was initiated for 12 weeks, followed by peginterferon-ribavirin dual-therapy until week 48. The outcome measurement was HCV RNA after silibinin lead-in, at weeks 2, 4, and 12, and at end of treatment.

Baseline characteristics of six HIV/Hepatitis c coinfected patients

Patient	Age (year)	Sex	CD4+ (cells/µl)	ART	GT	METAVIR	Fibroscan (kPa)	Preceding Tx
A	49	m	396	RGV ATV/r TDF	1a	F3	35.8	Null-response
B	48	f	520	RGV TDF/FTC	1e	F3	19.8	Null-response
C	50	m	627	RGV ATV/r TDF	1a	F3	18.4	Viral breakthrough
D	47	m	686	RGV ABC/3TC	1b	F3	NA	Partial response
E	56	m	678	RGV ATV/r 3TC	1a	F3	14.3	Relapse
F	38	m	175	RGV EFV TDF/FTC	1a	NA	24.6	Null-response

Abbreviations: ART: antiretroviral therapy; GT: genotype; Tx: Therapy; NA: not available
RGV: Raltegravir; ATV/r: Atazanavir/Ritonavir; EFV: Efavirenz; TDF: Tenofovir; FTC: Emtricitabine; 3TC: Lamivudine

Silibinin is the main component of silymarin, an extract of the milk thistle *Silybum marinum.*

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Results

We examined six HIV/HCV-coinfected patients. Median age was 49 years (range 38-56). For five individuals the transmission mode was intravenous drug use. Genotype 1a, which is associated with poorer response to triple therapy, was most prevalent (5/6) and all had a fibrosis grade METAVIR F3. All were under successful antiretroviral treatment (HIV-RNA <20c/ml) with a median CD4+ cell count of 574/µl (range 175-686). Mean HCV-RNA decline under silibinin therapy was 2.6log10 copies/ml (range 2-3). Five of six patients were virologically suppressed at weeks 2 and 4, and 6/6 at week 12 of triple therapy. One experienced a viral breakthrough thereafter. At the end of treatment, 5/6 (83%) patients had an undetectable HCV RNA.

Figure 1: Previous treatment failure in six HIV/HCV-coinfected patients with pegylated interferon alfa-2a plus ribavirin dual therapy (PR). The dotted line indicates the failing patient in the silibinin plus subsequent triple therapy, shown in Figure 2.

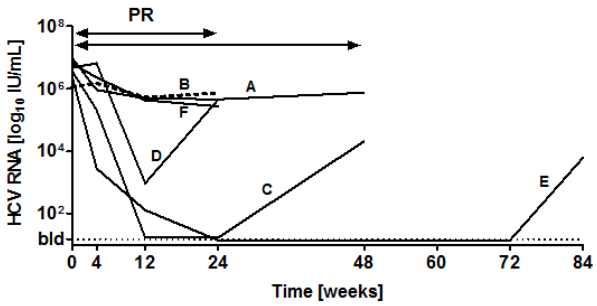
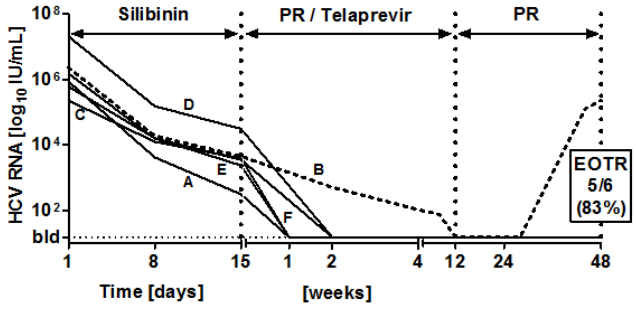


Figure 2: HCV RNA viral load in the same six patients during lead-in therapy with intravenous silibinin for 14 days followed by initiation of triple therapy on day 15 (i.e. week 0) for 48 weeks. The black arrows indicate the different treatment durations with PR in the six patients.
bld: below level of detection, EOTR: end of treatment response, PR: pegylated interferon alfa-2a plus ribavirin



Summary and Conclusion

A lead-in with silibinin before triple therapy is highly effective and may increase the probability of HCV treatment success in difficult-to-treat HIV/HCV-coinfected patients with advanced liver fibrosis and previous failure of peginterferon-ribavirin. It might be a treatment alternative where latest direct acting agents against HCV are not available or affordable.

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