Silibinin is a potent antiviral agent in patients with chronic hepatitis C not responding to pegylated interferon/ribavirin therapy

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BACKGROUND & AIMS: Oral Silibinin (SIL) is widely used for treatment of hepatitis C, but its efficacy is unclear. Substantially higher doses can be administered intravenously (IV).

METHODS: Pedigreed nonresponders to full-dose pegylated (Peg)-interferon/ribavirin (PegIFN/RBV) were studied. First, 16 patients received 10 mg/kg/day SIL IV (Legalon Sil; Madaus, Köln, Germany) for 7 days. In a subsequent dose-finding study, 20 patients received 5, 10, 15, or 20 mg/kg/day SIL for 14 days. In both protocols, PegIFN alpha-2a/RBV were started on day 8. Viral load was determined daily.

RESULTS: Unexpectedly, in the first study, HCV-RNA declined on IV SIL by 1.32 +/- 0.55 log (mean +/- SD), P < .001 but increased again in spite of PegIFN/RBV after the infusion period. The viral load decrease was dose dependent (log drop after 7 days SIL: 0.55 +/- 0.5 [5 mg/kg, n = 3], 1.41 +/- 0.59 [10 mg/kg, n = 19], 2.11 +/- 1.34 [15 mg/kg, n = 5], and 3.02 +/- 1.01 [20 mg/kg, n = 9]; P < .001), decreased further after 7 days combined SIL/PegIFN/RBV (1.63 +/- 0.78 [5 mg/kg, n = 3], 4.16 +/- 1.28 [10 mg/kg, n = 3], 3.69 +/- 1.29 [15 mg/kg, n = 5], and 4.85 +/- 0.89 [20 mg/kg, n = 9]; P < .001), and became undetectable in 7 patients on 15 or 20 mg/kg SIL, at week 12. Beside mild gastrointestinal symptoms, IV SIL monotherapy was well tolerated.

CONCLUSIONS: IV SIL is well tolerated and shows a substantial antiviral effect against HCV in nonresponders.