

PRIMARY SCLEROSING CHOLANGITIS

Minocycline treatment improves some biochemical markers of disease

No effective therapy exists for primary sclerosing cholangitis (PSC), a chronic liver disease associated with high morbidity and mortality. PSC is characterized by chronic inflammation, mainly mediated by nitric oxide produced by the inducible nitric-oxide synthase. Minocycline, a second-generation tetracycline, displays anti-inflammatory activity by inhibiting inducible nitric-oxide synthase and suppressing the function of T and B cells. In a pilot study, patients with PSC, who were treated with minocycline, had few adverse events and experienced significant decreases in serum levels of alkaline phosphatase, a diagnostic marker for PSC, and in the Mayo risk score for PSC.

“No effective therapy exists for primary sclerosing cholangitis...”

Dr Silveira *et al.* investigated the effects of 1 year of treatment with minocycline (100 mg twice daily) on 16 patients with PSC. Potentially drug-related adverse events were observed in nine patients, with three patients having to abandon the study. However, the symptoms of these three patients improved shortly after discontinuation of treatment. Among the

12 patients who completed the treatment (one patient abandoned the study for personal reasons), the median serum level of alkaline phosphatase decreased significantly, from 330 U/l at baseline to 265 U/l at 1 year (reference range 45 U/l–142 U/l). Although levels of no other markers of liver biochemistry changed significantly from baseline, a significant reduction in median PSC Mayo risk score was observed (0.55 at baseline versus 0.02 at 1 year). The Mayo risk score—a function of the patient's age, variceal bleeding status and serum levels of bilirubin, aspartate aminotransferase and albumin—estimates 4-year survival in patients with PSC, and tracking it over time can help establish the natural history and prognosis of this disease.

Silveira and colleagues conclude that the infrequent and minor adverse events and the improvements in surrogate markers for PSC recorded in their study warrant initiation of randomized studies of minocycline, alone or as part of a combination therapy.

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Original article Silveira, M. G. *et al.* Minocycline in the treatment of patients with primary sclerosing cholangitis: results of a pilot study. *Am. J. Gastroenterol.* **104**, 83–88 (2009).