Melatonin trial in patients with irritable bowel syndrome

Sleep disturbance is highly prevalent in irritable bowel syndrome (IBS) patients. As melatonin has been associated with both sleep promotion and the regulation of gastrointestinal motility, Song and colleagues carried out a randomized, placebo-controlled study to assess its efficacy in treating symptoms of IBS and sleep disturbance.

In total, 40 patients with IBS and sleep disturbance were randomized 1:1 to receive either 14 days treatment with melatonin 3 mg daily at bedtime, or placebo. Bowel symptoms, sleep disturbance and the psychological status of participants were recorded at baseline and after completion of 14 days of therapy, by means of questionnaires: rectal manometry and overnight polysomnography were also performed at these two evaluation points.

After 2 weeks, patients receiving melatonin had a significantly greater decrease in abdominal pain and significantly increased sensory thresholds for urgency and pain, compared with those receiving placebo. The quality and quantity of patients' sleep, however, did not differ significantly between the two groups. In addition, there was no significant difference in the anxiety and depression scores of patients receiving melatonin compared with placebo.

The authors conclude that melatonin is effective in reducing abdominal pain and enhancing rectal pain thresholds in IBS patients, but this effect is independent of its effect on sleep and psychological parameters.

Katy Cherry

Original article Song GH *et al.* (2005) Melatonin improves abdominal pain in irritable bowel syndrome patients who have sleep disturbances: a randomised, double-blind, placebo controlled study. *Gut* **54:** 1402–1407

Hepatic stellate cells: early activation predicts fibrosis in HCV-infected transplant recipients

End-stage liver disease due to hepatitis C virus (HCV) infection is an indication for liver transplantation. Recurrent HCV infection is universal in these patients, and leads to the development of fibrosis or cirrhosis in around 20% after 2 years and 30% after 5 years. Treatment with interferon-based therapies and ribavirin has limited efficacy and is poorly tolerated in liver-transplant patients. The aim of two recent studies was to identify a marker for those patients at highest risk of fibrosis that might allow more effective targeting of therapy. Both studies looked at hepatic stellate cells (HSCs), the main source of extracellular matrix and collagen in the liver. Activation of HSCs is known to be the earliest stage of hepatic fibrogenesis, but data are lacking on the association of HSC activation and the subsequent development of advanced fibrosis and cirrhosis in liver-transplant patients.

Gawrieh and colleagues used α-smooth-muscle actin (αSMA), detected immunohistochemically, as a marker of HSC activation. Liver biopsies performed 4 months post-transplantation were stained for αSMA and assessed retrospectively by a pathologist blind to the patients' clinical and laboratory data. A semi-quantitative scoring system was used to give regional and total HSC activation scores. The 4-month scores were then correlated with the fibrosis score at 1 year post-transplant. They found that total HSC scores were similar between patients with severe (fibrosis score ≥2; $n = 13$) and those with mild (fibrosis score 0; $n = 13$) HCV infection. Regional scores differed, however (parenchymal zones 1, 2 and 3; mesenchymal portal tracts and fibrous septa). Higher mesenchymal scores were predictive of progression, and mesenchymal activation of HSCs had a specificity and positive predictive value of 100% for the development of progressive fibrosis. The authors conclude that assessment of HSC activity at 4 months post-transplant could help identify a population of patients at particular risk of cirrhosis who might benefit most from antiviral therapy.

Russo and colleagues used the same marker (αSMA) to detect activated HSCs in their study, which also assessed HSC activation at 4 months as a predictor of the subsequent development of advanced fibrosis. Their study included 46 HCV-infected liver-transplant recipients, divided into rapid fibrosers ($n = 21$), defined by the development of fibrosis or cirrhosis within 2 years of transplantation, and slow fibrosers ($n = 25$). A computerized image and data analysis system was used to analyze αSMA retrospectively (expressed as the proportion of cellular area positive on immunohistochemistry) detected in 4-month post-transplant biopsy samples. The authors found that HSC activity was associated