Anson W. Lowe and Richard H. Moseley, Section Editors

Endoscopic Index of Disease Severity in Crohn's and Ulcerative Colitis

Endoscopy plays an essential role in the management of patients with inflammatory bowel disease and in the evaluation of the efficacy of new treatment modalities. Interobserver variation in the assessment of endoscopic severity of disease in patients with ulcerative colitis and patients with Crohn's disease has led to the development of several activity indices, including the Mayo Clinic Index, the Ulcerative Colitis Disease Activity Index, the Ulcerative Colitis Index of Severity (UCEIS), and the Crohn's Disease Endoscopic Index of Severity (CDEIS), and the Simplified Endoscopic Score for Crohn's Disease (SES-CD), respectively. In this issue of GASTROENTEROLOGY, 2 studies provide important information about use of endoscopic activity scoring indices in patients with inflammatory bowel disease.

Ferrante et al have performed a subgroup analysis of 172 patients enrolled in the SONIC trial, who had endoscopic lesions at baseline, underwent endoscopy at week 26, and had the Crohn's Disease Activity Index and C-reactive protein concentration assessed both at baseline and week 26 to determine the minimally necessary improvement in endoscopic activity after 26 weeks of treatment with infliximab, azathioprine, or both, that could serve to define endoscopic response and predict sustained clinical benefit, as defined by corticosteroid-free clinical remission (CFREM) at week 50. Complete mucosal healing, a secondary endpoint of the SONIC trial, was achieved in 48% of patients and predicted CFREM at week 50 with 56% sensitivity and 65% specificity. A decrease from baseline in the SES-CD of $\geq$50% at week 26 was found to best define an endoscopic response. This less stringent criterion was achieved in 65% of patients and predicted CFREM at week 50 with 74% sensitivity and 48% specificity. A decrease from baseline in the CDEIS of $\geq$50% at week 26 was achieved in 65% of patients and predicted CFREM at week 50 with 73% sensitivity and 46% specificity. Although changes in ulcer subscores of the CDEIS and SES-CD indices did not improve the predictability of CFREM at week 50, segmental mucosal healing (ie, disappearance of mucosal ulcerations in $\geq$1 evaluated segment at week 26) was predictive with 85% sensitivity and 37% specificity (Table 1). These findings support the use of response defined by endoscopic scoring indices in pharmacologic or treatment strategy trials in patients with Crohn's disease.

Similarly, Travis et al, using a video library of flexible sigmoidoscopies from clinical trials of patients with active ulcerative colitis evaluated by an independent cohort of 25 investigators throughout the world, examine the reliability of the UCEIS, calculated as the sum of vascular pattern (scored from 0 to 2), bleeding (0 to 3), and erosions and ulcers (0 to 3), in assessing disease severity. A high level of correlation (0.93) was found between UCEIS score and overall assessment of severity. Intra- and interinvestigator reliability ratios for the UCEIS were 0.96 and 0.88, respectively. Of note, intrainvestigator variability in determining UCEIS scores was unaffected by addition of clinical details with a video. This simple-to-use endoscopic scoring system may become an important tool in clinical trials or in routine clinical management of patients with ulcerative colitis.

See pages 978 and 987.

Management of Anemia in Patients Treated for HCV Infection

Anemia is a common adverse event observed during the treatment of

Table 1. Corticosteroid-Free Clinical Remission at Week 50 as a Function of Clinical and Endoscopic Response at Week 26 (N = 172)

Clinical or endoscopic evaluation at week 26	Total	Sensitivity (95% CI)	Specificity (95% CI)	PLR (95% CI)	NLR (95% CI)	AUC (95% CI)	*P* value[a]
Corticosteroid-free clinical remission (n = 116)	172	84% (77%–91%)	56% (45%–68%)	1.93 (1.46–2.54)	0.28 (0.17–0.46)	0.702 (0.634–0.771)	<.001
Clinical remission (n = 122)	172	86% (79%–93%)	51% (39%–62%)	1.75 (1.36–2.24)	0.27 (0.16–0.46)	0.684 (0.617–0.752)	<.001
Clinical response with ΔCDAI ≥100 (n = 133)	172	90% (84%–96%)	41% (29%–52%)	1.52 (1.24–1.87)	0.24 (0.13–0.46)	0.655 (0.590–0.719)	<.001
Clinical response with ΔCDAI ≥70 (n = 139)	172	93% (88%–98%)	37% (25%–48%)	1.47 (1.22–1.77)	0.19 (0.09–0.40)	0.648 (0.587–0.710)	<.001
Mucosal healing (n = 82)	172	56% (47%–66%)	65% (54%–76%)	1.60 (1.12–2.29)	0.67 (0.51–0.89)	0.606 (0.532–0.680)	.006
ΔSES-CD ≥50% (n = 112)	172	74% (66%–83%)	48% (36%–60%)	1.42 (1.11–1.83)	0.54 (0.36–0.81)	0.611 (0.538–0.683)	.003
ΔCDEIS ≥50% (n = 112)	172	73% (65%–82%)	46% (35%–58%)	1.37 (1.07–1.75)	0.58 (0.38–0.86)	0.599 (0.526–0.671)	.007
Segmental mucosal healing (n = 125)	165	85% (77%–92%)	37% (25%–48%)	1.34 (1.09–1.64)	0.42 (0.24–0.73)	0.607 (0.538–0.675)	.002

NOTE. ΔCDAI, decrease in CDAI between baseline and week 26; ΔCDEIS, decrease in CDEIS score between baseline and week 26; mucosal healing, absence of mucosal ulcerations at week 26; segmental mucosal healing, disappearance of ulcers in at least one of the evaluated segments at week 26; ΔSES-CD, decrease in SES-CD between baseline and week 26.

[a]*P* value is derived from a χ^2 test for association between each variable and corticosteroid-free clinical remission at week 50.

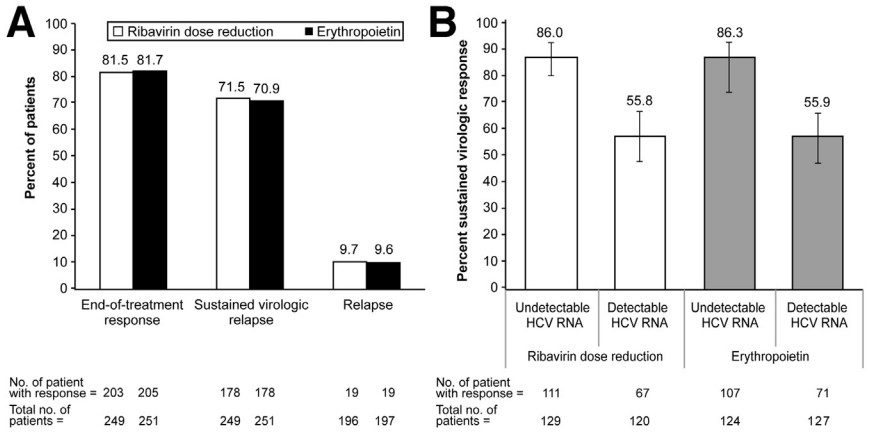

Figure 1. End-of-treatment response, sustained virologic response (SVR), and relapse rates for the 2 anemia management strategies (*A*) and SVR rates by HCV RNA levels at start of primary anemia management (*B*).

patients infected with hepatitis C virus (HCV) with pegylated interferon, ribavirin, and the recently approved protease inhibitors, boceprevir and telaprevir. Management of anemia during treatment consists of dose reduction of ribavirin and/or the use of erythropoietin. However, these management strategies have not been compared and there have been concerns about the effect of ribavirin dose reduction on rates of sustained virologic response (SVR) and the cost and safety of erythropoietin. In this issue of GASTROENTEROLOGY (accompanied by an editorial), Poordad et al have assessed the relative efficacy and safety of these anemia management strategies in 687 treatment-naïve patients with chronic HCV genotype-1 infection treated with the combination of pegylated interferon, ribavirin, and boceprevir. Patients who developed anemia (defined as a hemoglobin decline, or an expected decline before the next protocol-specified visit, of <10 g/dL) during treatment were randomized to ribavirin dose reduction (n = 249) or erythropoietin (40,000 IU/wk) therapy (n = 251). End-of-treatment response, relapse, and SVR rates were similar for the ribavirin dose reduction and erythropoietin arm. Regardless of the primary anemia management strategy, higher SVR rates (86%) were observed in patients who were HCV RNA undetectable at the start of primary anemia management, compared with 56% for patients with detectable HCV RNA at the start of primary anemia management (Figure 1). However, patients receiving <50% of the assigned total ribavirin dose had significantly lower SVR rates compared with the other groups. Low baseline hemoglobin level, normal inosine pyrophosphatase activity, age >40 years, and higher degrees of fibrosis were risk factors for the development of anemia during treatment. Eleven thromboembolic adverse events occurred in 9 of the patients receiving erythropoietin compared with 1 patient who did not receive erythropoietin. These findings suggest no benefit of erythropoietin as a first-line anemia management strategy and support ribavirin dose reduction as the primary intervention in an algorithm for managing anemia in patients receiving pegylated interferon, ribavirin, and boceprevir.

See page 1035; editorial on page 930.

Role of Mitochondrial DNA Variation in Experimental Colitis

Reduced intestinal mucosal adenosine triphosphate (ATP) levels were previously observed in patients with ulcerative colitis. A potential role for ATP was further supported by the discovery of genetic associations for ulcerative colitis that identified genes such as SLC22A5 and UCP2 that are involved with energy generation. Additional studies supported a role for defects in mitochondrial-based respiration in ulcerative colitis. How such defects may affect the pathogenesis of ulcerative colitis was not known. In this issue of GASTROENTEROLOGY, Bär et al from Lübeck, Germany, report on studies performed in murine models of colitis that differed in their abilities to generate ATP.

The role of ATP produced by mitochondrial respiration in murine models of ulcerative colitis was explored using genetically determined mice. Mitochondria contain their own genomes that encode for 32 genes. The authors utilized murine conplastic inbred strains in which the nuclear genome was identical but differed with respect to naturally occurring mitochondrial polymorphisms. Four different mouse strains were studied and included (1) control C57BL/6; (2) BL6.NOD that express differences from the controls in 3 mitochondrial genomic positions and is known to express higher brain ATP levels; (3) BL6.NZB mice that express 85 polymorphisms in their mitochondrial genomes and 2 DNA variations from BL6.NOD in their genome; and (4) BL6.AKR, which differ in 2 nucleotide positions located within the D-loop region of the mitochondrial $tRNA^{Arg}$ gene and at the mt-ND3gene. Only the BL6.NOD mice possessed a DNA polymorphism that resulted in an amino acid difference from controls of a mitochondrial gene, mt-COX3 (Val>Ile). Analysis of colonic mucosa from these mice revealed that the BL6.NOD and BL6.NZB exhibited ≥2-fold higher levels of ATP than the BL6.AKR and C57BL/6 mice. The increased ATP levels in BL6.NOD and BL6.NZB mice were associated with increased levels of 2 protein complexes associated with oxidative phosphorylation.

Download English Version:

https://daneshyari.com/en/article/6094802

Download Persian Version:

https://daneshyari.com/article/6094802

Daneshyari.com