CORRESPONDENCE

Readers are encouraged to write letters to the editor concerning articles that have been published in GASTROENTEROLOGY. Short, general comments are also considered, but use of the Correspondence section for publication of original data in preliminary form is not encouraged. Letters should be typewritten double-spaced and submitted in triplicate.

Insulin Resistance Influences Iron Metabolism and Hepatic Steatosis in Type II Diabetes

Dear Sir:

We read with interest the article by Mendler et al.[1] who described the association of hepatic iron overload, steatosis, and presence of one or more components of the insulin resistance syndrome. They suggested a role for insulin resistance in the development of hepatic iron overload, steatosis, and increased serum ferritin levels, although the mechanisms whereby insulin resistance would induce alterations in iron metabolism remain to be elucidated. Insulin resistance is very common among subjects with metabolic disorders, but its prevalence varies substantially among clinical conditions.[2] Type II diabetes is one of the metabolic conditions with the higher rate of insulin resistance and is frequently associated with increased serum ferritin levels.[2,3] We have evaluated iron indices in patients with type II diabetes before and after improvement of metabolic control to provide some insights into the relationship between iron and metabolic disorders. From 1989 to 1990, in our Department of Medicine, 10 outpatients with poorly controlled diabetes were enrolled to evaluate the incidence of hepatic steatosis and its reversibility after correction of the glycemic control. Results of this study have not been published. Chronic alcoholism, acute and chronic liver diseases, malignancies, and inflammatory and iron overload disorders were excluded. After baseline evaluation, patients received a strict diet regimen for 12 months in addition to antidiabetic therapy. The study schedule included monthly measurements of mean blood glucose, fructosamine, glycosylated hemoglobin, cholesterol, and triglyceride levels; assessment of uricemia and liver function tests for 12 months; and hepatic ultrasound examination and liver biopsy at baseline and after 12 months. Small aliquots of the serum samples were collected and stored at −80°. The study was approved by the Hospital's ethical committee. All patients gave their informed consent to the study. Four denied liver biopsy. We then retrospectively evaluated serum iron, transferrin, and ferritin levels of the patients on each sample and hepatic iron concentration (HIC) at baseline and at the end of study. HIC was determined by atomic absorption spectrophotometry (Perkin-Elmer S2380; Norwalk, CT) in deparaffinized specimens. Table 1 shows the main data of the patients at baseline and during the study. Significant improvement of glycemic control was obtained in each patient. At baseline, serum ferritin levels were significantly higher than those in 20 normal age-matched controls (223 ± 139 vs. 122 ± 66 μg/L; $P < 0.01$) and significantly decreased at the end of the study. Serum ferritin correlated with triglyceride at baseline ($r = 0.69$; $P = 0.026$) and with HIC only at the end of the study ($r = 0.87$; $P = 0.024$). Liver function test results were normal at baseline and did not change during the study. Hepatic steatosis, as defined by ultrasound examination and histology, was present in 80% of the patients at baseline and in 25% after 12 months; it was mild and often associated with very mild necroinflammatory activity. In 5 patients, HIC decreased after 12 months, but did not change in 1 patient. The results suggest the existence of a relationship between glucose metabolism, fatty liver, serum ferritin, and hepatic iron. Hyperinsulinemia, the main manifestation of insulin resistance, favors the accumulation of free fatty acid in the liver and increases the risk of steatosis.[4] High serum ferritin levels are common in patients with metabolic disorders and nonalcoholic steatosis or steatohepatitis, and some of them also have increased HIC.[4,5] In our patients, serum ferritin levels at baseline were increased to a degree disproportionate to liver iron stores because they significantly decreased after metabolic improvement when the expected correlation with HIC finally appeared. Also, the mild but significant decrease of HIC at the end of the study suggests a possible influence of diabetic-associated metabolic alterations on hepatocellular iron metabolism. The improvement of the glycemic control observed in the patients can be ascribed to increased insulin action in the liver and in the peripheral tissues. The concomitant improvement of steatosis and the decrease of serum ferritin and hepatic iron levels suggest that these alterations are distinct consequences of a common factor (probably insulin resistance in this case) and that they are at least partially reversible by the improvement of metabolic control. Hypertriglyceridemia is another condition typically associated with the insulin resistance syndrome,[2] and the correlation observed in our patients at baseline between serum ferritin and triglyceride further supports the hypothesis of a relationship between insulin resistance and alterations in iron metabolism.

Table 1. Iron and Metabolic Indices in 10 Patients With Poorly Controlled Type II Diabetes at Baseline and During Treatment

	Baseline	2nd month	6th month	12th month
Transferrin saturation (%)	29 ± 12	24 ± 9	24 ± 7	27 ± 12
Serum ferritin (μg/L)	223 ± 139	156 ± 102	140 ± 100	121 ± 101[b]
Mean blood glucose (mg/dL)	252 ± 53	157 ± 45	151 ± 27	157 ± 49[c]
Fructosamine (mmol/L)	350 ± 62	271 ± 43	273 ± 49	263 ± 100[c]
Glycosylated hemoglobin (%)	12.3 ± 2.5	9.1 ± 2.5	8.5 ± 2.1	8.6 ± 1.6[d]
HIC[a] (mg/100 mg)	109.2 ± 32			89.7 ± 45.6[e]

NOTE. Results are means ± SD.
[a]Measured in 6 patients.
[b]$P < 0.0001$, Kruskal–Wallis nonparametric analysis of variance (ANOVA) test.
[c]$P < 0.0001$ and [d]$P = 0.0011$, ANOVA.
[e]$P = 0.049$, paired t test.

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Short-Segment Barrett's: A Significant Lesion

Dear Sir:

We read with interest the study by Sorbi et al.[1] in the December 1999 issue of GASTROENTEROLOGY, in which they evaluated a small-caliber endoscope with an outer diameter of 6 mm. We would like to make two points. First, the title on the cover page "Unsedated Small Intestinal EGD" is misleading. The study evaluated esophagogastroduodenoscopy using a small-caliber endoscope in the upper gastrointestinal tract proximal to the distal duodenum and not the conventional small intestine. Second, we were disappointed to note that short-segment Barrett's esophagus (SSBE) was not included in the list of significant lesions in the upper gastrointestinal tract.

SSBE is suspected endoscopically when the length of apparent columnar-lined esophagus is less than 3 cm.[2] Any endoscope looking to replace the current videoendoscopes should be able to identify not only columnar-appearing epithelium less than 3 cm but also much shorter tongues and fingers of possible Barrett's esophagus, for the following reasons:

1. SSBE is being reported with increasing frequency[2,3] and is suspected in up to 33% patients with reflux symptoms undergoing endoscopy.[4] In a similar comparative study from our center, the length of involvement was less than 3 cm in 17 of the 18 patients with suspected Barrett's esophagus.[5]
2. SSBE can progress to dysplasia,[2,6–8] with the reported incidence being as high as 8.5%.[9]
3. The association of SSBE with adenocarcinoma is well established.[6–8,10]
4. Surveillance for SSBE is recommended by experts.[2]

With advances in technology, endoscope diameters are likely to shrink further. Prospective studies comparing these newer endoscopes with existing instruments will follow. We recommend that apparent columnar-lined epithelium less than 3 cm in the esophagus always be included as a significant finding. Endoscopes unable to diagnose this lesion reliably would have difficulty being accepted by the medical community.

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Reply. Unsedated small-caliber endoscopy is a procedure that is growing in interest for various reasons. The interpretation of our study title by Drs. Mokhashi and Hawes is confusing to us. We did not intend this experience to suggest that endoscopy was a component of the examination. The study design in phase 1 limited the technical assessment of the endoscope to passage into the second portion of the duodenum only. The title of the study, including the running titles, accordingly do not contain reference to the small intestine. There is an incorrect bullet-type notation of the manuscript on the cover of the issue that should not be a problem for readers.

Our intent for this study was to explore the technical feasibility of unsedated small-caliber endoscopy, patient tolerability, as well as diagnostic accuracy. The latter was accomplished by accepting incontrovertible findings. These findings included a classic definition of Barrett's esophagus.

We recognize and understand the points of Drs. Mokhashi and Hawes on SSBE, which is a clinical management issue in evolution. In principle, we agree that current and future small-caliber instruments,