Metabolic Syndrome Impairs Hep C Treatment

In one study, all components of metabolic syndrome but one—low HDL—predicted a poor response.

BY BRUCE JANCIN

FROM THE ANNUAL INTERNATIONAL LIVER CONGRESS

VIENNA — Metabolic syndrome predicts a poor response to treatment for chronic hepatitis C viral infection, according to results from a large trial—but there's a twist.

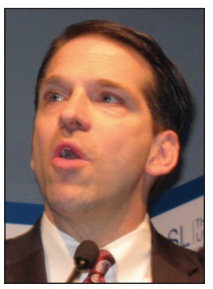
In the 3,070-patient study, each of the individual components of metabolic syndrome was a negative predictor of sustained virologic response to 48 weeks of antiviral therapy, except one: Surprisingly, a low HDL predicted a favorable response to treatment. And a cardioprotective high HDL level was an independent predictor of treatment failure, Dr. Mark S. Sulkowski reported at the congress.

Another study presented at the congress suggested that intensified doses of the standard antiviral agents—pegylated interferon and ribavirin—could significantly improve treatment success rates in difficult-to-cure hepatitis C genotype 1 patients with metabolic syndrome.

Dr. Sulkowski noted that all of the more than 3,000 participants in the IDEAL study (Individualized Dosing Efficacy versus Flat Dosing to Assess Optimal Pegylated Interferon Therapy) had genotype 1 hepatitis C.

At baseline, 30% met the criteria for metabolic syndrome from the American Heart Association/International Diabetes Federation. Their sustained virologic response (SVR) rate of 35% after 48 weeks of pegylated interferon plus ribavirin was significantly lower than the 42% rate for patients without metabolic syndrome.

The difference was significant in both men and women, although the outcome gap was bigger in women. The SVR in women with metabolic syndrome was



For each additional component of metabolic syndrome, the SVR dropped further.

DR. SULKOWSKI

35%, compared with 43% in women without metabolic syndrome. Men with metabolic syndrome had a 35% SVR, compared with 41% in those without the syndrome, reported Dr. Sulkowski, medical director of the viral hepatitis center at Johns Hopkins University, Baltimore.

For each additional component of metabolic syndrome that a patient had, the SVR dropped further. Multivariate regression analysis revealed that an elevated fasting blood glucose was the strongest negative predictor of SVR, with an odds ratio of 1.72 for missing this key end point.

Unexpectedly, a secondary analysis revealed that an HDL of at least 40 mg/dL in men or 50 mg/dL in women was another independent predictor of not attaining an SVR, with an odds ratio of 1.5. The 18% of IDEAL participants with both a high fasting blood glucose and a high HDL at baseline had a twofold increased likelihood of not achieving an SVR after 48 weeks of antiviral therapy.

Six months after completion of therapy, 56% of patients with metabolic syndrome at baseline no longer met criteria for the disorder, Dr. Sulkowski said at the congress, which was sponsored by the European Association for the Study of the Liver.

In an interim analysis of an observational study involving 2,501 German patients being treated for chronic hepatitis C, three factors were found to be independent predictors of failure to achieve an early virologic response at week 12: hypertriglyceridemia, elevated fasting blood glucose, and body mass index of 27 kg/m^2 or more. But a total cholesterol level higher than 190 mg/dL was associated with a threefold greater likelihood of early virologic response compared with that seen in patients with a lower cholesterol level, reported Dr. Elmar Jaeckel of Hannover (Germany) Medical School.

The relapse rate in those treated with the most intensive regimen was half that of those on standard therapy.

DR. SHIFFMAN

The strongest predictor of an early virologic response was hepatitis C genotype 2 or 3. These genotypes were associated with a 7.6-fold greater likelihood of early virologic response compared with genotypes 1, 4, 5, or 6, Dr. Jaeckel said.

Dr. Mitchell L. Shiffman presented a retrospective analysis of 1,135 patients with chronic hepatitis C genotype 1 infection who were treated with pegylated interferon alfa-2a (Pegasys) plus ribavirin in a variety of dosing schedules. Among the 34% of patients classified as having metabolic syndrome, the relapse rate in those randomized to the most intensive treatment regimen was only about half that of patients on standard therapy—24% vs. 47%—reported Dr. Shiffman of Bon Secours Health System, Newport News, Va.

Similarly, the SVR rate at week 72 in patients assigned to the most intensive regimen was 43%, compared with 24% in patients on the standard approved regimen.

The most intensive regimen consisted of pegylated interferon alfa-2a at 360 mcg/week for the first 12 weeks followed by 180 mcg/week out to week 48, accompanied by weight-based dosing of ribavirin at either 1,400 or 1,600 mg daily. The standard regimen was pegylated interferon alfa-2a at 180 mcg/week plus ribavirin at 1,200 mg daily.

This finding, that intensified treatment increases the treatment success rate in difficult-to-cure genotype 1 patients with metabolic syndrome, must be considered hypothesis generating, and requires confirmation in prospective randomized trials, Dr. Shiffman said.

The studies presented by Dr. Shiffman and Dr. Jaeckel were funded by F. Hoffmann-La Roche Ltd.; they serve as consultants to the company. The IDEAL study was supported by Schering-Plough Corp. Dr. Sulkowski disclosed serving as an adviser to Schering-Plough and nine other pharmaceutical companies. ■

DXA More Accurate Than BMI as Measure of Obesity

BY MIRIAM E. TUCKER

FROM THE ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS

BOSTON — Dual energy x-ray absorptiometry was a more accurate predictor of obesity than was body mass index in a retrospective comparison of the two measures in 1,234 adults.

Despite its widespread use, BMI is not an accurate indicator of body fat. Direct measures of adiposity, such as those obtained by dual energy x-ray absorptiometry (DXA), are far more precise, Dr. Eric R. Braverman and his associates reported in a poster at the meeting.

'We have a big problem with the BMI. You could retitle it the "baloney mass index." '

DR. BRAVERMAN

"We have a big problem with the BMI. You could retitle it the 'baloney mass index.' It's a mathematical equation. … The scientific standard is clearly subpar compared to our other endocrinology standards," Dr. Braverman of the department of neurological surgery at Weill Cornell Medical College, New York, said at a press briefing.

Dr. Braverman and his colleagues analyzed medical records of 1,234 private adult outpatients (490 men, 744 women) who had both BMI and DXA measurements during 2003-2009.

The subjects had a mean age of 51 years, a mean BMI of 26.2 kg/m^2, and a mean percentage body fat of 29.5%. They were classified as obese or nonobese for both parameters based on the American Bariatric Society's definitions: BMI of at least 30 mg/kg^2, and body fat percentages of 25% for males and 30% for females based on DXA.

When the researchers used BMI, 249 (20%) were classified as obese. DXA measurement showed that of those 249, 95% (237) were obese and 5% (12) were nonobese on the basis of body fat percentage.

When the researchers used DXA, 689 (56%) were classified as obese. Of those 689, 34% (237) were obese and 66% (452) were not obese based on BMI.

Thus, 37% of patients were misclassified by BMI: A total of 452 were found to be obese by DXA but nonobese by BMI and 12 were obese by BMI but not by DXA.

The 66% of patients classified as obese by DXA but who were "missed" by BMI had lower muscle and lean body mass, Dr. Braverman and his associates noted.

The BMI measurement of obesity in this study was approximately identical to the national percentage of obesity, which is also determined by BMI. "However, we have shown that BMI is a highly insensitive measure, resulting in an underdiagnosis of obesity. If we can extrapolate from the rest of our data on the national scale, it is very likely that obesity is a much bigger epidemic than is currently acknowledged," the investigators said in the poster.

Dr. Braverman said in an interview that he foresees DXA becoming a routine part of clinical practice in the future, to measure bone density as well as assess obesity.

"In the 21st century, the physical is really quite outdated and almost no yield to silent disease that every endocrinologist works in. DXA and an efficiency system that can deliver it at $3 a test will make it simply a part of the physical," he said. ■

VITALS

Major Finding: BMI failed to detect obesity in 37% and falsely detected it in 5% in a study of 1,234 adults who had both BMI and DXA measurements.

Data Source: Medical chart review of private adult outpatients.

Disclosures: Study funded by the nonprofit PATH (Place for Achieving Total Health) Research Foundation NY. Dr. Braverman, director of the PATH centers in New York and Philadelphia, had no other financial disclosures.