

LIPOWATCH[®] NEWS

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The LipoWatch[®] fax program from Visionary Health Concepts supports providers and patients with education that integrates scientific data with a "real world" focus. This month's topic is lipodystrophy-related insulin resistance.

Insulin helps move glucose from the blood into body tissues and inhibits production of glucose by the liver. With insulin resistance, the body needs higher than normal amounts of insulin. This is not very different from the situation early in type II diabetes mellitus (adult onset).

Insulin resistance is associated with high triglycerides and glucose, hypertension, and low HDL-cholesterol – all documented risk factors for cardiovascular disease.

Insulin Resistance and HIV

Insulin resistance was linked with lipodystrophy in 1998, and most strongly to protease inhibitor use, even without changes in body composition. For example, indinavir (Crixivan) can induce insulin resistance in HIV-negative volunteers. Also, insulin sensitivity improved in studies of switching from a protease inhibitor to a non-nucleoside reverse transcriptase inhibitor or to abacavir (Ziagen).

The mechanism for insulin resistance is not clear. For example, one study of the protease inhibitor ampre-

navir (Agenerase) found no changes in insulin sensitivity through 24 weeks of therapy. However, by week 48 insulin resistance had increased and so had truncal fat, a known correlate of insulin resistance. It's not clear whether the insulin resistance was caused by amprenavir, or by the increase in visceral fat. The loss of peripheral fat (lipoatrophy), which was not seen in this study, might also stimulate insulin resistance.

There is no simple test for insulin resistance. Fasting glucose, random glucose, and fasting insulin measurements each have their weaknesses. The "gold standard" test is a lengthy "clamp" procedure that entails timed intravenous infusions of glucose and insulin.

Although not studied in people with HIV, non-drug treatment for insulin resistance includes dietary changes and increased physical exercise. Switching from a protease inhibitor to efavirenz (Sustiva), nevirapine (Viramune), or abacavir (Ziagen) might help. However, any decision to change a regimen must carefully weigh possible metabolic benefits against other characteristics of both the current and prospective regimen.

Metformin (Glucophage) and the glitazones are generally used to treat non-HIV-related insulin resistance.

Metformin, which reduces the liver's production of glucose, appears well tolerated by patients with HIV. In one study, body weight declined evenly, so it did not appear to worsen peripheral lipodystrophy. Blood lipids, however, did not decrease. In fact, in one study in people with HIV lipodystrophy, metformin increased total cholesterol and triglycerides.

Glitazones, by improving insulin sensitivity, increase the uptake of glucose into body tissues. In non-HIV infected patients, they improve glucose metabolism, and – in one study – decreased abdominal fat while increasing some subcutaneous fat. Troglitazone (Rezulin) was pulled from the market because of liver toxicity. Two other glitazones are being studied.

One ongoing trial (ACTG 5082) is examining the effects of metformin and rosiglitazone (Avandia), separately or in combination, in people with HIV who have high insulin levels and abdominal fat accumulation. ■

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