Diabetes Drug Avandia Helps Reverse Lipoatrophy

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Avandia (rosiglitazone), a member of the “glitazone” drug class approved for the treatment of diabetes, may help reverse fat loss in HIV-positive people with lipoatrophy, according to a new study reported by Grace McComsey, MD, of Case Western Reserve University in Cleveland and her colleagues on Monday, February 9, at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal. The encouraging results counter those of several other studies, likely because patients in this most recent trial were no longer treating their HIV with either zidovudine (found in Retrovir, Combivir and Trizivir) or stavudine (Zerit)—the two thymidine analogue members of the nucleoside reverse transcriptase inhibitors (NRTIs) drug class believed to cause lipoatrophy.

Glitazones have been eyed as a potential lipoatrophy treatment for several years. Test tube studies suggest that they stimulate the production of a protein called PPAR-gamma, which in effect promotes the healthy activity of adipocytes (fat cells). Clinical trials have also found that glitazone therapy is associated with gains in subcutaneous fat—fat immediately below the skin—in people with diabetes.

Results from eight clinical trials involving HIV-positive people completed to date have been mixed—four showed increases in limb fat (mostly legs and arms) associated with the use of a glitazone, whereas four did not. However, many studies yielding lackluster results often involved HIV-positive individuals who remained on either zidovudine or stavudine for the duration of the trials. In turn, McComesey explained, the ongoing damage to adipocytes (fat cells) caused by thymidine analogues may blunt the potential benefit of glitazone treatment.

Side effects are potential concern of glitazone treatment, including increases in total cholesterol and harmful non-HDL cholesterol—existing concerns among many people with HIV, notably those with body fat changes. In turn, if glitazones are to be used for the treatment of lipoatrophy, they must be proven safe and effective.

Promoted as the first study of a glitazone for lipoatrophy involving HIV-positive patients being treated with a regimen not containing either zidovudine or stavudine, McComsey’s study enrolled 71 HIV-positive individuals with documented fat loss to take either Avandia (4 mg twice daily) or placebo for 48 weeks. All volunteers had been off a tNRTI for at least 24 weeks before enrolling in the study.

All study volunteers had the amount of subcutaneous fat in their limbs measured using dual energy X-ray absorptiometry (DEXA) during the trial. Disappointingly, the researchers did not specifically evaluate the effect of Avandia treatment of facial wasting—often the most distressing manifestation of HIV-associated lipopatrophy.

Blood tests to measure viral load, lipid levels, glucose and insulin were also conducted. The average age upon entering the study was 40 year, 83 percent were men and approximately 50 percent were white.

At the start of the trial, patients had about 6.5 kilograms of limb fat—“normal” is 8 kg or more. After three months of treatment, patients receiving Avandia saw their limb fat increase by about 0.9 kg, compared with a 0.25 kg increase in the placebo group. This translates into a 15 percent gain in limb fat associated with Avandia treatment, compared with a 5 percent gain in limb fat associated with placebo. This difference between the two groups after 48 weeks was statistically significance, meaning it was too large to have occurred by chance.

About 98 percent of patients enrolled in the study maintained viral loads below 400 copies for the duration of the study. Not surprisingly, insulin levels—which were abnormally high in about 37 percent of the patients enrolled—fell in the Avandia group but not in the placebo group.

As for lipid levels, total cholesterol levels were significantly higher in the Avandia group after 48 weeks compared with those in the placebo group. No significant differences in non-HDL or triglyceride levels were reported. Similarly, body mass indexes—a measure of weight in relation to height—were not statistically different after 48 weeks of treatment.

Dr. McComsey said that further analysis of the data is ongoing, including a closer look at the effect of glitazone treatment on adipocyte functioning in people with HIV and lipoatrophy. More data regarding the effects of glitazone treatment on facial fat volume and patient satisfaction with therapy are also needed, though it is not clear if this particular study will answer these important questions.

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