



8th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

San Francisco, California - September 24 - 26, 2006

EFFECT OF PIOGLITAZONE ON LIMB FAT AND CIRCULATING ADIPOKINES IN HIV-RELATED LIPODYSTROPHY (ANRS113: LIPIOT)

Antiviral Therapy 2006; 11:L16 (abstract no. 23)

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Lipodystrophy (LD) is a frequent adverse event of antiretroviral therapy. Contradictory results have been reported regarding the ability of thiazolidinediones to reverse peripheral lipodystrophy in these patients. We performed a randomized, double-blind, prospective placebo-controlled study with 130 HIV-infected LD patients. Patients received 30 mg pioglitazone or a matching placebo, once daily, for a 48-week study period. Efficacy was assessed by measurement of anthropometric parameters. Metabolic parameters and circulating adipokines were evaluated. Pioglitazone had a beneficial effect on limb fat mass with a mean increase of 0.38 (SD 0.78) kg between W0 and W48 while no significant change was observed in patients in the placebo group. This effect was only seen in patients not receiving stavudine. There was no difference between the two groups as regards the mean changes in VAT between W0 and W48. No difference was observed between the pioglitazone and the placebo groups in the mean changes in glycaemic parameters, triglycerides, total cholesterol or LDL cholesterol between W0 and W48. By contrast, HDL-cholesterol was improved: the mean change was +0.09 mmol/L (SD 0.18) with pioglitazone and -0.08 mmol/l (SD 0.66) with placebo ($P=0.005$). No significant change of plasma levels of leptin, resistin and soluble TNF receptor I (sTNFR I) was observed at W48 in the pioglitazone as compared to the placebo group. By contrast, plasma adiponectin levels were increase at W48 in the pioglitazone group [3.9 (SD 3.3) versus 8.7 (SD 7.7) ng/ml] while no significant change was observed in the control group [2.3 (SD 2.2) versus 2.4 (SD 2.2) ng/ml]; $P<0.0001$. Interestingly, this effect was observed both in patients not receiving and receiving stavudine. The delta change of limb fat mass between W0 and W48 correlated with both plasma pioglitazone concentration

($r=0.476$, $P<0.001$, $n=51$) and leptin variation between W0 and W48 ($r=0.365$, $P<0.01$, $n=57$). Overall, the results of this study support the use of pioglitazone in the treatment of peripheral lipotrophy in HIV-1-infected patients. We report here that pioglitazone has a positive impact on limb fat and adipose tissue endocrine function by improving adipokines secretion.

2006-09-24
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