Letters To The Editor

Leptin and insulin resistance: good, bad, or still unclear?

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TO THE EDITOR: the article by Paz-Filho et al. (13) addresses the physiological changes with reduction in intrahepatic and intra-

muscular fat, decreased energy intake, and improvement in triglyceride levels (1, 10, 11, 14). Although the overwhelming evidence points toward improved insulin sensitivity in the patients with lipodystrophy, whether these are direct effects of leptin on insulin sensitivity or indirect effects related to other accompanying changes caused by leptin therapy remains to be sorted out in humans.

Given this alternative explanation of findings reported by Paz-Filho et al. (13), along with the positive effect on insulin sensitivity of leptin in patients with lipodystrophy, it is premature to implicate leptin as a contributor to the insulin resistance of obesity. Furthermore, no apparent worsening of glucose metabolism was evident or reported during the trials with recombinant methionyl human leptin (5) and pegylated leptin (6, 7).

Finally, it is certainly understandable why the present studies were not undertaken when subjects were at steady weight. A lengthy withdrawal period to get the subjects to a stable weight is not an ethical approach, taking into consideration all the beneficial effects of leptin therapy in these individuals. Studying insulin sensitivity during a shorter withdrawal period is unlikely to be helpful unless a caloric restriction can be achieved to maintain the reduced weight. These authors should be congratulated for undertaking a difficult set of translational studies in patients with a rare syndrome. Taking the time to design and execute studies in patients who are presented in the community is clearly important. Despite design problems that are inherent in performing research in patients undergoing community is clearly important. Despite design problems that are inherent in performing research in patients undergoing bariatric surgery.

Previous studies in lipodystrophic patients and in patients with mutations of the insulin receptor have indicated that leptin therapy is associated with a marked improvement in the metabolic state of the patients with remarkable improvements in insulin sensitivity. This is supported by direct measurement of glucose disposal and suppression of hepatic glucose output before and after leptin therapy as well as the indirect evidence of improved glucose control and/or lowering or discontinuation of insulin therapy. When withdrawal from leptin therapy was attempted in one patient with lipodystrophy, this was accompanied by an immediate worsening of glucose and insulin levels within 48 h of withdrawal (11). However, like those of Paz-Filho et al. (13), these patients are undergoing significant physiological changes with reduction in intrahepatic and intra-

REFERENCES


