



## Short Communication

# Leptin deficiency due to lipid apheresis: a possible reason for ravenous hunger and weight gain

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**OBJECTIVE:** To investigate how extracorporeal cholesterol lowering therapy affects circulating leptin levels in patients with ravenous hunger after treatment and permanent weight gain.

**DESIGN:** A case report.

**SUBJECT:** 51 y old caucasian male patient with moderate chronic renal failure.

**MEASUREMENTS:** Serum Leptin concentration (RIA, Linco Research Inc, St. Louis, MO, USA), total cholesterol, low density lipoprotein cholesterol, blood glucose levels, calorie intake by food records.

**RESULTS:** During treatment total cholesterol was reduced by 50%. Serum Leptin levels showed a 42% reduction at the end of treatment, that by far exceeds the physiological diurnal variation. Calorie intake was significantly increased on days of treatment.

**CONCLUSION:** We conclude that this artificial reduction in circulating leptin plays an important role in the pathogenesis of ravenous hunger and weight gain under extracorporeal cholesterol lowering therapy in this case.

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**Keywords:** lipidapheresis; leptin; cholesterol; appetite; obesity

Leptin, the protein of the *ob* gene, is thought to be involved in the regulation of body weight by transmission of a 'lipostatic' signal from fat stores to the central nervous system resulting in appetite suppression and increased thermogenesis.<sup>1</sup> As a consequence, leptin deficiency has been shown to result in excessive obesity in both mice<sup>1</sup> and men.<sup>2</sup>

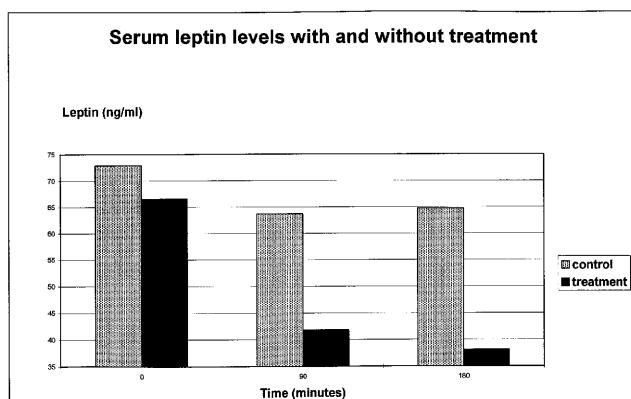
Hereby we report on a 51 y old caucasian male patient with moderate chronic renal failure (serum creatinine of 3.1 mg/dl) on a chronic extracorporeal cholesterol lowering therapy due to drug resistant hyperlipidaemia for 14 months. Therapy was performed with Cascadeflo AC-1770 (Asahi Medical Co. Ltd, Frankfurt, Germany) once a week for 3 h. Since the onset of therapy the patient showed permanent weight gain of 18 kg up to an actual body weight of 96 kg (body mass index 32.7 kg/m<sup>2</sup>). Assessment of body composition by bio impedance (BODY4, Data input, Frankfurt, Germany) revealed a fat mass of 34.3 kg corresponding to 35.7% of total body weight. Additionally the patient complained of ravenous hunger with excessive food intake after treatment. Food records, performed periodically, revealed

a significant increase of energy intake on days of treatment (3178 kcal ± 37 vs 2053 kcal ± 208 on days without treatment). Diet was quantified by computed analysis (EWP, dato Denkwerkzeuge, Vienna, Austria).

The hypothesis of our investigation was to test the possibility that, additionally to lipid particles, plasma leptin might be eliminated during apheresis therapy. Therefore leptin concentrations were measured before, during and after therapy and 2 days later following the same time protocol, but without treatment. On both occasions, the sampling was started at 7.30 a.m. after an overnight fast and a standardized evening meal (at 7 p.m.) the day before. During lipid apheresis, total cholesterol was reduced by 50% from 294 to 148 mg/dl. Thereby, low density lipoprotein cholesterol fell from 167 to 64 mg/dl and lipoprotein (a) was reduced from 203 to 69 mg/dl. Blood glucose concentration remained stable (4.95 mmol/l baseline value, 5.05 mmol/l at the end of treatment).

Serum leptin was found to be reduced from 67 ng/ml at baseline to 39 ng/ml after treatment (42% reduction, Figure 1). In the eluate a leptin concentration of 20 ng/ml was found. Two days later circulating leptin concentration was 72 ng/ml under baseline condition and showed only a slight decrease to 65 ng/ml (10% reduction) after three hours without treatment (Figure 1), which corresponds to the diurnal leptin variation. Leptin reduction due to lipid apheresis by far exceeds the physiological diurnal variation.

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**Figure 1** Serum leptin concentrations before, during and at the end of treatment and without treatment for control. Leptin concentrations were measured by RIA (Linco Research Inc, St Louis, MO, USA)

Based on these data we suggest that in this patient during extracorporeal cholesterol lowering therapy with Cascadeflo not only lipid particles were reduced but also circulating leptin concentrations. This suggestion is based on the findings that (I) significant amounts of leptin could be determined in the eluate and (II) the decline of plasma leptin concentration observed during treatment by far exceeds the physiological decline<sup>3</sup> and is in the range of reduction observed by a weight loss of about 10 kg body weight.<sup>4</sup>

In human obesity increased concentrations of circulating leptin<sup>4</sup> are found, suggesting a possible resistance to leptin action. Fasting leptin concentration observed in our patient fits into the range observed for an amount of body fat as high as 35% of total body weight. Chronic renal failure has been reported to be accompanied by increased concentrations,<sup>5</sup> possibly explaining the high values in our patient.

No information exists on the effect of artificial reduction of serum leptin concentration on food intake and body weight. In our case elevated circulating baseline leptin concentrations were significantly decreased by lipid apheresis. Energy intake on the day of treatment was significantly higher than on days without treatment. This regular energy excess can explain the weight gain in our patient. Two days after treatment baseline leptin was slightly higher than the preapheresis value. This restoration of the patient's serum leptin concentration is possibly triggered by the excessive food intake.

Such a 'relative' short-term hypoleptinaemia might play an important role in triggering food intake via disturbances in the leptin signalling pathway. Food intake and body weight, however, are determined by a complex interaction of regulatory hormones. Further evaluations are required to clarify the role of leptin and other satiety regulating hormones, which also might be disturbed by lipid apheresis.

#### References

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