

**Intramyocellular Lipids (IMCL), Plasma Leptin System and Glucose Uptake in Women with a History of Gestational Diabetes (GDM).**

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**Introduction**

Insulin resistance is a common feature of metabolic syndrome, in which alterations of lipid metabolism play an important role. Recent studies have introduced (1) and validated (2) the quantitation of intramyocellular lipid (IMCL) content using localized in vivo 1H NMR spectroscopy and have shown a correlation between intramyocellular lipid content and insulin sensitivity in lean and obese healthy humans (3,4), and offspring of type 2 diabetic patients (4,5).

Leptin is involved in the regulation of body weight and energy metabolism. In humans plasma leptin relates to plasma insulin and plasma lipid concentration. Recent studies have shown a relation between free and bound leptin to insulin secretion in patient with impaired insulin tolerance and increased soluble leptin receptors levels in diabetic women (6).

Gestational diabetes (GDM) characterizes insulin resistant women at high risk for Type 2 diabetes mellitus and represents an ideal model for studies of prediabetic state.

This study aims to examine the relationship of IMCL content with insulin sensitivity, total plasma leptin (PL), bound plasma leptin (BL), and plasma leptin receptor (LR) concentrations, intravenous glucose tolerance (KG), insulin sensitivity (SI) and glucose effectiveness (SG) in women with a history of gestational diabetes (postGDM)

**Study Groups and Methods**

28 postGDM women were studied 4-10 months after delivery (age: 31.9±1.5 years, BMI: 26.1±1.1 kg.m⁻², waist-hip-ratio (WHR): 0.82±0.02, triglycerides: 118±6.3 mg/dl). Control data are taken from the literature (7).

IMCL content was measured in the soleus muscle by means of 1H NMR spectroscopy in 3T MedSpec 30/80 NMR system (Bruker, Germany) using a 25 cm standard birdcage head coil. STEAM sequence (TR= 20 ms, TM= 33 ms, TR= 6 sec, 1024 data point, SW= 2500 Hz, NS= 32) with CHESS water suppression scheme was applied on the cubical volume of interest (VOI: 1.73 - 3.38 cm³) positioned solely in the soleus muscle. Spectrum without water suppression from the same VOI was also acquired (NS=1, other parameters identical). Spectral analysis was done offline using line fitting routine included in the MacNUTS software package (AcornNMR, Ca.). IMCL content was quantified by comparison of the intensity of the -(CH2)n- group resonance line at 1.25 ppm with that of water from water unsuppressed spectrum after a T2 relaxation correction was done. IMCL content is expressed in percent of water resonance intensity. Intradividual variation of IMCL quantitation was assessed in 9 young healthy subjects each measured 4 times. None of the series showed significant variation. IMCL content was in the range of 0.8% - 1.4% of water resonance intensity and standard error of the mean ranged from 0.01%–0.03% of water resonance intensity.

Insulin sensitivity (SI), glucose effectiveness (SG) and disposition indexes were derived from the insulin-modified frequently sampled glucose tolerance test (FSIGT) using mathematical model analysis (8). The basal metabolic rate and body fat content were assessed from bioimpedance measurements (Akern-RJL Systems). Plasma concentration of total plasma leptin (PL) was measured by radioimmunoassay kit (Linco Research). Plasma concentration of total plasma leptin (PL), bound plasma leptin (BL), and leptin receptor (LR) were measured by specific radioimmunoassay methods according to Lewandowski et al.(7). Total plasma leptin (PL) correlated with amount of body fat (r=0.5, p<0.001) BMI (r=0.6, p<0.0005) and insulin secretion (r=0.4, p<0.02), while bound leptin (BL) correlated positively only with leptin receptor concentration (LR, r=0.36, p<0.01), disposition index (r=0.69 p<0.01) and negatively with glucose effectiveness (SG, r=0.35, p<0.01).

**Discussion**

Results of the study support the hypothesis of a correlation between the IMCL content and the glucose utilization. Interestingly, IMCL are related to insulin-independent glucose dependent glucose uptake and not to the insulin sensitivity as was already demonstrated in other insulin resistant populations (4,5).

**References**


**Fig.1 Localized proton spectrum of human soleus muscle.**

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**Results**

The postGDM women featured moderate insulin resistance as assessed by model-parameters SI (4.47±0.54.10⁻⁴.min⁻¹.(µU.ml)⁻¹; -25% vs. Control) and SG (0.021±0.001 min⁻¹; -30% vs. Control), as well as increased (20% vs. Control) plasma concentrations of BL (4000±40 pmol/l) and LR (3400±300 pmol/l).