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Role of Visfatin in the Pathogenesis of Gestational Diabetes Mellitus

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Abstract

Background The recently discovered adipocytokine visfatin has insulin-like properties. It lowers blood glucose and improves insulin sensitivity; however, clinical data on visfatin are limited.

Objective To evaluate the role of visfatin in GDM (gestational diabetes mellitus), we determined visfatin levels in women with GDM and healthy pregnant women.

Methods A total of 60 women were evaluated: 30 women with gestational diabetes mellitus and 30 healthy pregnant women to serve as control subjects. Serum visfatin concentrations were analyzed using an enzyme-linked immunosorbent assay the study was done in Al-Yarmouk Teaching Hospital during the period from November 2010 to March 2011.

Results Serum visfatin concentrations were significantly lower in the gestational diabetes mellitus group (0.27±0.1 ng/ml) than in the healthy control group (1.37±0.25ng/ml) (P=0.0001).

Conclusions Our results show that there are decreased concentrations of serum visfatin in gestational diabetes mellitus subjects and this may indicate that visfatin plays a role in the pathogenesis of gestational diabetes mellitus .However; further experiments are needed to clarify this role.

Key Words Visfatin, Gestational Diabetes Mellitus

Introduction

Gestational Diabetes mellitus is defined as carbohydrate intolerance that begins or is first recognized during pregnancy [(1)]. It occurs in 3% to 5% of pregnant women and is associated with adverse effects for both mother and fetus [(1)]. Gestational diabetes mellitus share a number of epidemiologic, physiological, and genetic characteristics with diabetes mellitus type two and seems to be a significant risk factor for the development of diabetes mellitus type 2 in later life [(2)].

A variety of polypeptides secreted from adipose tissue, such as TNF-α (tumour necrosis factor-α) [(3)], resistin [(4)] and leptin [(5)], might play an important role in metabolic homoeostasis and the development of Type II diabetes, dyslipidaemia and artherosclerosis [(6)]. Recently reported, the novel adipocytokine visfatin (52 kDa cytokine with 491amino acids), which was previously known as PBEF (pre-B-cell colony-enhancing factor). It was originally isolated as a secreted factor that synergizes with interlukine-7 and stem cell factor to promote the growth of B-cell precursors [(7)].

Visfatin is a peptide that is predominantly expressed in, and secreted from, visral adipose tissue [(8,9)] and exerts insulin-mimicking effects through activation of an insulin receptor, although in a manner distinct from that of insulin [(9)]. The role of visfatin in human physiology and pathophysiology remains to be elucidated, while, according to some authors, plasma concentrations of visfatin are elevated in

obesity [10] and type 2 diabetes [11], which are states characterized by insulin resistance (IR) and typically also observed in gestational diabetes mellitus (GDM).

Acute administration of recombinant visfatin to mice leads to a reduction of plasma glucose independent of changes in plasma levels of insulin. Thus it works synergistically with insulin to lower blood glucose concentrations [9]. Chronic elevation of visfatin in mice reduces insulin plasma concentrations [9], and it was suggested that visfatin improves insulin sensitivity [12]. Visfatin affects the insulin signal transduction pathway by inducing tyrosine phosphorylation of the insulin receptor and IRS1 and 2 (insulin receptor substrate 1 and 2) in the liver. Furthermore, an autocrine/paracrine function on visceral adipose tissue as well as an endocrine role modulating insulin sensitivity in peripheral organs might be modes of action [12].

To evaluate the role of visfatin in GDM we determined this novel adipocytokine in women with GDM and healthy pregnant controls.

Methods

All subjects were carefully instructed about the aims of the study and written informed consent was given. Thirty women with GDM (mean age, 36±2 years) diagnosed during pregnancy weeks 24-28 and 30 healthy pregnant controls (mean age, 29±2 years) were included in the study. All subjects were non-smokers.

Women were diagnosed as GDM if two or more of the four glucose levels in the tolerance test exceeded the National Diabetes Data Group Criteria as follows:

Fasting more than ≥5.3 mmol/l

1-hour postload 75-g glucose value ≥10.0 mmol/l

2-hour postload glucose value ≥8.6 mmol/l

3-hour postload glucose value ≥7.5 mmol/l

The (OGTT) was performed between 24th and 28th weeks of gestation.

Blood samples were obtained directly from a cannulated vein for the purpose of a routine glucose challenge test at 24-28 weeks of gestation. The serum was separated by centrifugation, and stored at -20 ^{o}C until further analysis. Serum visfatin was analyzed using kit manufactured by (BIO VISION).

Inclusion criteria were signed informed consent, absence of a clinically relevant illness, normal findings in the medical history and physical examination except for GDM, and normal laboratory values. Subjects were excluded if any clinically relevant abnormality was found as part of the screening or in any of the laboratory tests including circulating anti-insulin antibodies and anti-islet cell antibodies. No subject was on a special diet or reported to have any medication, including "over-the-counter" drugs, at the time of blood sampling.

Results

Table 1 shows the clinical results of our subjects, both those with GDM and those with healthy control groups. Serum visfatin concentration was significantly lower in the GDM group (Mean= 0.27±0.1) than in the healthy control group (Mean= 1.37±0.25) (p-value= 0.0001) as shown in and Figure 1.

Table 1. Clinical Data

Parameters	Controls	GDM	P-Value
Visfatin Level (ng/ml)	1.37±0.25	0.27±0.1	0.0001

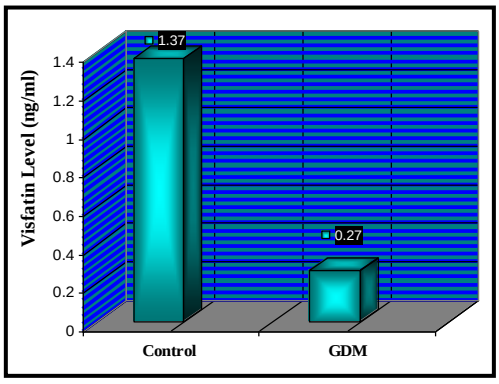

Figure 1. Serum Visfatin Level plotted for both GDM subjects and those who were in the healthy group

Discussion

This study describes the recently identified adipocytokine visfatin in women with GDM and healthy pregnant controls.

The results of this study suggest an inverse association of plasma visfatin concentrations with gestational diabetes mellitus.

The cause of reduced fasting visfatin and mitigated response to glucose challenge in women with GDM is not directly accessible from this study. It has been demonstrated that plasma visfatin concentrations are inversely correlated to progressive-cell deterioration in patients with type 1 or type 2 diabetes [(13)].

The present data argue against an assumption that altered pancreatic insulin secretion has contributed to reduced plasma visfatin in GDM because insulin plasma concentrations were comparable in fasting conditions. This is important, as insulin is known to suppress glucose induced visfatin release in vitro and in vivo [(14)].

On the contrary, as it is known that glucose induces visfatin release, which is also a consistent finding in this study, one might have expected higher visfatin concentrations in women with GDM. Thus, factors other than glucose and insulin alone seem to influence the regulation of visfatin in pregnancy, such as proinflammatory cytokines [(15)]. Indeed, an association between plasma tumor necrosis factor-α and visfatin mRNA in subcutaneous adipose tissue has recently been reported [(16)].

The finding in this study that gestational diabetes mellitus subjects have lower plasma visfatin concentrations suggests that an insufficiency of visfatin may play a role in the pathogenesis of gestational diabetes mellitus, these finding are in agreement with study done by chan et al 2006 and haider et al 2007.

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