Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1765–1767

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

Prolactin effect on blood glucose and insülin in breastfeeding women

Hatice Ozisik [a,*], Aslı Suner [b], Sevki Cetinkalp [a]

[a] Ege University, Faculty of Medicine, Department of Endocrinology, İzmir, Turkey
[b] Ege University, Faculty of Medicine, Department of Biostatistics, İzmir, Turkey

ARTICLE INFO

Article history:
Received 10 March 2019
Accepted 29 March 2019

ABSTRACT

Introduction: Prolactin plays a significant role in lactation and prolactin levels are increasing physiologically in pregnancy and breastfeeding period. There might be different mechanisms during breastfeeding between prolactin and insülin levels. In order to highlighten this mechanisms we compared the plasma levels of glucose, insülin, prolactin, C-peptid in basal situations and after taking 75 gr carbonhydrate, 20 gr protein, 23 gr fat in breastfeeding and in non lactating women.

Material and methods: Participants and measurements: The study population included 12 breastfeeding women and 11 healthy non lactating women as a control group. We collected information on age, history of gestational diabetes mellitus, family history of diabetes mellitus, natality, the symptoms of hypoglycemia. Weight, height and waist circumference were measured and body mass index (BMI) was calculated as weight (kg)/height (m^2).

Results: Prolactin was inversely correlated with HbA1c and 2. hour C peptide ($p=0.005$, $r=-0.564$; $p=0.008$, $r=-0.539$). Prolactin was not significantly correlated with HOMA-IR, HOMA-IS, AUC-I or AUC-G. Prolactin levels were higher in breastfeeding women (median:34.98 μg/L) than in non lactating women (median:12.21 μg/L, $p<0.001$). There was a significant association between age and fasting glucose ($p=0.018$, $r=-0.665$), 2. hour glucose ($p=0.049$, $r=0.578$) in breastfeeding women.

Discussion: In our study, we displayed prolactin was inversely correlated with HbA1c and 2. hour C peptide. Some studies in the past demonstrated that higher prolactin levels had importantly lower prevelance of type 2 diabetes. Our findings supported this situation.

1. Introduction

Prolactin plays a significant role in lactation and prolactin levels are increasing physiologically in pregnancy and breastfeeding period [1]. Prolactin is related with pancreatic cell growth and insülin functions [2]. It has a multifunctional role in different conditions such as immunregulation, reproduction and osmoregulation [3–5]. In addition, prolactin has various isoforms with different biological activities because of post-transcriptional modifications [6]. It has reported that high prolactin levels are associated with lower glucose, lipid levels and greater insülin sensitivity [7,8]. Prolactin receptors are found in the hypothalamus, adipose tissue, liver, pancreas and mammary gland [9]. Prolactin has insulinotropic effects but not in breastfeeding period [10]. There might be different mechanisms during breastfeeding between prolactin and insülin levels. In order to highlighten this mechanisms we compared the plasma levels of glucose, insülin, prolactin, C-peptid in basal situations and after taking 75 gr carbonhydrate, 20 gr protein, 23 gr fat in breastfeeding and in non lactating women.

2. Material and methods

2.1. Participants and measurements

The study population included 12 breastfeeding women and 11 healthy non lactating women as a control group. All participants were involved after signing informed consent. We collected information on age, history of gestational diabetes mellitus, family history of diabetes mellitus, natality, the symptoms of hypoglycemia (whipple's triad). Weight, height and waist circumference were measured and body mass index (BMI) was calculated as weight (kg)/height (m^2). In addition, a baseline blood samples were collected for prolactin, lipid profile, Hba1c, fasting plasma glucose, C-peptid and fasting insülin. The participants fasted after 21.00 on the day before the test and took 587 kcal in the early morning, they

* Corresponding author.
E-mail address: yasdikhatice@yahoo.com (H. Ozisik).

https://doi.org/10.1016/j.dsx.2019.03.045
1871-4021/

ate 75 gr carbonhydrate, 20 gr protein, 23 gr fat. Corrected insülin glucose ratios were calculated and we estimated HOMA-IR (homeostatis model assesment-Insulin resistance), HOMA-IS(homeostatis model assesment-Insulin sensitivity), AUC-I (Area Under The Curve Insulin), AUC-G (Area Under The Curve Glucose).

2.2. Statistical methods

Categorical variables were examined with frequency tables for each patient group and descriptive statistics for continuous variables were calculated. While continuous variables were presented as mean ± standard deviation (SD), categorical variables were presented as frequencies and percentages. Shapiro-Wilk normality test was used to examine whether the continuous variables were normally distributed. Since data were not distributed normally, the Spearman's correlation coefficient was used to examine the correlation between prolactin and other variables such as insulin, glucose, c-peptide, BMI, waist circumference. Mann-Whitney *U* test was used to compare the variables of breastfeeding women and control group. Categorical variables such as history of GDM, family history of DM, presence of natality and Whipple's triad were compared by the Chi square test. A p value of less than 0.05 was accepted as statistically significant. In all statistical analysis, IBM SPSS Version 25.0 statistical package was performed.

3. Results

Baseline characteristics of study participants are demonstrated in Table 1. Characteristics of study population according to lactation status are presented in Table 2. Prolactin was inversely correlated with HbA1c and 2. hour C peptide ($p = 0.005$, $r = -0.564$; $p = 0.008$, $r = -0.539$). Prolactin was not significantly correlated with HOMA-IR, HOMA-IS, AUC-I or AUC-G. Prolactin levels were higher in breastfeeding women (median:34.98 μg/L) than in non lactating women (median:12.21 μg/L, $p < 0.001$). There were statistically significant differences between breastfeeding women and non-lactating women for BMI ($p = 0.027$), parity ($p = 0.031$), number of chidren ($p = 0.031$), number of natality ($p = 0.031$).

The relationships between prolactin concentrations, baseline characteristics and parameters of MMTT are displayed in Table 3. Nevertheless, there were no statistically significant correlations between prolactin and continuous variables ($p > 0.05$). There was a significant association between age and fasting glucose ($p = 0.018$, $r = -0.665$), 2. hour glucose ($p = 0.049$, $r = 0.578$) in breastfeeding women. Similarly, weight and BMI ($p < 0.001$, $r = 0.947$), waist circumference ($p = 0.001$, $r = 0.840$), 3. hour glucose ($p = 0.002$, $r = 0.796$), fasting insulin ($p = 0.049$, $r = 0.579$), 3. hour insulin ($p = 0.020$, $r = 0.660$), 4. hour insulin ($p = 0.019$, $r = 0.663$), 5. hour insulin ($p = 0.001$, $r = 0.846$), fasting C peptide ($p = 0.017$, $r = 0.670$), 1. hour C peptide ($p = 0.001$, $r = 0.825$), 4. hour C peptide ($p < 0.001$, $r = 0.863$), 5. hour C peptide ($p < 0.001$, $r = 0.870$), ratio of insülin glucose ($p = 0.032$, $r = 0.619$), corrected insülin glucose ratio ($p = 0.038$, $r = 0.604$), AUC-I ($p = 0.005$, $r = 0.755$) ve AUC-G ($p = 0.050$, $r = 0.576$) variables are positively correlated in breastfeeding women.

The diffence between history of gestational diabetes mellitus, family history of diabetes mellitus, whipple's triad in these two groups were not statistically significant ($p > 0.05$). However, there were statistically significant differences between BMI ($p = 0.027$), parity ($p = 0.031$), number of natality ($p = 0.031$), prolactin ($p < 0.001$) levels in these two groups ($p < 0.05$).

Table 1
Baseline characteristics of study participants.

Characteristics	Breastfeeding women	Non-lactating women
Age (y)	34.75 ± 4.75	34.72 ± 8.87
History of GDM (n, (%))	2 (16.7)	–
Family history of DM (n, (%))	3 (25.0)	1 (9.1)
Natality (n, (%))	12 (100.0)	11 (100.0)
Whipple's triad (n, (%))	3 (25.0)	1 (9.1)
Weight (kg)	76.05 ± 17.03	62.00 ± 10.56
Height (cm)	163.58 ± 5.10	164.63 ± 4.54
Waist circumference (cm)	92.87 ± 14.91	81.31 ± 13.59
BMI (kg/m2)	28.36 ± 6.15	22.82 ± 3.41

Table 2
Characteristics of study population according to lactation status.

Characteristics	Breastfeeding women	Non-lactating women
Prolactin	35.59 ± 4.67	12.38 ± 1.32
Triglyceride	95.91 ± 17.29	112.90 ± 21.72
Total cholesterol	188.33 ± 11.94	196.45 ± 14.33
HDL cholesterol	65.83 ± 4.52	64.72 ± 2.96
LDL cholesterol	103.41 ± 8.66	109.18 ± 13.42
HbA1c	5.04 ± 0.59	5.24 ± 0.88
Fasting glucose	81.16 ± 1.61	88.09 ± 2.95
Fasting insulin	11.91 ± 2.82	8.04 ± 1.12
Fasting C-peptid	1.47 ± 0.21	1.36 ± 0.17
1. hour plasma glucose	96.08 ± 6.88	86.36 ± 8.28
2. hour plasma glucose	85.58 ± 1.99	84.63 ± 4.04
3. hour plasma glucose	78.41 ± 1.98	83.18 ± 4.60
4. hour plasma glucose	76.50 ± 2.35	81.72 ± 2.44
5. hour plasma glucose	78.50 ± 1.66	82.72 ± 2.11
1. hour serum insulin	63.51 ± 19.97	47.72 ± 8.00
2. hour serum insulin	35.63 ± 11.30	29.57 ± 5.63
3. hour serum insulin	18.92 ± 8.63	10.15 ± 1.38
4. hour serum insulin	9.41 ± 3.74	5.88 ± 1.00
5. hour serum insulin	8.70 ± 3.62	5.65 ± 0.74
1. hour C peptide	4.46 ± 0.64	5.20 ± 0.58
2. hour C peptide	3.51 ± 0.48	4.16 ± 0.59
3. hour C peptide	2.30 ± 0.44	2.21 ± 0.30
4. hour C peptide	1.51 ± 0.30	1.43 ± 0.21
5. hour C peptide	1.36 ± 0.28	1.12 ± 0.16

4. Discussion

Physiologically elevated prolactin may preserve from the impairment of glucose homeostasis although extremely high levels of prolactin increase insülin resistance and damage insülin-secretory capacity in situations such as prolactinoma [11]. Patients having prolactinoma have hyperglycemia, obesity, insülin resistance [12]. Prolactin arranges insülin sensitivity, glucose metabolism, enhancing hepatic insülin sensitivity, and regulating immun function [13,14].

In our study, we displayed prolactin was inversely correlated with HbA1c and 2. hour C peptide. Some studies in the past demonstrated that higher prolactin levels had importantly lower prevelance of type 2 diabetes [7]. Our findings supported this situation. The negative corelation between Hba1c, C peptide and prolactin may display the rise in peripheral insulin sensitivity. To our knowledge this was the first time to demonstrate the association between prolactin and peripheral insulin sensitivity.

Lots of changes are seen in glucose metabolism, increasing peripheral insulin resistance in pregnancy and lactation period, commencing with beta cell mass contraction, probably even apoptosis, and decreased insulin secretion [15].

There are several reports demonstrating that systematic or circulating factors can arrange beta cell replication and mass. Several hormones such as insulin, placental lactogen and prolactin have a role in regulating beta cell mass [16,17]. Betatrophin is a hormone that controls pancreatic beta cell proliferation [18]. Betatrophin arranges lipoprotein lipase activity and plays

Table 3
Spearman's correlations of prolaction with variables in all subjects for each group.

Groups	Variables	Spearman's rho	p-value
Breastfeeding women			
N = 11	Age	0.014	0.966
	Height	0,070	0829
	Weight	−0,081	0803
	BMI	−0,126	0697
	Waist circumference	−0,018	0957
	Fasting glucose	0,324	0304
	Fasting insulin	−0,112	0729
	Fasting C peptide	−0,245	0443
	1. hour plasma glucose	−0,357	0255
	2. hour plasma glucose	−0,347	0269
	3. hour plasma glucose	−0,063	0845
	4. hour plasma glucose	−0,133	0680
	5. hour plasma glucose	0,270	0396
	1. hour serum insulin	−0,012	0729
	2. hour serum insulin	−0,343	−0,276
	3. hour serum insulin	−0,531	0075*
	4. hour serum insulin	−0,385	0217
	5. hour serum insulin	−0,224	0484
	1. hour C peptide	−0,028	0443
	2. hour C peptide	−0,490	0106
	3. hour C peptide	−0,252	0430
	4. hour C peptide	−0,294	0354
	5. hour C peptide	−0,259	0417
Non-lactating women			
N = 12	Age	−0.350	0.291
	Height	0,279	0407
	Weight	−0,059	0863
	BMI	−0,264	0433
	Waist circumference	−0,191	0573
	Fasting glucose	−0,096	0780
	Fasting insulin	−0,300	0370
	Fasting C peptide	−0,245	0467
	1. h plasma glucose	−0,342	0304
	2. hour plasma glucose	−0,519	0102
	3. hour plasma glucose	−0,573	0066
	4. hour plasma glucose	−0,128	0708
	5. hour plasma glucose	0,202	0552
	1. hour serum insulin	−0,145	0670
	2. hour serum insulin	−0,418	0201
	3. hour serum insulin	−0,245	0467
	4. hour serum insulin	−0,145	0670
	5. hour serum insulin	−0,314	0346
	1. hour C peptide	−0,282	0401
	2. hour C peptide	−0,583	0060
	3. hour C peptide	−0,618	0043
	4. hour C peptide	−0,282	0401
	5. hour C peptide	−0,500	0117

*p < 0.05 statistically significant.

significant roles in lipid and fatty acid metabolism [19]. Hence, prolactin can take part in the arrangement of glucose and lipid metabolism similar as betathrophin. This relationship may have an effect on breastfeeding.

Several limitations must be considered in our study. We had small number of participants which might potentially conclude in a lack of statistical power to find associations.

In conclusion, serum prolactin levels are associated with HbA1c and possibly HOMA-IS. More studies are warranted to understand these associations.

Conflicts of interest

We have no conflicts of interest.
All participants were involved after signing informed consent.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.03.045.

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