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Nesfatin-1 Differences in Cesarean Section Compared to Natural Vaginal Delivery

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Abstract

Objective: According to previous research, delivery is known as an inflammatory process. Recently discovered Adipokine has been proved with an anti-inflammatory and anti-apoptotic role. Hence, this study aimed to investigate changes of maternal Nesfatin-1 concentrations before and after delivery

Methods: We conducted a nested case–control study within a cohort of 166 pregnant women that meeting the inclusion criteria, were followed up during 28-32 weeks of gestational age and until after delivery. Serum Nesfatin-1 levels were measured during 28-32 weeks of gestation and first 24 hours after elective Cesarean section (case group, n=23) and Natural vaginal delivery (control group, n=22) by using ELISA. P-value of <0.05 was considered statistically significant. Analysis was performed with SPSS v.16

Results: The results showed that the serum Nesfatin-1 level was significantly elevated after delivery in the Natural vaginal delivery group (P=0.037) but was decreased after delivery in the Cesarean section group (p>0.05). Also, Nesfatin-1 difference before and after delivery was significantly higher in the Natural vaginal delivery group compared to the Cesarean section group (P=0.025)

Conclusion: It has been found that the concentrations of Serum Nesfatin-1 level were significantly elevated after Natural vaginal delivery. So considering to anti-inflammatory effects of this peptide and inflammatory effect process of delivery Nesfatin-1 might increase to suppress the inflammation process as its physiological anti-inflammatory effect.

Keywords: Nesfatin-1; Pregnancy; Cesarean Delivery; Natural Vaginal Delivery

Introduction

Spontaneous vaginal delivery at term has long been regarded as the preferred outcome for pregnancy because of the perceived

health, economic, and societal benefits, taken from vaginal deliveries [1].Meanwhile, enhancement in rate of caesarean delivery is associated with an increase in use of postpartum antibiotics, greater violent maternal morbidity and mortality, and higher fetal and neonatal morbidity [2]. Evidence shows that human parturition is an inflammatory process. An apparent increase in pro-inflammatory cytokines within tissues of the labouring uterus has been previously demonstrated [3]. Nesfatin-1, produced and secreted by adipose tissue, is Adipokine which is activated during infection and inflammation. The hormone has an anti-inflammatory effect [4]. According to previous studies, Nesfatin-1 was discovered in 2006 as an anti-appetite polypeptide by Oh *et al.* [5].This is derived from nucleobindine-2 (NUCB2) during a transition process [6]. Studies revealed that Nesfatin-1 is secreted from various body organs (pancreas, stomach mucus, stomach glands, intestine duodenum sub mucus, cardiomyocytes and testis) besides the brain and its peripheral tissues (brainstem, pituitary, hypothalamus, dorsal motor nucleus of the vagus, supraoptic nucleus, paraventricular nucleus, arcuate nucleus and nucleus of the solitarious tracts). It is influenced by diet and inflammatory cytokines and insulin [7-10]. The NUCB2 expression has been detected in the amnion and decidua of the rat placenta. Placenta has a considerable role as a source of circulating Nesfatin-1 level in a pregnant rat and the fetus in the mid-pregnancy. The serum Nesfatin-1 levels are reduced considerably as pregnancy progresses in rats from gestational day 12 to the end of the pregnancy [11,12]. However, due to the lack of sufficient information about the physiological difference of Nesfatin-1 in pregnancy and after delivery cannot be argued absolutely. To investigate the difference of Nesfatin-1 in pregnancy and after delivery, we measured serum Nesfatin-1 levels during 28-32weeks of gestational age and 24 hours after delivery in an Iranian population.

Materials and Methods

This study was conducted on pregnant women referring to the prenatal clinic of Mahdiyeh Hospital of Tehran. In this nested case–control study within a cohort of 166 pregnant women, aged 18-40 and meeting the inclusion criteria, were followed up during 28-32 weeks of gestational age and until after delivery in prenatal clinic of Mahdiyeh Hospital of Tehran from 2013 to 2015. First mother's blood serum sample was taken in the third trimester to measure Nesfatin-1. Twenty-three of these subjects underwent elective Caesarean section (C/S) and were considered as the case group. C/S, individuals with Cesarean indications such as abnormal presentation, macrosomia, repeated Cesarean section that had not experienced labor pain in their recent pregnancy. Then, from the women with Natural vaginal delivery (NVD), twenty-two were made homogeneous concerning demographic characteristics including age, husband's and mother's occupation and education, family income, gravidity, parity, and abortion and Gestational age at the Third trimester and at the 24 hours after delivery and Body mass index (BMI) of before pregnancy, in the third trimester and delivery time with case group and selected as the control group. Finally, the second blood sample was taken to measure mother's serum nesfatin-1 twenty-four hours after delivery.

Sampling

In order to obtain a written consent, the process was explained to each participant. In the weeks 32-28 of gestation, next in the first 24 hours after C/S and NVD, the non-fasting blood samples were taken from the antecubital vein of the mothers and transferred to the test tubes containing antiproteases blood sample. Then, blood samples were transferred to the endocrinology and metabolism laboratories of Shahid Beheshti University of Medical Sciences, Tehran within 72 hours of receiving, and centrifuged at 3000 rpm for 10 minutes at 4 °C by a laboratory technician for plasma isolation, and the plasma was frozen at -20° -70 °C until analysis. Concentration of Nesfatin-1 after delivery was measured by Enzyme-linked immunosorbent assay method (ELISA) using the Human Nesfatin-1 ELISA kit, ZellBio GmbH, Ulm Germany. Inclusion criteria were age of 18-40 years, singleton pregnancy, and being Iranian. Data collection instruments for assessing maternal serum Nesfatin-1 levels were the routine questionnaire of prenatal care, prepared by Iranian Ministry of Health, observation of clinical examinations, the first mother's ultrasound and using last menstrual period (LMP) and Estimated delivery date (EDC). Exclusion criteria were mental health problems, systemic diseases such as lupus, diabetes mellitus, use of tobacco and alcohol, any pregnancy complications (gestational diabetes, pre-eclampsia and other complications.), emergency Cesarean section and taking any medications except for pregnancy supplements.

Statistical Analysis

Normality of the data was tested using the Kolmogorov-Smirnov test. Because maternal plasma Nesfatin-1 levels were not normally distributed, Kruskal-Wallis tests and Mann-Whitney U-tests were used for comparisons of continuous variables between the two groups. Comparison of proportions was performed by Chi-square or Fisher's exact tests. Analysis was performed with SPSS v.16. A P-value of <0.05 was considered statistically significant.

Policy of Ethics

This study was carried out after being approved by the research council of Tarbiat Modarres University in Tehran, Iran, being licensed in Medical Ethics Committee of the Faculty of Medical Sciences (registration number: IR.TMU.REC.1394.1111) and presenting a research introduction letter to the university to Mahdieh Hospital.

Result

The concentrations of serum Nesfatin-1 in the third trimester of pregnancy and in the first 24 hours after delivery were 1360.6±2153.4

and 1296.8±1925.5 (Ng/L) in the C/S group and 1483.3±1980.4 and 1853.8±2285.7 (Ng/L) in the NVD. Wilcoxon test showed that the concentrations of serum Nesfatin-1 significantly increased 25% (P=0.037) in the NVD group, But was decreased after delivery in C/S group (p=0.455) (Table1). It has been found that there was no significant difference between mean serum level of Nesfatin-1 in the third trimester of pregnancy and in the first 24 hours after delivery in the C/S and the NVD groups (P=0.237), (P=0.899). Moreover, Nesfatin-1 difference level after delivery from third trimester in the NVD group was significantly more than the C/S group (P=0.025) (Table2).

Table 1: Variations in Nesfatin-1 level in each groups (n= 45)

Mother's serum Nesfatin-1 level (Ng/L) / *type of Delivery*	*Third trimester of pregnancy Mean±SD*	*24 hours After delivery Mean±SD*	*P-value**
CS (n=23)	1360.6±2153.4	1296.8±1925.5	**0.455**
NVD (n=22)	**1483.3±1980.4**	**1853.8±2285.7**	**0.037**

* Statistical Wilcoxon test

Table 2: Comparison of serum level of Nesfatin-1 in groups (n= 45)

Mother's serum Nesfatin-1 level (Ng/L) / *type of Delivery*	*Third trimester of pregnancy Mean±SD*	*The first 24 hours after delivery Mean±SD*	*Difference * Mean±SD*
C/S (n=23)	1360.6±2153.4	1296.8±1925.5	**-63.8571±3081.0**
NVD (n=22)	1483.3±1980.4	1853.8±2285.7	**3704.7±7164.8**
*P-value***	**0.237**	**0.890**	**0.025**

*Difference of Nesfatin-1 after delivery from the third trimester of pregnancy

** Statistical Mann-Whitney test

Discussion

Serum Nesfatin-1 level was significantly elevated after delivery in control group (P=0.037) but was decreased after delivery in case group that was not significant (p>0.05). According to previous studies, Nesfatin-1 as a protein produced in the gastrointestinal tract and the brain, acts as a satiety molecule, and has been involved in the regulation of food intake and energy homeostasis. However, not much is known about the regulation of Nesfatin-1 and its NucB2 precursor whose amounts change during pregnancy in different physiological or physiopathological conditions [5,9,13-15]. NucB2 mRNA placental levels are reduced significantly as pregnancy progresses. As both are significantly low or undetectable at the end of gestation, placental NucB2 mRNA and protein expression patterns are in agreement [16]. The concentration of serum Nesfatin-1 in the pregnant rat is reduced since gestational 12th day to the end of the pregnancy [11,12]. During mid-gestation, the placenta plays an important role as a source of circulating levels of Nesfatin-1 in pregnant rats and fetus .Placenta may also play an important role in the regulation and the input levels of maternal and fetal Nesfatin-1 during a period of gestation, but as the fetus regulates and controls its own production and acts as an additional source, it may be deleterious, and therefore, it decreases in synthesis toward the end of gestation [12]. Neurons of the central nesfatinergic system are sensitive to peripheral inflammatory stimulus; therefore, they belong to the specific immunosensitive neurocircuitry that is activated during infection or inflammation [4]. These results point out to the important role of Nesfatin-1 in the process of anti-inflammation [17]. Due to the fact that at the time of NVD, inflammatory factors such as IL-1h, sIL-2R, sIL-4R, IFN-g, TNF-a and sTNF RI increase and since the Nesfatin-1 has a repressive role for the same inflammatory factors that increase at delivery , and as this peptide also increases after NVD, it can be concluded that Nesfatin-1 may act as a postpartum anti-inflammatory element. In elective Cesarean section, the inflammatory phase is practically eliminated, which may be due to the decrease in the amount of this peptide or a significant change in it [18,19]. So considering to anti-inflammatory effects of this hormone and inflammatory effect process of delivery, this study has shown that Nesfatin-1 might increase in the inflammatory process of initiation of labor at term gestation in humans to suppress the inflammation process as its physiological anti-inflammatory effect [4,20-22].

The difference of this peptide levels before and after delivery was significantly higher in the NVD group compared to the C/S group (P=0.025), a recently discovered satiety peptide, is said to be vastly responsible for provision of appetite and metabolic regulation in hypothalamus [23,24]. According to previous studies, Nesfatin-1 inhibits food intake and suppresses appetite. So, it is known as an anti-obesity hormone that reduces body weight [5,25]. Peripheral Nesfatin-1 administration can provide a new choice in the treatment of obesity [26,27]. The expression of Nesfatin-1 not only in central nervous system but also in peripheral tissues including pancreatic beta cells suggests the possible involvement of Nesfatin-1 in the regulation of insulin secretion from pancreatic beta cells having an anti-hyperglycemic role [28]. Besides the anorexigenic and antihyperglycemic effects of Nesfatin-1 , there are several studies indicating its important possible role in metabolic control [29]. Several studies reported the association between the low Nesfatin-1 levels and the elevated systolic and diastolic blood pressure indicating that Nesfatin-1 might play an important

role in blood pressure regulation [30,31]. Low Nesfatin-1 levels have been reported to be responsible for Insulin resistance, raise of systolic and diastolic hypertension and metabolic syndrome [6,30,32]. In Metabolic syndrome patients, significantly lower levels of Nesfatin-1 were detected, compared to non- Metabolic syndrome patients, which is consistent with the previous literature findings [32]. Clinical significance of Nesfatin-1 in several metabolic diseases including obesity, Type 2 DM, and insulin resistance was indicated in various studies in the literature, but its difference in delivery is unknown. According to our study, NVD group may benefit from the increasing effect of Nesfatin-1 due to its beneficial effects on the organs of the body. This effect possibly may not be present in the women who undergo C/S. Since, there are no studies on the changes of this peptide with regard to the mode of delivery, more research is needed.

Conclusion

Summing up the results, it can be concluded that Nesfatin-1 increasing levels in NVD group was along with physiology of labor initiation. Furthermore, Nesfatin-1 difference before and after delivery was significantly higher in NVD group compared to C/S group. So the existence of the important role of Nesfatin-1 in obesity and metabolic syndrome implies the necessity to investigate the role of this hormone in pregnancy.

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