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Ischemia Modified Albumin as an Antioxidant: Maternal Serum Levels in IVF Pregnancies

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Abstract

In vitro fertilization (IVF) being an artificial method for conceiving may cause some co-morbidity on the on-going pregnancy after an infertile period. Assisted fertilization outside the reproductive tract and implantation via artificial methods may cause something go different from natural conceptions.

This study, to the best of our knowledge, is the first one in this field searching the oxidative status of IVF pregnancies with respect to the infertility causes. Because the infertility itself and the artificial processes of implantation in IVF may cause oxidative stress in the proceeding pregnancy, we expected an imbalanced oxidation in favour of an increased IMA levels in low-risk IVF pregnancies of third trimester, but the results were not so. Conceiving via IVF because of unexplained or DOR seem not to have detrimental effects on the oxidation.

Keywords: Albumin; Serum levels; Pregnancies

Introduction

In vitro fertilization (IVF) being an artificial method for conceiving may cause some co-morbidity on the on-going pregnancy after an infertile period. Assisted fertilization outside the reproductive tract and implantation via artificial methods may cause something go different from natural conceptions. Not the IVF procedure itself but also the cause of the infertility may interfere the molecular state of the related pregnancy and may result at likely negative impacts. Among pregnancy complications related to IVF conceptions, placenta previa, premature rupture of the membranes, abruption, preeclampsia, abnormal umbilical cord insertion have been reported [1], but what about of the IVF pregnancies of low risk group? It is not known whether the low risk IVF pregnancy is affected in the same dysfunctional manner. Even the pregnancy goes in a normal route; there may be some molecular abnormalities in such conceptions.

Reactive oxygen species (ROS) is a group of molecules with highly reactive properties within the cell [2]. Where limited amount of ROS is necessary for all physiological processes, an imbalanced state between the oxidants and the antioxidants causes oxidative stress that is toxic for the cell and the on-going biological pathways as well [3].

Women infertility has also been studied from the view of oxidative status. Elevated oxidative markers were shown in serum of infertile women [4]. A likely oxidative damage in the reproductive functions has been concluded in the women going to assisted reproductive treatments [5]. Oxidative damage has also been studied according to the cause of the infertility. In a group of unexplained infertile patients going to IVF, fertilization failure was bind to increased oxidative markers in the embryo culture media [6]. Diminished ovarian reserve (DOR) being another cause of female infertility, has also been linked to oxidative stress. Cyclical ROS production has been associated with oophoritis which later causes DOR and premature ovarian failure [7]. In a cell culture study, granulosa and luteal cells prone to ROS presented diminished gonadotropin secretion and antiestrogenic actions seen like in poor ovarian response [7].

Ischemia-modified albumin (IMA) is one the new oxidative markers which has been announced mostly in cardiological researches [8]. It has been concluded to increase in the ischemic status. In our study we used IMA as an oxidative marker. We analysed IMA in low-risk IVF pregnancies of women who have unexplained infertility and diminished ovarian reserve. We hypothesised that the infertility itself and the artificial processes related to embryo transfer may affect the IVF pregnancy; even it is low-risk pregnancy, in a manner of increased oxidation.

Material Method

This prospective cross-sectional study was conducted between October 2014 and January 2015 in Zekai Tahir Burak Women's Health Centre, Ankara, Turkey. A total of 43 IVF pregnancies were included. Eleven of them were male factor infertility and were excluded, and 8 pregnant of high risk pregnancies and four of women who refused to give blood samples were also excluded. The study was completed with a

total of 20 low risks, IVF pregnancies. High risk pregnancy is defined as the pregnancy with health problems related to mother, baby or both. Hypertension, gestational or presentational diabetes mellitus, preterm birth, premature rupture of membranes, placental adhesion abnormalities, intrauterine growth retardation, multiple pregnancy, and pregnancies with the systemic diseases of mother are all included in high risk pregnancy. Pregnancies free of maternal or fetal risks are defined as low risk pregnancies. All procedures performed in this human study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. As increased oxidative status is seen as a physiological requirement for trophoblast invasion during the first and the late second trimester, so the study and the control patients were selected from the third trimester. A total of 20 low-risk IVF pregnancies of third trimester were compared to 22 non-IVF, low risk and spontaneous conception pregnancies in the third trimester as well. The study and the control group were matched to age and body mass index (BMI). Groups were compared with respect to the maternal serum IMA levels and IMA/Albumin ratios.

Laboratory measurements

Serum IMA level was analyzed using the rapid and colorimetric method developed by Bar-Or et al. [9,10]. Briefly 200 µl was incubated with 50 µl cobalt chloride solution of 1g/L for 10 minutes. 50 µl of 1.5 g/L dithio-erthreitol and 1 mL of 0.09% NaCl were added. The absorbance was read against blank at 470 nm. Results were given as absorbance unit (ABSU).

Statistical analysis

Statistical analysis was performed using SPSS for Windows Version 15.0 (SPSS Inc., Chicago, IL, USA). Data were shown as mean ± standard deviation (SD) or median (minimum-maximum). The differences between groups were compared by Student's t test. Otherwise, Mann Whitney U test was used for comparison of values which do not meet parametric test criteria. Correlation between numeric variables was reported by Spearman correlation coefficient. A p value less than 0.05 was considered statistically significant.

Results

Tables 1 and 2 show the demographic analysis of the patients. Age and BMI were insignificant between the groups, p>0.05 for all. Serum IMA levels were insignificant; 0.013 ± 0.01 ABSU and 0.012 ± 0.007 ABSU for the IVF and the non-IVF patients, respectively (p>0.05). IMA/Albumin ratios were also similar between the groups, 0.003 ± 0.002 and 0.003 ± 0.002 for group A and B, respectively (p>0.05).

Table 1: Demographic variables of the IVF and non-IVF pregnancies.

	IVF Pregnancy (n=20)	Non-IVF Pregnancy (n=22)	P value
Age (years)	29.1 ± 5.1	28.4 ± 5.9	NS
BMI (kg/m^2)	29.9 ± 4.1	29.1 ± 4.6	NS

Table 2: Ischemia modified albumin and the serum albumin levels of the IVF and the non-IVF pregnancies.

	IVF pregnancies (n=20)	Non-IVF pregnancies (n=22)	p value
IMA (ABSU)	0.013 ± 0.01	0.012 ± 0.007	>0.05
IMA/Albumin ratio	0.003 ± 0.002	0.003 ± 0.002	>0.05

Discussion

This study, to the best of our knowledge, is the first one in this field searching the oxidative status of IVF pregnancies with respect to the infertility causes. Because the infertility itself and the artificial processes of implantation in IVF may cause oxidative stress in the proceeding pregnancy, we expected an imbalanced oxidation in favour of an increased IMA levels in low-risk IVF pregnancies of third trimester, but the results were not so. Conceiving via IVF because of unexplained or DOR seem not to have detrimental effects on the oxidation.

There are many published data related to the OS in high risk pregnancies and in most of them OS has been concluded to be one of the pathophysiological mechanisms leading a low-risk pregnancy to a high-risk one. In spite of the fact that ROS production in balanced amounts is a physiological requirement for normal placentation in a healthy uterus of early pregnancy period, an unbalanced status with a higher production of oxidative molecules more than needed or more than the neutralizing antioxidants during the advanced gestational weeks may develop micro-environmental harms [11].

Related to IMA and the high-risk pregnancies, an increased level has been concluded to take role in the pathology of recurrent pregnancy losses [12]. IMA has also been studied in intrauterine growth restriction and concluded to be both a predictive and the etiological factor with the demonstration of the increased levels in maternal serum [13].

Pregnancies conceived via IVF are also prone to become a high-risk pregnancy because of advanced maternal age, the cause of infertility itself and additive morbidities like thrombophilia, diabetes mellitus, metabolic syndrome, etc. Usage of high doses of ovulation induction medications and the contact of the embryo with many kinds of chemicals before transfer may be another risk factors. It is hard to analyse the IVF effect on a pregnancy if it becomes a high-risk one because of many confounding, but may be possible to analyse on a low-risk group of IVF pregnancy which is thought to be free of likely negative effects. In a study of mouse model comparing the OS in the placentas of IVF pregnancies to spontaneous conception pregnancies showed an increased OS in IVF pregnancies [14]. Placental site OS may affect the maternal circulation in the same manner as increased oxidative marker, the IMA. In the highlights

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of the same IMA levels both in the IVF and the non-IVF pregnant shown in this study, we may say that conceptions of IVF pregnancies of DOR and unexplained infertility do not go with increased oxidation in the maternal site. Conceptions of DOR and unexplained reasons of IVF may be away from the OS as long as long as the pregnancy is a low-risk one. Related to the weakness of our study, fetal cord blood IMA analyses together with the placental IMA levels would have serve the best results when compared with the maternal serum IMA levels, but because of the unfavourable conditions to attend to each IVF patient's birth since they delivered in different hospitals, these results are absent in our study.

In conclusion, maternal serum IMA levels of the IVF pregnancies with the indications of DOR and unexplained infertility were not different from the spontaneous conception pregnancies. Even though DOR and the unexplained infertility itself have been thought to go with an increased oxidative status, this did not affect the circulatory oxidative status during the pregnancy. Low-risk IVF pregnancies of DOR and unexplained infertility indications may be free of an increased oxidation and the infertility together with the artificial methods of IVF may not cause detrimental effects in the molecular state. The results of our study need to be supported with a higher population and with other kinds of oxidants.

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