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CHANGES IN INFLAMMATORY PARAMETERS AND FACTORS AFFECTING THE FOLLICULAR MEMBRANE DURING INTRAUTERINE FETAL GROWTH RESTRICTION: BASIC RESEARCH

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ABSTRACT

We experienced changes in inflammatory parameters, i.e., neutrophils, macrophages, and lymphocytes, in the follicular membrane during IUGR and analyzed the factors that influence it.

Background and Aim: Intrauterine growth Restriction (IUGR) is a predictor of weight loss below 10% or −1.5SD of the mean fetal growth curve for gestational age, with inhibition of fetal growth and maturation in utero. Intrauterine growth retardation (IUGR) is an important health problem worldwide. In developed countries, more than 9% of all pregnancies are complicated by IUGR, which is equivalent to about 30 million neonates worldwide. IUGR is defined as the fetus not reaching its genetic developmental potential and is secondary to preterm birth as the major cause of perinatal death. It is commonly caused by a condition known as placental hypofunction, placental insufficiency, which causes chronic hypoxemia and reduces the supply of nutrients to the fetus, and consequently affects organogenesis and fetal body development. In this regard, many countries are working on this topic.

Object: The experiments were conducted in 200-250 g rats.

Methodology: LPS was administered intraperitoneally in rats to provide an IUGR model. On day 20 after conception, the placenta was removed and the follicle was harvested and microscopically examined for neutrophils, macrophages, and lymphocyte infiltration in the follicle as an indicator of inflammation. Then, the experimental group was divided into three groups, group 1 was under ischemic conditions, group 2 was under hypoxic conditions, and group 3 was subjected to indirect smoking conditions to model and observe inflammatory parameters.

Results: In the intrauterine fetal growth retardation model, the number of neutrophils and gestational phagocytes infiltrated into the oocyte membrane was significantly higher than in the normal group, but there was no significant difference in lymphocyte count. Ischemia, hypoxia, and passive smoking during intrauterine fetal growth retardation showed significant changes in inflammatory parameters, neutrophils, macrophages, and lymphocyte infiltration in the membrane.

Conclusion: There was a significant inflammatory change in the membranes of rats with delayed intrauterine fetal growth when exposed to ischemia, passive smoking, and hypoxia.

Keywords: Intrauterine fetal growth retardation; Fallopian membranes; Inflammatory parameters; Ischemia; Indirect smoking; Hypoxia.

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INTRODUCTION

Intrauterine growth Restriction (IUGR) is a result of the suppression of fetal growth and maturation in utero, with predicted body weight below 10% or below −1.5SD of the mean fetal growth curve for gestational age.

Intrauterine growth retardation (IUGR) is an important health problem worldwide.

In developed countries, more than 9% of all pregnancies are complicated by IUGR, which is equivalent to about 30 million neonates worldwide.

IUGR is defined as the fetus not reaching its genetic developmental potential and is secondary to preterm birth as the major cause of perinatal death (Bernstein et al., 2000).

It is caused by conditions commonly known as placental hypofunction, placental insufficiency, which cause chronic hypoxemia and reduce the supply of nutrients to the fetus, and consequently generally affect organogenesis and fetal body development.

The main factors causing IUGR are chronic hypertension, pregnancy diabetes, cardiovascular disease, substance abuse, and autoimmune conditions.

Some are the result of fetal conditions, such as infection, malformation, chromosomal abnormalities, placental outcome, choroidal hemangioma, infarction, localized placental mosaicism, and obstructive vascular disease of the placental layer.

In addition, accumulation of toxic metals in placental tissue can lead to abnormal placental function and impaired nutrient transport, which may cause fetal growth restriction.

We further investigated this by examining the presence of oocyte membranes under different conditions to determine which factors contribute to IUGR.

2. MATERIALS AND METHODS

2.1 Object

Females of 200-250 g Wistar strain were used as experimental animals.

2.2 Materials and Instruments

LPS, dissection apparatus, microscope

2.3 Method

To determine the changes in inflammatory parameters in the follicle during IUGR, a model of IUGR was created by intrauterine LPS administration once in the rat peritoneal cavity at 50 mg/kg 7 days after mating and sperm identification by vaginal smears.

At 14 days after pregnancy, the oocyte was obtained and the specimens were prepared according to the conventional histopathology sampling technique, and the degree of neutrophil, macrophage and lymphocyte infiltration deposited in the oocyte membrane was observed as an inflammatory-related index under light microscopy at 400-fold field of view.

The parameters calculated at any five fields of each sample were averaged and calculated.

To identify factors affecting inflammatory parameters changes in the follicle during IUGR, we performed mating and then administered LPS at a dose of 50 mg/kg intraperitoneally in both the model and experimental rats 15 days after sperm identification by vaginal smears.

Three groups of the experimental group were divided into three groups: one blood collection of 20% of total blood by capillary blood collection in the orbital venous plexus of rats was performed in a single blood collection, and in group 2, 6-hour daily in a box, 5-day hypoxic exposure and 2-hour daily exposure to cigarette smoke in group 3 were allowed to continue for 5 days under indirect smoking.

On day 20 after conception, the placenta was removed and the oocyte membrane was obtained and the specimens were prepared according to the conventional histopathology sampling technique and observed under a light microscope at 400-fold field of view.

As an indicator of inflammation, neutrophils, macrophages, and lymphocyte infiltration in the oocyte membrane were observed.

3. RESULTS

3.1Changes in inflammation-related parameters in the follicle during intrauterine fetal growth restriction

3.1.1Changes in neutrophil infiltration during intrauterine fetal growth restriction

As shown in Table 1, the number of neutrophils infiltrated into the oolemma was 4.3±0.3/field of view in the model group, significantly higher than 3.1±0.2/field of view in the normal group (P<0.01).

As shown in Table 2, the number of macrophages infiltrating the oolemma was significantly higher than 2.3±0.2/field of view in the normal group, with 3.5±0.2/field of view in the model group (P<0.01).

As shown in Table 3, the number of lymphocytes infiltrating the oolemma was 4.4±0.4/field in the model group, less than 5.2±0.5/field in the normal group, but there was no significant difference.

Table1: Changes of neutrophil infiltration

Group	number of observations	Number per field of view			
		1-3	4-6	7-9	
Control	30	19	11	-	3.1±0.2
Model	30	9	19	2	4.3±0.3**

** indicates p<0.01

Table 2: Changes of macrophage infiltration

Group	number of observations	Number per field of view			
		1-3	4-6	7-9	
Control	30	25	5	-	2.3±0.2
Model	30	14	15	1	3.5±0.2**

** indicates p<0.01

Table 3: Changes of lymphocyte infiltration

Group	number of observations	umber per field of view			
		1-5	6-10	11-15	
Control	30	16	13	1	5.2±0.5
Model	30	20	10	-	4.4±0.4

** indicates p<0.01

3.2Changes in inflammatory-related parameters in response to conditions during intrauterine fetal growth restriction

As shown in Table 4, neutrophil and macrophage infiltration in the oolemma during IUGR was significantly increased in the anemic condition by 6.2±0.9, 7.1±1.3, and hypoxic condition by 6.6±0.9, 8.2±1.7, and indirect smoking condition by 6.8±1.2 and 7.8±1.2/field of view, respectively, compared with the model condition (4.3±0.3 and 3.3.3, respectively) and the model condition by 6.3±0.3 and 0.3/3, respectively, respectively, respectively, under the anemic condition, and the model condition by 6±0.3 and 0.3 and 3/3, respectively, respectively.3 and 0.3 and 0.3 and 0.3 and 0.3 and 3 and 0.3 and 3 by the indirect field of the hypoxic condition (4, respectively).

Table 4: Changes of inflammatory index according to condition

Group			No. of observations	Neutrophil	Macrophage	Lymphocyte
Control			30	3.1±0.2	2.3±0.2	5.2±0.5
Model			30	4.3±0.3	3.5±0.2	4.4±0.4
Exp.l Gr.	A	Ischemia	30	6.2±0.9*	7.1±1.3*	3.3±0.3*
	B	Hypoxia	30	6.6±0.9*	8.2±1.7*	3.2±0.3*
	C	Indirect smoking	30	6.8±1.2*	7.8±1.2*	2.8±0.3*

Exp. Gr.: Experimental Group ** indicates p<0.01

4. DISCUSSION

According to ACOG guidelines, a fetus with intrauterine growth restriction (IUGR) is a fetus with an estimated weight less than the 10th percentile for gestational age [1]. With a prevalence of the 5–8% in the general population, IUGR can complicate 10% to 15% of all pregnancies [2]. Frequently the etiology of IUGR is unknown; however in several cases it is possible to identify fetal (infection, malformation, and chromosomal aberration [3]), placental [4] (chorioangioma, infarction, circumvallated placenta, obliterative vasculopathy of the placental bed, etc.), maternal (chronic hypertension [5], pregestational diabetes, cardiovascular disease [6], substance abuse, autoimmune conditions, etc.), and external factors that modulate the normal fetal growth, by acting on a genetically predetermined potential growth [7].

IUGR represents the second cause of perinatal mortality, after prematurity, and it is related to an increased risk of perinatal complication as hypoxemia, low Apgar scores, and cord blood acidemia, with possible negative effects for neonatal outcome [8, 9].

The exposure of pregnant women to cigarette smoke is an important risk factor for the development of IUGR, spontaneous abortion and premature birth [10].

Modern lifestyle promotes unhealthy behavior such as alcohol, tobacco and drugs abuse.

The simultaneous exposure to alcohol and environmental toxics may have an amplifying effect on health [11].

Present data pointed out that chronic maternal cigarette smoking and alcohol intake during pregnancy produced not only lowered birth weight but also retarded physical growth and restricted fetus development (e.g. the liver weight, the lengths of body and tail), which indicated IUGR formation [12].

In addition, accumulation of toxic metals in placental tissue can lead to abnormal placental function and impaired nutrient transport, which may cause fetal growth restriction.

We used LPS to model IUGR and to determine which factors contribute to IUGR, and to determine the changes in inflammatory parameters in the oocyte membrane by providing ischemia, hypoxia, and indirect smoking conditions.

As a result, ischemia, hypoxia, and passive smoking conditions have made the changes of inflammatory parameters in the membrane more severe.

5. CONCLUSION

In the intrauterine fetal growth retardation model, the number of neutrophils and gestational phagocytes infiltrated into the oocyte membrane was significantly higher than in the normal group, but there was no significant difference in the number of lymphocytes.

In addition, ischemia, hypoxia, and passive smoking during intrauterine fetal growth retardation showed significant changes in inflammatory parameters, neutrophils, macrophages, and lymphocyte infiltration in the egg membrane.

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