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CLINICAL ARTICLE

L-Arginine treatment for asymmetric fetal growth restriction

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Abstract

Objectivities: To investigate the effects of L-Arginine in treating asymmetric fetal growth restriction (FGR). *Methods:* A total of 66 pregnant women whose fetuses were diagnosed with asymmetric fetal growth restriction were divided into two groups. Group 1 consisted of 36 women who were given routine therapy alone; group 2 consisted of 30 women who were given L-Arginine and routine therapy; and the control group consisted of 30 more women with a normal pregnancy. *Results:* Before treatment, mean maternal serum levels of NO_2^-/NO_3^- were significantly lower in groups 1 and 2 than in the control group ($P<0.01$). After treatment, maternal serum levels of NO_2^-/NO_3^- were considerably higher in group 2 than in group 1 ($P<0.01$). Mean birth weight was significantly higher in group 2 than in group 1 ($P<0.05$), but still lower in group 2 than in the control group ($P<0.01$). *Conclusions:* A deficiency in nitric oxide may play an important role in the development of asymmetric fetal growth restriction. L-Arginine can be used to increase maternal NO_2^-/NO_3^- levels and newborn birth weight.

1. Introduction

Fetal growth restriction (FGR) can be divided into two subtypes, "symmetrical," when the fetus is small but well proportioned and "asymmetrical," when the fetus' abdominal growth is restricted. Most asymmetric FGR is associated with uteroplacental insufficiency [1]. Nitric oxide (NO) is an important regulator of placental perfusion, as it plays a role in placental vascular endothelial function [2]. Nitric oxide is synthesized from the physiologic precursor L-Arginine by the stereospecific enzyme NO synthase in what is called the L-Arginine/NO pathway, and L-arginine is the only substrate for the production of NO [3]. Recently, case reports on the use of L-arginine for treating FGR were published [4]. This study, however, uses

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L-Arginine to treat 30 cases of asymmetric FGR, analyzes maternal and umbilical serum levels of NO_2^-/NO_3^- and their effects on pregnancy, and determines whether L-Arginine is effective in treating FGR.

2. Materials and methods

2.1. Patients and methods of treatment

Between September 2001 and March 2003, 66 women with a singleton pregnancy, whose fetuses had been diagnosed with asymmetric FGR by clinical and ultrasonic examination, were recruited for this study at the First Affiliated Hospital of Jinan University. The fetuses had normal head circumferences and body lengths, but a head circumference—abdominal circumference ratio below the 10th percentile [5]. The women had a regular menstrual cycle before pregnancy; they had a normal volume of amnionic fluid; and antepartum fetal surveillance was uneventful, except that initially they had been diagnosed with TORCH syndrome, pathological pregnancy, obstetric complication, and fetal malformation. After informed consent was obtained, all women were voluntarily assigned to two groups. In group 1, 36 women received routine therapy (oral salbutamol, intravenous dan-shen root, low-molecular-weight dextran, glucose, and amino acids); in group 2, 30 women received routine therapy plus 20 g/day of L-Arginine intravenously (Shanghai Sine Pharmaceutical, Shanghai, China). Both groups received treatment for 7 days. Ultrasonic examinations and antepartum fetal surveillance were performed periodically. As long as there was continuous growth and fetal evaluation remained satisfactory, pregnancy was allowed to go on. Otherwise, delivery was considered. In addition, 30 women experiencing uneventful pregnancies, with fetuses of appropriate growth for gestational age, constituted the control group. The general characteristics of the three groups were not significantly different (Table 1).

2.2. Clinical data and statistical analysis

One day before treatment initiation and after 7 days of treatment, maternal serum levels of NO_2^-/NO_3^- were measured in the three groups. After delivery, the umbilical vein serum levels of NO_2^-/NO_3^- were measured and the pregnancy outcome was recorded. Concentrations of NO_2^-/NO_3^- were measured by the Griess reaction after reduction with nitrate reductase. All data were entered in statistical software SPSS, version 10.0 (SPSS, Chicago, IL) for analysis. The differences were tested for statistical significance using the *t*-test and the Fisher exact test. $P<0.05$ was considered significant.

3. Results

3.1. Maternal and umbilical serum NO_2^-/NO_3^- levels in the three groups

- Before treatment, maternal serum NO_2^-/NO_3^- concentrations in groups 1 and 2 were 19.17±5.15 and 20.25±5.50 μmol/L, respectively. They were significantly lower than those of the control group (75.03±11.12 μmol/L) ($P<0.01$).
- After treatment, maternal serum NO_2^-/NO_3^- concentrations were 43.49±20.27 μmol/L in group 1 and 58.42±23.12 μmol/L in group 2. They were significantly increased in both groups compared with those obtained before treatment ($P<0.01$). The values however, were significantly higher in group 2 than in group 1 ($P<0.01$).
- Umbilical serum NO_2^-/NO_3^- were, in decreasing order, 41.01±12.49 μmol/L in the control group;

Table 1 Comparison of general conditions in three groups of pregnant women[a]

	Group 1 (n=36)	Group 2 (n=30)	Control group (n=30)	P value
Age, years	27.4±3.1	27.0±3.6	27.6±2.8	0.761
Body height, cm	157.8±3.6	158.0±3.4	157.6±4.0	0.910
Body mass index, kg/m^2	0.24±0.02	0.23±0.02	0.24±0.02	0.225
Systolic pressure, kPa	14.6±1.1	14.3±1.4	14.0±1.3	0.178
Diastolic pressure, kPa	9.5±0.8	9.2±0.8	9.2±0.9	0.287
Gestation age at beginning of observation, weeks	33.06±2.43	33.03±2.59	32.77±2.55	0.884
Gestation age at labor, weeks	39.13±1.79	39.37±1.07	39.17±1.28	0.786
Gravidity	3.0±1.3	3.0±1.3	3.1±1.3	0.846

[a] Values are given as mean±S.D. unless otherwise indicated.