ORIGINAL RESEARCH PAPER

Obstetrics And Gynaecology

L-ARGININE SUPPLEMENTATION IN IUGR AND ITS EFFECT ON FETAL OUTCOME IN IUGR.

KEY WORDS:

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ABSTRACT

Objective: Intrauterine growth restriction (IUGR), a condition in which the foetal growth is restricted pathologically in utero, remains a serious health problem. The main aim of this study was to evaluate the effect of L-Arginine administration on the fetal outcome in pregnancies complicated by intra uterine growth restriction.

Methods: This randomized control study was undertaken in the Department of Obstetrics and Gynaecology at Narayana Medical College and Hospital, Nellore from March 2021 to November 2021. The study included 80 randomly chosen pregnant women diagnosed with intrauterine growth restriction (IUGR). 40 women received 3 g of L-Arginine daily as a supplement to standard therapy (case Group) and 40 women received only routine therapy (control group). The ultrasound and clinical examination were done on the first day of hospitalization and then every week in both the groups.

Results: In the group treated with L-Arginine, we observed higher Estimated fetal weight after 4 weeks of treatment , and Apgar score at 5 minutes compared to control group. There were no significant differences in IUGR (at entry and at delivery) between two groups. We also observed that there was an improvement in the liquor status of the group treated with L-Arginine.

Conclusion: Our study demonstrated that L-Arginine administration to pregnant women with IUGR may improve fetal condition and neonatal outcome after delivery by prolonging pregnancy and delivering a child with higher birth weight, better Apgar score and decrease the rate of caesarean sections. However, these benefits require confirmation by larger, more-powered study.

INTRODUCTION

The control of fetal growth is a complex process confounded by multiple variables such as maternal height, race , socioeconomic status and other factors. At the biological level, Fetal growth depends on genetic potential and substrate supply. An adequate substrate supply is essential to achieve the genetic potential. This supply is derived from the placenta, which is dependent on uterine and placental blood supply. Any alterations may result in the restriction of growth of the foetus. Among the intrauterine factors, nutrition plays the most important role in affecting placental and foetal growth. The current view in embryology is that a foetus has an inherent potential to grow into a healthy appropriately sized new born. However, if there is an imbalance in one or more of these critical growth and development factors, the foetus may fail to achieve appropriate size & weight.

IUGR : Intrauterine growth restriction (IUGR), a condition in which the foetal growth is restricted pathologically in utero, remains a serious health problem; as it affects not only the neonatal period, but also the adult phenotype and quality of life. ACOG defines FGR as fetal weight less than 10^{th} percentile for gestational age. IUGR represents the second most common 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 academia, with possible negative effects on neonatal outcome. It has been proven by studies that there is an increased risk of premature birth, reduced survival of the neonate and long-term sequel like impairment of neuro-developmental progress in childhood and insulin-resistance in adulthood, associated with IUGR.

Role of L-Arginine in Pregnancy and Foetal growth : L-Arginine is a semi-essential amino acid with a wide range of biological functions. The "L" in the name refers to the lefthanded configuration of the molecule. It serves as a precursor not only to proteins but also nitric oxide which has been identified as endothelium-derived relaxing factor. There are several proposed mechanisms by which Arginine supplementation might improve foetal growth.

a. Increasing utero placental perfusion by increasing local nitric oxide (NO) concentrations.
b. A second mechanism is Arginine mediated stimulation of maternal growth hormone secretion.
c. A third potential mechanism is enhancement of placental growth and development via the promotion of polyamine synthesis.
d. Arginine is a potent foetal insulin secretagogue, and insulin is a major anabolic hormone in the foetus.
e. Finally, Arginine has been shown to stimulate skeletal muscle protein synthesis.

FDA Category It is a category B drug.
Recommended Dosage L-Arginine has been studied at oral doses of 6 to 30 g/day for a variety of conditions. Many formulations have been used.

OBJECTIVE

The main aim of this study was to evaluate the effect of L-Arginine administration on the fetal outcome in pregnancies complicated by intra uterine growth restriction.

METHODS

The randomized control study was undertaken in the Department of Obstetrics and Gynaecology at Narayana Medical College and Hospital, Nellore from March 2021 to November 2021. The study included 80 randomly chosen pregnant women diagnosed with intrauterine growth restriction (IUGR). 40 women received 3 g of L-Arginine daily as a supplement to standard therapy (case Group) and 40 women received only routine therapy (control group). The ultrasound and clinical examination were done on the first day of hospitalization and then every week in both the groups.

RESULTS

In the group treated with L-Arginine, we observed higher Estimated fetal weight after 4 weeks of treatment, and Apgar score at 5 minutes compared to control group. There were no significant differences in IUGR (at entry and at delivery) between two groups. We also observed that there was an improvement in the liquor status of the group treated with L-Arginine.

Table:1 Showing Pretreatment Efw(gms)

PRETREATMENT EFW (GMS)	CASES	%	CONTROLS	%
≤1100 GMS	5	12.5	5	12.5

1101-1300 GMS	19	47.5	18	45
1301-1500 GMS	9	22.5	9	22.5
1501-1700 GMS	7	17.5	8	20
TOTAL	40	100	40	100

Table:2 Showing Posttreatment Efw(gms)

POSTTREATMENT EFW(GMS)	CASES	%	CONTROLS	%
≤1500 GMS	0	0	3	7.5
1501-1700 GMS	6	15	19	47.5
1701-1900 GMS	19	47.5	10	25
1901-2100 GMS	9	22.5	7	17.5
2101-2300 GMS	6	15	1	2.5
TOTAL	100	100	100	100

Table: 3 Showing Birth Weight(gms)

BIRTH WEIGHT (GMS)	CASES	%	CONTROLS	%
≤1600 GMS	0	0	7	17.5
1601-1800 GMS	6	15	18	45
1801-2000 GMS	20	50	10	25
2001-2200 GMS	10	25	5	12.5
2201-2400 GMS	4	10	0	0
TOTAL	100	100	100	100

Type of resuscitation in cases group, routine care (n=30,75%), bag and mask(n=6, 15%) endotracheal intubation (n=2,5%).

Control group shows 17 cases routine care (42.5%) and 15 cases (37.5%) bag and mask, 4 cases(10%) requiring endotracheal intubation.

Table: 4 Showing Complications

COMPLICATIONS	CASES	%	CONTROLS	%
RD	14	35	18	45
HYPOGLYCEMIA	6	15	9	22.5
HYPOTHERMIA	5	12.5	5	12.5
VH,NEC	3	7.5	4	10

RD - Respiratory distress ,VH - ventricular haemorrhage

NEC - necrotising enterocolitis.

Out of 38 babies in cases group 9 required nicu admission, and out of 36 babies in control group 15 required nicu admission .Results being statistically insignificant.

The decreased percentage difference in complication status in cases group and control group was found to be statistically insignificant.

DISCUSSION:

In my study In my study, majority of the study subjects in cases group were distributed in 26-30 years age group and same age group in control group. The difference in the mean age of the cases group and control group was found to be statistically insignificant . In both the groups in the study, gestational age at entry was around 30 weeks, in case group (n=14, 46.67%) and in control group (n=14, 46.67%), with the difference in the mean gestational age at entry in cases group (30.60) and control group (30.60) being statistically insignificant.

The characteristics in study and control groups Pre-treatment EFW was similar in both the groups between 1101-1300 GMS in case group (n=19, 47.5%) and in control group (n=18, 45%). The post- treatment EFW analysed in both the groups, after a period of 4 weeks, showed 1701-1900 GMS (n=19, 47.5%) in cases group and 1501-1700 GMS in control group (n=19, 47.5%). The difference in the mean in cases group (1848.17) and control group (1680.60) and the increased difference in mean post- treatment EFW in cases group compared to control group (167.57, 9% higher) was found to be statistically significant. The ultrasound estimation of fetal weight at the start and at the end of the treatment showed a mean increase of 642 g.

Table: 5

CHARACTERISTICS	CASES	%	CONTROLS	%
LIVE BIRTHS	38	95	36	90
IUD	2	5	4	10
MEAN BIRTH WEIGHT	40	1.9±0.12	40	1.7±0.14
GA AT DELIVERY	30	35±0.7	30	34.9±0.94
VAGINAL DELIVERY	33	82.5	32	80
LSCS RATE	7	17.5	8	20

In case group, intrauterine deaths were 2 (5%) and there were 4 in control group (10%), difference being statistically insignificant. Of the above, there were 5 neonatal deaths in case group (18.52%) and 3 in control group (12%).Though the gestational age at delivery was found to be more in Arginine therapy group around 35weeks whereas it was around 34 weeks in control group, the difference was statistically insignificant.

The mean birth weight of the neonates in case group was 1801- 2000 GMS (50%) compared to 1601-1800GMS (45%) in control group. This implies that the difference in the mean birth weight in cases group (1946.93GMS) and control group (1711.80GMS) and the increased difference in mean birth weight of 235.13GMS in cases group compared to control group (12% higher) was found to be statistically significant. Postnatal assessment showed that Apgar score at 1st and 5th minute was higher in the L-Arginine group . On analysing the difference in the mean APGAR score at 5 minutes in cases group (7.85) and control group (7.04), it was found to be statistically significant.

CONCLUSION

The conclusion drawn from my study is that after oral administration of L- Arginine, in women where fetal wellbeing is good and no placental insufficiency as indicated by decreased Umblical Artery S/D ratio, there was increase in the birth weight of the baby, improved APGAR of the neonates and thereby good perinatal outcome. There was reduction in complications and need for NICU admissions. L-Arginine improves foetal weight more significantly in cases with idiopathic IUGR or where mother is nutritionally deficient rather than in those pregnancies affected by anemia or preeclampsia. Hence, during antenatal care all pregnant women and high risk cases should be screened to detect IUGR in earlier stages which will decrease perinatal mortality and morbidity. Apart from the routine fetal surveillance in IUGR, Umbilical Artery S/D ratio done by Doppler ultrasonography helps in detecting increased resistance and monitoring of a compromised fetus. The IUGR cases should be supplemented oral L-Arginine, a nitric oxide donor, to reduce the resistance in feto-placental circulation.

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