Effect of L-Arginine on Intrauterine Growth Restriction Fetuses Measured by Birth weight: Randomised Controlled Trial

Thesis

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List of Contents

Subject *Page No.*

List of Abbreviations ..... **i**

List of Tables ..... **ii**

List of Figures ..... **vii**

Introduction **1**

Aim of the Work **5**

Review of Literature

Intrauterine Growth Restriction (IUGR) 6

L-Arginine 27

Patients and Methods **40**

Results **47**

Discussion **66**

Summary and Conclusion **71**

Recommendations ..... Error! Bookmark not defined.

References **74**

Arabic Summary ..... **—**

List of Abbreviations

Abbr.	Full-term
AC	**:** Abdominal circumference
ACOG	**:** American College of Obstetricians and Gynecologists
AFI	**:** Amniotic fluid index
CMV	**:** Cytomegalovirus
CPR	**:** Cerebroplacental Ratio
EFW	**:** Estimated fetal weight
FGR	**:** Fetal growth restriction
FL	**:** Femur length
GA	**:** Gestational age
HC	**:** Head circumference
IUGR	**:** Intrauterine growth restriction
LMP	**:** Last menstrual period
MAS	**:** Meconium aspiration syndrome
MCA	**:** Middle cerebral artery
NEC	**:** Necrotizing enterocolitis
NO	**:** Nitric Oxide

PI **:** Pulsatility index

PPHN **:** Persistent pulmonary hypertension

RCOG **:** Royal College of Obstetricians and Gynecologists

SD **:** Standard deviation

SFH **:** Symphysis–fundal height

SGA **:** Small for gestational age

SPSS : Statistical package for social science

T2DM **:** Type 2 diabetes mellitus

UA **:** Umbilical artery

List of Tables

Table No.	Title	Page No.
Table (1):	Demographic characteristics among the studied groups	49
Table (2):	Umbilical artery PI among the studied groups	50
Table (3):	Umbilical artery RI among the studied groups	52
Table (4):	Umbilical artery SD among the studied groups	54
Table (5):	AFI among the studied groups	56
Table (6):	Fetal GA (weeks) among the studied groups	58
Table (7):	Estimated fetal weight (gm) among the studied groups	60
Table (8):	Rate of estimated fetal weight increase (gm/week) among the studied groups	62
Table (9):	Neonatal condition among the studied groups	64

List of Figures

Figure No.	Title	Page No.
Figure (1):	Uterine artery with increased resistance and protodiastolic Notch	19
Figure (2):	Flow velocity waves of umbilical arteries: normal and with reverse diastolic component	21
Figure (3):	Flow velocity waves of the middle cerebral arteries: normal and with altered, low resistance	22
Figure (4):	Flow velocity waves of the ductus venosus: normal and altered	24
Figure (5):	Chemical structure of L-arginine	31
Figure (6):	Delocalization of charge in guanidinium group of L-Arginine	32
Figure (7):	Role of L-arginine in preeclampsia	33
Figure (8):	Advantages of L-arginine	39
Figure (9):	Flow chart of the studied cases	48
Figure (10):	Umbilical artery PI among the studied groups	51
Figure (11):	Umbilical artery RI among the studied groups	53
Figure (12):	Umbilical artery SD among the studied groups	55
Figure (13):	AFI among the studied groups	57
Figure (14):	Fetal GA among the studied groups	59

Figure (15): Estimated fetal weight among the studied groups..... 61

Figure (16): Rate of estimated fetal weight increase among the studied groups..... 63

Figure (17): Neonatal condition among the studied groups 65

Abstract

Background An area of fetal medicine research interest is to determine whether the enhancement of NO productivity could boost fetal growth patterns . There are attempts to the treatment of IUGR pregnancies by L-Arginine but the results are still inadequate**.**

Objective this study investigate the effect of L-arginine supplementation on fetal growth and pregnancy outcome.

Methodology A prospective interventional randomised controlled research trial, conducted at Ain Shams University Maternity Hospital. From 2017 till 2018**,** 260 pregnant females as research study Categorized randomly into two equal numbered research groups, 12 cases were dropped out due to loss of contact with them. Finally249 pregnant women were diagnosed with IUGR and have been categorized into two groups according to the results:**Group I:**125 pregnant women with IUGR recived 3g L_arginine and 75 mg of Acetylesalicylic daily. **Group II:** 124 pregnant women with IUGR recived 75mg Acetylesalicylic ic acid daily only . Both research groups were followed up by daily fetal movement counting, day after day cardiotocography (CTG) ,doppler twice weekly , Pelvic sonographic assessment weekly for: Head Circumference(HC) , Abdominal circumference(AC) , Femur Length (FL), Estimated fetal weight(EFW) , Amniotic fluid index(AFI) or Mean Vertical Pocket **.**

Results

The Rate of estimated fetal weight increase, birth weight and Apgar score were statistically significantly higher among L-Arginine research group than among control group(p values<0.001). NICU admission and preterm delivery were statistically significantly less frequent among L-Arginine group than among control group(p value<0.001).

Conclusions

L-arginine seems to be useful management agent for improving asymmetrical mild IUGR fetuses via raising nitric oxide levels which enhances the fetomaternal circulatory functional performance .

Keywords: L_arginine ,IUGR,nitric, oxide.

Introduction

Intrauterine growth restriction (IUGR) is an important problem in perinatal care, and has always been of great interest to obstetricians and pediatricians. It is one of the main reasons for perinatal mortality and morbidity of pregnancy which affects up to 8% of pregnancies **(Sieroszewski *et al*., 2001).**

Intrauterine growth restriction (IUGR) is defined as a fetal weight below the 10^{th} percentile for gestational age and is a common complication of pregnancy **(Gilbert *et al*., 2003).**

IUGR is not synonymous with Small for gestational age (SGA). 30-50% of SGA are IUGR while 50–70% of SGA fetuses are constitutionally small, with fetal growth appropriate for maternal size and ethnicity. The likelihood of IUGR is higher in severe SGA infants. Growth restriction implies a pathological restriction of the genetic growth potential. As a result, growth restricted fetuses may manifest evidence of fetal compromise (abnormal Doppler studies, reduced liquor volume) **(Alberry*et al*., 2007).**

IUGR can be divided into small non–placenta mediated growth restriction, for example; structural or chromosomal anomaly, inborn errors of metabolism and fetal

infection; and placental-mediated growth restriction. Maternal factors can affect placental transfer of nutrients, for example; low pre-pregnancy weight, under nutrition, substance abuse or severe anaemia. Medical conditions can affect placental implantation and vasculature and hence transfer, for example; pre-eclampsia, autoimmune disease **(Alberry*et al*., 2007).**

So IUGR is classified into two types which are: symmetrical when the fetus is small but well-proportioned and asymmetrical when the fetus abdominal growth is restricted. Most of asymmetrical cases are linked to placental insufficiency **(Ropacka *et al*., 2007).**

A variety of approaches have been undertaken to prevent fetal growth restriction. There is no consistent evidence that either inpatient or outpatient bed rest prevents fetal growth restriction or reduces the incidence of SGA births **(ACOG, 2003).**

Some experts have advocated for the use of aspirin to prevent placental insufficiency, however, there is insufficient evidence for such therapy to be routinely indicated for fetal growth restriction prevention **(Bujold *et al*., 2010).**

Vascular tone is crucial in maintaining fetoplacental perfusion. Nitric Oxide (NO) synthesized in the placental

vasculature may be essential in maintaining a sufficient placental flow by reducing placental vascular tone **(RCOG, 2007).**

Reduced NO availability may have an important role in the pathophysiology of IUGR. Therefore, NO donors as glyceryl trinitrate and isosorbide mononitrate precursors (L-arginine) and NO mediator as sildenafil citrate may be possible therapeutic approaches for IUGR **(Becker *et al*., 2000).**

It is not known whether an improvement of NO production could enhance fetal growth. There are attempts to the treatment of IUGR pregnancies by L-Arginine but the results are still insufficient **(Ropacka *et al*., 2007).**

L-arginine is possibly safe when taken by mouth appropriately for a short-term during pregnancy. Not enough is known about using L-arginine long-term in pregnancy or during breast-feeding. Stay on the safe side and avoid use **(McRae, 2016).**

L-arginine can cause an allergic response or make swelling in the airways worse. If you are prone to allergies or asthma and decide to take L-arginine, use it with caution **(Resnick et al., 2002).**

There is a concern that L-arginine might make herpes worse. There is some evidence that L-arginine is needed for the herpes virus to multiply **(Grinde, 203).**

L-arginine might lower blood pressure. This could be a problem if the patient already has low blood pressure **(Dong *et al.*, 2011).**

The primary goal of this study was to investigate the effect of dietary intake of NO donor L-arginine on IUGR pregnancy outcome.