

# Treatment of restriction in fetal growth with L-arginine

<b>Submission date</b> 26/01/2018	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 12/03/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 06/11/2024	<b>Condition category</b> Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Intrauterine growth restriction (IUGR) is a condition in which an unborn baby is smaller than it should be because it is not growing at a normal rate inside the womb. Children with IUGR have a higher risk of perinatal mortality, infant mortality, sudden infant death syndrome, cerebral palsy, and alterations in cognitive development and physical growth. The aim of this study is to find out whether giving an L-arginine supplement to pregnant women with IUGR decreases the risk of the newborn being diagnosed as being small for gestational age and the perinatal morbidity and mortality associated with this problem.

### Who can participate?

Pregnant women between 24 and 32 weeks of gestation, with a single fetus with IUGR

### What does the study involve?

Participants are randomly allocated to one of two groups to take either one packet a day of L-arginine or a placebo (dummy) supplement until the time of delivery. Outcomes are measured including birth weight, perinatal morbidity, perinatal mortality, preterm delivery, and admission to the neonatal intensive care unit (NICU).

### What are the possible benefits and risks of participating?

L-arginine may reduce the risks of IUGR. Although it has no serious side effects, nausea, diarrhea and weakness have been reported with excessive consumption of this substance.

### Where is the study run from?

Hospital Clínico Universitario Virgen de la Arrixaca (Spain)

### When is the study starting and how long is it expected to run for?

January 2015 to June 2024

### Who is funding the study?

Fundación para Formación e Investigación Sanitaria (Spain)

Who is the main contact?  
Catalina De Paco Matallana  
katy.depaco@gmail.com

## Contact information

### Type(s)

Public

### Contact name

Miss Catalina De Paco Matallana

### Contact details

Unidad Materno Fetal-Hospital Maternal  
Hospital Clínico Universitario Virgen de la Arrixaca  
Cta. Madrid-Cartagena s/n 30120  
El Palmar - Murcia  
Spain  
30120  
+34 (0)968395588  
katy.depaco@gmail.com

## Additional identifiers

### Protocol serial number

2017-4-14-HCUVA

## Study information

### Scientific Title

Treatment of restriction in fetal growth with L-arginine: randomized clinical trial, double-blind, controlled with placebo

### Acronym

ARCIR

### Study objectives

To assess whether oral administration of L-arginine in pregnant women with IUGR decreases the risk of newborn diagnosed as being small for gestational age and the perinatal morbidity and mortality associated with this problem.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

1. Approved 30/03/2015, Comité Ético de la Región de Murcia (Carretera Madrid-Cartagena S/N, El Palmar (Murcia), 30120, Spain; +34 968 369031; rosariogarcia7@carm.es), ref: 2017-4-14-HCUVA
2. Approved 24/04/2017, Ethics Committee H.C.U. Virgen de la Arrixaca, ref: 2017-4-14-HCUVA

## **Study design**

Single-centre double-blind placebo-controlled trial

## **Primary study design**

Interventional

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Intrauterine growth restriction (IUGR)

## **Interventions**

Pregnant women with an ultrasonographic diagnosis of IUGR will be invited to participate in the study. After signing informed consent, women will be randomised and assigned to one of two study groups:

1. Women in the L-arginine group will take 1 packet/day containing 7.84 gram of L-arginine
2. The placebo group will take 1 packet/day, identical in weight, size, color and flavor to those of L-Arginine but that will only contain excipient without pharmacological activity (96% corn starch)

Women will be instructed to take the packet at least one hour before breakfast in order not to interfere with the absorption of other constituents of the diet. The maximum treatment duration will be 20 weeks and the follow-up will be done every week.

## **Intervention Type**

Supplement

## **Primary outcome(s)**

Birth weight below the 10th percentile for gestational age and sex, according to local reference curves. The estimation of fetal weight is made by combining the cephalic perimeter, abdominal perimeter and femur length. This weight estimation is usually done every two weeks when the estimated fetal weight percentile is between the 3rd and 10th percentile and each week when it is below the 3th percentile.

## **Key secondary outcome(s)**

Secondary objectives will be analyzed at the postnatal level, except for the diagnosis of the development of hypertension in pregnancy, either preeclampsia or gestational hypertension:

1. Birth weight
2. Gestational age at birth
3. Size of the newborn
4. Abdominal perimeter of the newborn
5. Cephalic perimeter of the newborn
6. Weight index of the newborn
7. Placental weight
8. Placental weight/weight ratio of the newborn

9. Low weight (<2500 g)
10. Very low weight (<1500 g)
11. Preterm delivery <37 weeks of gestation
12. Preterm delivery <32 weeks gestation
13. Preterm delivery <28 weeks gestation
14. Apgar score at minute 1 and 5
15. Perinatal mortality (early fetal and neonatal mortality)
16. Respiratory distress syndrome
17. Bronchopulmonary dysplasia
18. Intraventricular hemorrhage
19. Periventricular leukomalacia (selene)
20. Neonatal sepsis
21. Necrotizing enterocolitis
22. Retinopathy of prematurity
23. Compound of perinatal morbi-mortality
24. Admission to the neonatal intensive care unit
25. Congenital malformations
26. Induction of labor
27. Cesarean section
28. Preeclampsia
29. Gestational hypertension
30. Antepartum hemorrhage
31. Postpartum hemorrhage
32. Maternal infection
33. Need for maternal hospitalization
34. Maternal adverse effects

**Completion date**

01/06/2024

## Eligibility

**Key inclusion criteria**

1. Age  $\geq 18$  years
2. Single pregnancy
3. Ultrasonographic diagnosis of IUGR: estimated fetal weight lower than the 10th percentile for gestational age according to local or national reference values, independently of the results of the Doppler parameters of the umbilical, middle cerebral and/or uterine arteries
4. Live fetuses at 11 and 13 at weeks gestation
6. Gestational age between 24 and 32 weeks
7. No indication of imminent or planned birth
8. Availability to participate in the study and sign the consent

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

Female

**Total final enrolment**

73

**Key exclusion criteria**

1. Women with medical complications such as preeclampsia, chronic hypertension, kidney disease, diabetes mellitus, liver dysfunction, autoimmune disease or other significant medical complications
2. Women with a history of major mental disorders (schizophrenia, manic-depressive illness)
3. Women in labor or with imminent or planned delivery
4. Fetal malformation
5. Acute fetal distress
6. IUGR associated with infectious disease
7. Multiple pregnancy

**Date of first enrolment**

05/02/2018

**Date of final enrolment**

23/01/2024

**Locations****Countries of recruitment**

Spain

**Study participating centre**

Hospital Clínico Universitario Virgen de la Arrixaca

Murcia

Spain

30008

**Sponsor information****Organisation**

Fundación para Formación e Investigación Sanitaria

**ROR**

<https://ror.org/05m5has32>

# Funder(s)

## Funder type

Research organisation

## Funder Name

Fundación para Formación e Investigación Sanitaria

# Results and Publications

## Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

## IPD sharing plan summary

Data sharing statement to be made available at a later date