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Treatment of restriction in fetal growth with L-arginine

Submission date	Recruitment status	[_] Prospectively registered
26/01/2018	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
12/03/2018	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
06/11/2024	Pregnancy and Childbirth	[X] 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?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

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 measure
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.

Secondary outcome measures
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

Overall study start date
01/01/2015

Completion date
01/06/2024

Eligibility

Key inclusion criteria
1. Age ≥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

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
130

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

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Sponsor type
Research organisation

Website
https://www.ffis.es

ROR
https://ror.org/05m5has32

Funder(s)

Funder type
Research organisation

Funder Name
Fundación para Formación e Investigación Sanitaria

Results and Publications

Publication and dissemination plan
Throughout 2019 and 2020 the statistical analysis of the results will be carried out, followed by publications.

Intention to publish date
01/12/2021

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