Clinical trial results:
Sulfato de magnesio en pauta continua versus discontinua en la conducta expectante de la preeclampsia grave: ensayo clínico aleatorizado

Summary

EudraCT number	2011-002095-17
Trial protocol	ES
Global end of trial date	30 May 2016

Results information

Result version number	v1 (current)
This version publication date	18 November 2021
First version publication date	18 November 2021

Trial information

Trial identification

Sponsor protocol code	MAGSPET

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	VHIR
Sponsor organisation address	Passeig Vall Hebron 119-129, Barcelona, Spain, 08035
Public contact	Joaquin Lopez-Soriano, VHIR, 34 934894779, joaquin.lopez.soriano@vhir.org
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether continuous administration of magnesium sulfate prolongs pregnancy more days compared to discontinuous administration

Protection of trial subjects:

During the course of the study, the United States Food and Drug Administration (FDA) alerted against prolonged use (more than 5-7 days) of magnesium sulfate, due to concern about fetal and neonatal bone demineralization. However, in these cases magnesium sulfate was used as tocolytic treatment, and prenatal exposure was longer (9.6 weeks) and higher (total maternal dose of 3700 g) than in our study. Spanish Agency of Medicines and Medical Devices (AEMPS) was informed about this alert, and confirmed to continue with the study.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 March 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 95
Worldwide total number of subjects	95
EEA total number of subjects	95

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	95
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at Hospital Vall Hebron (Barcelona)

Pre-assignment

Screening details:

The inclusion criteria were pregnant women 18 years of age or older, gestational age between 24 weeks 0 days and 33 weeks 6 days, diagnosed with severe preeclampsia and suitable for expectant management after 24 hours of treatment with intravenous magnesium sulfate.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Continuous MgSulfate

Arm description:

Continuous treatment: keeping magnesium sulfate perfusion (1-1.5 g/h) to maintain a serum concentration of 4.8 to 9.6 mg/dL until 24 to 48 hours postpartum.

Arm type	Experimental
Investigational medicinal product name	Magnesium sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients were treated with intravenous magnesium sulfate according to Zuspan regimen (4 g loading dose, followed by an infusion of 1 g/h) up to 24 hours. After randomization, women were allocated to one of two groups; continuous or discontinuous

Arm title	Discontinuous MgSulfate

Arm description:

Discontinuous treatment: stopping magnesium sulfate until any indication of delivery. Magnesium sulfate (4 g loading dose, followed by an infusion of 1 g/h) was reinitiated before delivery until 24 to 48 hours postpartum

Arm type	Active comparator
Investigational medicinal product name	Magnesium sulfate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

All patients were treated with intravenous magnesium sulfate according to Zuspan regimen (4 g loading dose, followed by an infusion of 1 g/h) up to 24 hours. After randomization, women were allocated to one of two groups; continuous or discontinuous

Number of subjects in period 1	Continuous MgSulfate	Discontinuous MgSulfate
Started	48	47
Completed	45	47
Not completed	3	0
Consent withdrawn by subject	2	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	95	95	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	34.2		
inter-quartile range (Q1-Q3)	30.7 to 37.4	-	
Gender categorical Units: Subjects			
Female	95	95	
Male	0	0	

End points

End points reporting groups

Reporting group title	Continuous MgSulfate
Reporting group description:	
Continuous treatment: keeping magnesium sulfate perfusion (1-1.5 g/h) to maintain a serum concentration of 4.8 to 9.6 mg/dL until 24 to 48 hours postpartum.	
Reporting group title	Discontinuous MgSulfate
Reporting group description:	
Discontinuous treatment: stopping magnesium sulfate until any indication of delivery. Magnesium sulfate (4 g loading dose, followed by an infusion of 1 g/h) was reinitiated before delivery until 24 to 48 hours postpartum	

Primary: Days of delivery

End point title	Days of delivery
End point description:	
Primary end point is the interval, in days, between inclusion in the study and delivery, between continuous and discontinuous treatment groups	
End point type	Primary
End point timeframe:	
All the study	

End point values	Continuous MgSulfate	Discontinuous MgSulfate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: day				
arithmetic mean (full range (min-max))	4 (2 to 7)	5 (3 to 9)		

Statistical analyses

Statistical analysis title	Delivary day
Comparison groups	Continuous MgSulfate v Discontinuous MgSulfate
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.125
Method	t-test, 2-sided

Secondary: Maternal complications

End point title	Maternal complications

End point description:

End point type	Secondary

End point timeframe:

All the study

End point values	Continuous MgSulfate	Discontinuous MgSulfate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	47		
Units: number				
number (not applicable)	9	12		

Statistical analyses

Statistical analysis title	Maternal complications
Comparison groups	Continuous MgSulfate v Discontinuous MgSulfate
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.622
Method	t-test, 2-sided

Secondary: Newborn complications

End point title	Newborn complications

End point description:

End point type	Secondary

End point timeframe:

All the study

End point values	Continuous MgSulfate	Discontinuous MgSulfate		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45[1]	47[2]		
Units: Number				
number (not applicable)	17	19		

Notes:

[1] - They were actually 52 newborn in this group

[2] - There were actually 54 newborn in this group

Statistical analyses

Statistical analysis title	Newborn complications
Comparison groups	Continuous MgSulfate v Discontinuous MgSulfate
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.786
Method	t-test, 2-sided

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All the study

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Continuous
Reporting group description: -	
Reporting group title	Discontinuous

Reporting group description: -

Serious adverse events	Continuous	Discontinuous	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Intraventricular haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ventriculitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bilateral pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Continuous	Discontinuous	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 45 (60.00%)	33 / 47 (70.21%)	
Pregnancy, puerperium and perinatal conditions			
Uterine contractions during pregnancy			
subjects affected / exposed	4 / 45 (8.89%)	8 / 47 (17.02%)	
occurrences (all)	4	8	
Vulvar pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Genital herpes			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Vaginal bleeding			
subjects affected / exposed	2 / 45 (4.44%)	3 / 47 (6.38%)	
occurrences (all)	2	3	
Vaginitis			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
General disorders and administration site conditions			
Headache			
subjects affected / exposed	3 / 45 (6.67%)	0 / 47 (0.00%)	
occurrences (all)	3	0	
Neck pain			
subjects affected / exposed	1 / 45 (2.22%)	3 / 47 (6.38%)	
occurrences (all)	1	3	
Inferior extremity sensibility loss			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Suprapubic pain			

subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Fever			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Venous access haematoma			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Lumbar pain			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Hot flush			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Submaxilitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Acute pulmonary oedema			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Tracheobronchitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 45 (8.89%)	0 / 47 (0.00%)	
occurrences (all)	4	0	
Cardiac disorders			

Intraventricular haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Subacute ischaemic stroke			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Vasovagal syncope			
subjects affected / exposed	1 / 45 (2.22%)	1 / 47 (2.13%)	
occurrences (all)	1	1	
Ventriculitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 45 (8.89%)	8 / 47 (17.02%)	
occurrences (all)	4	8	
Phlebitis			
subjects affected / exposed	5 / 45 (11.11%)	8 / 47 (17.02%)	
occurrences (all)	5	8	
Hyperglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Otitis externa			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	

Diarrhoea			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Esophageal reflux			
subjects affected / exposed	2 / 45 (4.44%)	4 / 47 (8.51%)	
occurrences (all)	2	4	
Rectal haematoma			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Palmar pruritus			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Urticarial dermatitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Haematuria			
subjects affected / exposed	1 / 45 (2.22%)	0 / 47 (0.00%)	
occurrences (all)	1	0	
Acute renal failure			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Infections and infestations			
Acute upper respiratory infection			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	
Urinary tract infection			

subjects affected / exposed	12 / 45 (26.67%)	13 / 47 (27.66%)	
occurrences (all)	12	13	
Listeriosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 47 (2.13%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	3 / 47 (6.38%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported