Clinical trial results:
The pain relieving effect of nitrous oxide during bone marrow aspiration and biopsy - a placebo-controlled and randomized trial

Summary

EudraCT number	2012-004285-18
Trial protocol	FI
Global end of trial date	20 March 2014

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	00002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Helsinki and Uusimaa Hospital District
Sponsor organisation address	Haartmaninkatu 4, Helsinki, Finland, 00029
Public contact	Per Rosenberg, Helsingin yliopisto, +358 9471 72 510,
Scientific contact	Per Rosenberg, Helsingin yliopisto, +358 9471 72 510,
Sponsor organisation name	Helsinki University Hospital
Sponsor organisation address	Haartmaninkatu 4, Helsinki, Finland, 00029
Public contact	Anna-Maria Kuivalainen, Helsinki and Uusimaa Hospital District, Helsinki University Hospital, anna-maria.kuivalainen@helsinki.fi
Scientific contact	Anna-Maria Kuivalainen, Helsinki and Uusimaa Hospital District, Helsinki University Hospital, anna-maria.kuivalainen@helsinki.fi

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 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2014
Global end of trial reached?	Yes
Global end of trial date	20 March 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study was to find out if inhalation of a 50% mixture of N2O and oxygen is effective in relieving procedural pain in adults during bone maarow aspiration and/or biopsy compared to 50% oxygen.

Protection of trial subjects:

The ethics committee of Helsinki and Uusimaa Hospital District approved the study protocol before the start of the trial (Diary number 323/13/03/01/2012). The ethical principles of Helsinki declaration were followed during every step of the clinical trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2013
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	Finland: 70
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	46
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adult outpatients from the Division of Haematology undergoing bone marrow aspiration and/or biopsy were considered for inclusion. Patients were interviewed and screened for predetermined exclusion criteria before enrollment.

Pre-assignment

Screening details:

144 patients were considered for randomization. 74 patients were excluded and 70 patients were randomized.

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	Nitrous oxide arm

Arm description:

Patients receiving 50% mixture of nitrous oxide and oxygen

Arm type	Experimental
Investigational medicinal product name	50% mixture of nitrous oxide and oxygen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	Inhalation use

Dosage and administration details:

Patients started inhalation when the procedure was about to begin. After 2-3 minutes of inhalation, procedure was started. Patients inhaled countinuously throughout the procedure. After the procedure was completed, inhalation was stopped.

Arm title	Placebo arm

Arm description:

Patients receiving 50% oxygen arm

Arm type	Placebo
Investigational medicinal product name	50% oxygen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	Inhalation use

Dosage and administration details:

Patients started inhalation when the procedure was about to begin. After 2-3 minutes of inhalation, procedure was started. Patients inhaled continuously throughout the procedure. After the procedure, patients stopped inhalation.

Number of subjects in period 1	Nitrous oxide arm	Placebo arm
Started	35	35
Completed	35	35

Baseline characteristics

Reporting groups	
Reporting group title	Nitrous oxide arm
Reporting group description:	
Patients receiving 50% mixture of nitrous oxide and oxygen	
Reporting group title	Placebo arm
Reporting group description:	
Patients receiving 50% oxygen arm	

Reporting group values	Nitrous oxide arm	Placebo arm	Total
Number of subjects	35	35	70
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	58	60	
standard deviation	± 13	± 12	-
Gender categorical			
Units: Subjects			
Female	19	14	33
Male	16	21	37

End points

End points reporting groups

Reporting group title	Nitrous oxide arm
Reporting group description: Patients receiving 50% mixture of nitrous oxide and oxygen	
Reporting group title	Placebo arm
Reporting group description: Patients receiving 50% oxygen arm	

Primary: Pain during procedure

End point title	Pain during procedure
End point description:	
End point type	Primary
End point timeframe: Pain during bone marrow aspiration and/or biopsy procedure	

End point values	Nitrous oxide arm	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	35		
Units: Pain in NRS				
median (full range (min-max))				
Local anaesthetic infiltration	3 (0 to 7)	3 (1 to 8)		
Puncture	3 (0 to 9)	3 (0 to 8)		
Aspiration	4 (0 to 10)	4 (0 to 9)		
Biopsy	3.5 (0 to 10)	3.5 (0 to 10)		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description: The normality of the variables was assessed with the Shapiro–Wilk test. Ordinal regression analysis stratified by phase of the procedure was used to analyse the differences in pain felt during BMAB in both groups.	
Comparison groups	Nitrous oxide arm v Placebo arm
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)

Confidence interval	
level	95 %
sides	2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the start of study treatment until end of follow-up interview on the following day.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	1
Reporting groups	
Reporting group title	Treatment arm
Reporting group description: Patients receiving 50% mixture of nitrous oxide and oxygen	
Reporting group title	Placebo arm
Reporting group description: Patients receiving 50% oxygen	

Serious adverse events	Treatment arm	Placebo arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 35 (0.00%)	0 / 35 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Treatment arm	Placebo arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 35 (14.29%)	4 / 35 (11.43%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 35 (14.29%)	2 / 35 (5.71%)	
occurrences (all)	5	2	
Headache			
subjects affected / exposed	0 / 35 (0.00%)	3 / 35 (8.57%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Nausea			

subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	0 / 35 (0.00%) 0	

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29911602