Clinical trial results:
A prospective randomized open label study
Intranasal dexmedetomidine versus inhaled nitrous oxide for children age 3 – 15 years for procedural sedation and analgesia in pediatric emergency department.

Summary

EudraCT number	2016-003773-17
Trial protocol	SE
Global end of trial date	28 August 2020

Results information

Result version number	v1 (current)
This version publication date	19 February 2024
First version publication date	19 February 2024

Trial information

Trial identification

Sponsor protocol code	dex_version1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Karolinska University Hospital
Sponsor organisation address	AnnaStecksens gatan, Stockholm, Sweden,
Public contact	Astrid Lindgrens Childrens hospital, Karolinska University Hospital, 46 851770000,
Scientific contact	Astrid Lindgrens Childrens hospital, Karolinska University Hospital, 46 851770000,

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	03 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 August 2020
Global end of trial reached?	Yes
Global end of trial date	28 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Aim of this study is to measure whether intranasal dexmedetomidine is equally good as nitrous oxide (N2O) among children between 3 and 15 years of age with minor injuries with respect to analgesia during procedure measured by FLACC in a prospective randomized open-label study.
We are interested in finding out if dexmedetomidine could be used for PSA for painful procedures in combination with local anesthetics.

Protection of trial subjects:

This trial was approved by the Swedish Ethical Review Authority, Stockholm.
As all subject enrolled in this trial were minors and therefore vulnerable the risks and benefits of the treatments were carefully assessed.
Informed consent was required from all caregivers.
All data has been treated anonymously.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 May 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 156
Worldwide total number of subjects	156
EEA total number of subjects	156

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)	117
Adolescents (12-17 years)	39

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patient recruitment was carried out in the pediatric ED at Astrid Lindgren Children's hospital (ALB), Karolinska University Hospital in Stockholm, Sweden between August 2017 and October 2020

Pre-assignment

Screening details:

Swedish speaking, previously healthy children aged 3 to 15 years with an extremity fracture or luxation requiring reduction were eligible for this study.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	IN DEX

Arm description:

Intranasal dexmedetomidine for procedural sedation and analgesia

Arm type	Experimental
Investigational medicinal product name	dexmedetomidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intranasal use

Dosage and administration details:

2.0 mcg/kg intranasal with mucosal athomization devize (MAD)

Arm title	Nitrous oxide

Arm description:

Inhaled Nitrous oxide for procedural sedation and analgesia

Arm type	Active comparator
Investigational medicinal product name	nitrous oxide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	Inhalation use

Dosage and administration details:

N2O was administered with a facial mask held by an experienced ED nurse. N2O was titrated to a concentration 50% N2O : 50% O2 within 2-3 minutes. When N2O was discontinued supplemental 100% O2 was provided for 2-3 minutes.

Number of subjects in period 1	IN DEX	Nitrous oxide
Started	78	78
Completed	77	78
Not completed	1	0
Physician decision	1	-

Baseline characteristics

Reporting groups	
Reporting group title	IN DEX
Reporting group description:	
Intranasal dexmedetomidine for procedural sedation and analgesia	
Reporting group title	Nitrous oxide
Reporting group description:	
Inhaled Nitrous oxide for procedural sedation and analgesia	

Reporting group values	IN DEX	Nitrous oxide	Total
Number of subjects	78	78	156
Age categorical Units: Subjects			
Children (2-11 years)	59	58	117
Adolescents (12-17 years)	19	20	39
Gender categorical Units: Subjects			
Female	30	35	65
Male	48	43	91

End points

End points reporting groups	
Reporting group title	IN DEX
Reporting group description: Intranasal dexmedetomidine for procedural sedation and analgesia	
Reporting group title	Nitrous oxide
Reporting group description: Inhaled Nitrous oxide for procedural sedation and analgesia	

Primary: pain	
End point title	pain
End point description:	
End point type	Primary
End point timeframe: After procedure	

End point values	IN DEX	Nitrous oxide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	78		
Units: 10	77	78		

Statistical analyses

Statistical analysis title	dex vs N2O
Comparison groups	Nitrous oxide v IN DEX
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: sedation	
End point title	sedation
End point description:	
End point type	Secondary
End point timeframe: After procedure	

End point values	IN DEX	Nitrous oxide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	78		
Units: 6	77	78		

Statistical analyses

No statistical analyses for this end point

Secondary: parental and patient satisfaction

End point title	parental and patient satisfaction

End point description:

End point type	Secondary

End point timeframe:

After procedure

End point values	IN DEX	Nitrous oxide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	78		
Units: 5	77	78		

Statistical analyses

No statistical analyses for this end point

Secondary: phycisians opinion

End point title	phycisians opinion

End point description:

End point type	Secondary

End point timeframe:

After procedure

End point values	IN DEX	Nitrous oxide		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	78		
Units: 5	77	78		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: August 2018 - August 2020	
Adverse event reporting additional description: Reported to Swedish Medical authority	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	2.1

Reporting groups	
Reporting group title	dexmedetomidine
Reporting group description: -	
Reporting group title	Nitrous oxide
Reporting group description: -	

Serious adverse events	dexmedetomidine	Nitrous oxide	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 77 (0.00%)	0 / 78 (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: 0.7 %

Non-serious adverse events	dexmedetomidine	Nitrous oxide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 77 (6.49%)	9 / 78 (11.54%)	
Ear and labyrinth disorders			
tinnitus	Additional description: Short, passed quicky with discontinuation of nitrous oxide		
subjects affected / exposed	0 / 77 (0.00%)	1 / 78 (1.28%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
nausea and vomiting	Additional description: Symptoms passed quickly with cessation of nitrous oxide		
subjects affected / exposed	0 / 77 (0.00%)	7 / 78 (8.97%)	
occurrences (all)	0	0	
Psychiatric disorders			

Hallucinations, mixed	Additional description: Shortterm and no medications were required to treat these symptoms		
subjects affected / exposed	5 / 77 (6.49%)	1 / 78 (1.28%)	
occurrences (all)	5	1	

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