



Clinical trial results:

B.R.E.A.T.H.E. Bronchiolitis RCT: Emergency Assisted Therapy with Heliox - an Evaluation.

A Prospective, Double-Blinded, Randomised, Controlled Clinical Trial to assess the effect of helium-oxygen gas mixtures during the management of bronchiolitis.

Summary

EudraCT number	2005-003007-36
Trial protocol	GB
Global end of trial date	31 August 2007

Results information

Result version number	v1 (current)
This version publication date	22 January 2020
First version publication date	22 January 2020

Trial information

Trial identification

Sponsor protocol code	HP002A
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Additional study identifiers

ISRCTN number	ISRCTN18238432
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensington Campus, London, United Kingdom, SW7 2AZ
Public contact	Professor Parviz Habibi, Imperial College London, +44 020 3312 7683, p.habibi@imperial.ac.uk
Scientific contact	Professor Parviz Habibi, Imperial College London, +44 020 3312 7683, p.habibi@imperial.ac.uk

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	29 August 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2007
Global end of trial reached?	Yes
Global end of trial date	31 August 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial is to determine the efficacy of helium-oxygen mixtures in the management of bronchiolitis.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2005
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	United Kingdom: 319
Worldwide total number of subjects	319
EEA total number of subjects	319

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)	319
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 361 patients with clinically diagnosed bronchiolitis were considered for eligibility. Consent was obtained for 319 subjects who were randomized and enrolled in the study.

Pre-assignment

Screening details:

Infants presenting with any respiratory signs or symptoms were screened between the period of 2005 to 2008.

Period 1

Period 1 title	Allocation
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

The BREATHE study is the largest phase III, multicenter, double-blinded RCT of Heliox in bronchiolitis. It attempted to resolve the challenges of blinding. The use of special hosing material, identical in appearance for Heliox and Airox ensured that there was no difference in sound generation that could have alerted the investigator to identify the study gas.

Arms

Are arms mutually exclusive?	Yes
Arm title	Heliox

Arm description:

Participants received treatment with Heliox gas

Arm type	Experimental
Investigational medicinal product name	Heliox21
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gas and solvent for dispersion for injection/infusion
Routes of administration	Inhalation use

Dosage and administration details:

The intervention with additional oxygen titrated via Y-connection tubing, resulting in gas mixes with additional oxygen. Gas delivery was by a tight-fitting 3-valve, nonrebreathing facemask (FM; 1192; Intersurgical) or a nasal cannula (NC; BC 2745-20; Fisher & Paykel Healthcare) if the subject was FM intolerant. Gas drove the continuous positive airway pressure (CPAP) device (EME infant flow driver; CareFusion).

Arm title	AirOX
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Arm description:

Participants received a mixture of 21% oxygen + 79% nitrogen.

Arm type	Active comparator
Investigational medicinal product name	Medical Air
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gas and solvent for dispersion for injection/infusion
Routes of administration	Inhalation use

Dosage and administration details:

Treatment is a mixture of 21% oxygen + 79% nitrogen.

The intervention with additional oxygen titrated via Y-connection tubing, resulting in gas mixes with additional oxygen. Gas delivery was by a tight-fitting 3-valve, nonrebreathing facemask (FM; 1192; Intersurgical) or a nasal cannula (NC; BC 2745-20; Fisher & Paykel Healthcare) if the subject was FM

intolerant. Gas drove the continuous positive airway pressure (CPAP) device (EME infant flow driver; CareFusion).

Number of subjects in period 1	Heliox	AirOX
Started	160	159
Completed	140	141
Not completed	20	18
Consent withdrawn by subject	3	6
Physician decision	1	-
screening failure	4	8
therapy prematurely disrupted	8	-
Protocol deviation	4	4

Period 2

Period 2 title	Follow up
Is this the baseline period?	Yes ^[1]
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Heliox

Arm description:

Participants received treatment with Heliox gas

Arm type	Experimental
Investigational medicinal product name	Heliox21
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gas and solvent for dispersion for injection/infusion
Routes of administration	Inhalation use

Dosage and administration details:

The intervention with additional oxygen titrated via Y-connection tubing, resulting in gas mixes with additional oxygen. Gas delivery was by a tight-fitting 3-valve, nonrebreathing facemask (FM; 1192; Intersurgical) or a nasal cannula (NC; BC 2745-20; Fisher & Paykel Healthcare) if the subject was FM intolerant. Gas drove the continuous positive airway pressure (CPAP) device (EME infant flow driver; CareFusion).

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Treatment is a mixture of 21% oxygen + 79% nitrogen.

The intervention with additional oxygen titrated via Y-connection tubing, resulting in gas mixes with additional oxygen. Gas delivery was by a tight-fitting 3-valve, nonrebreathing facemask (FM; 1192; Intersurgical) or a nasal cannula (NC; BC 2745-20; Fisher & Paykel Healthcare) if the subject was FM intolerant. Gas drove the continuous positive airway pressure (CPAP) device (EME infant flow driver; CareFusion).

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Baseline characteristic provided only for participants that completed the study.

Number of subjects in period 2^[2]	Heliox	AirOX
Started	140	141
Completed	140	141

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Baseline characteristic provided only for participants that completed the study.

Baseline characteristics

Reporting groups

Reporting group title	Heliox
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Reporting group description:

Participants received treatment with Heliox gas

Reporting group title	AirOX
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Reporting group description:

Participants received a mixture of 21% oxygen + 79% nitrogen.

Reporting group values	Heliox	AirOX	Total
Number of subjects	140	141	281
Age categorical			
Units: Subjects			
Infants	140	141	281
Age continuous			
Units: weeks			
median	39	40	
inter-quartile range (Q1-Q3)	38 to 40	38 to 40	-
Gender categorical			
Units: Subjects			
Female	86	85	171
Male	54	56	110
Weight at presentation			
Units: kilogram(s)			
median	5.65	5.7	
inter-quartile range (Q1-Q3)	4.34 to 7.70	4.4 to 7.7	-
Modified Wood`s Clinical Asthma Score			
Maximum score 11.			
Units: score			
median	3	3	
inter-quartile range (Q1-Q3)	2 to 3	2 to 4	-

End points

End points reporting groups

Reporting group title	Heliox
Reporting group description:	
Participants received treatment with Heliox gas	
Reporting group title	AirOX
Reporting group description:	
Participants received a mixture of 21% oxygen + 79% nitrogen.	
Reporting group title	Heliox
Reporting group description:	
Participants received treatment with Heliox gas	
Reporting group title	AirOX
Reporting group description:	
Participants received a mixture of 21% oxygen + 79% nitrogen.	

Primary: Total length of treatment (LoT)

End point title	Total length of treatment (LoT)
End point description:	
End point type	Primary
End point timeframe:	
1 week	

End point values	Heliox	AirOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	141		
Units: days				
median (inter-quartile range (Q1-Q3))	1.9 (1.08 to 3.17)	1.87 (1.11 to 3.34)		

Statistical analyses

Statistical analysis title	LoT
Comparison groups	Heliox v AirOX
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Wilcoxon (Mann-Whitney)

Primary: Total length of treatment (LoT) for facemask tolerant participants

End point title	Total length of treatment (LoT) for facemask tolerant participants
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End point description:

Heliox - 44 participants, Aieox - 40 participants were facemask tolerant, used a nasal cannula

End point type	Primary
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End point timeframe:

1 week

End point values	Heliox	AirOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	40		
Units: day				
median (inter-quartile range (Q1-Q3))	1.46 (0.85 to 1.95)	2.01 (0.93 to 2.86)		

Statistical analyses

Statistical analysis title	LoT with facemask tolerant
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Statistical analysis description:

Heliox - 44 participants, Aieox - 40 participants were facemask tolerant, used nasal cannula

Comparison groups	Heliox v AirOX
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Number of subjects included in analysis	84
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Analysis specification	Post-hoc
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Analysis type	superiority
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P-value	= 0.03
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Method	Wilcoxon (Mann-Whitney)
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Secondary: Proportion of cases progressing to CPAP (continuous positive airway pressure)

End point title	Proportion of cases progressing to CPAP (continuous positive airway pressure)
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End point description:

End point type	Secondary
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End point timeframe:

1 week

End point values	Heliox	AirOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	141		
Units: percent	17	19		

Statistical analyses

Statistical analysis title	CPAP
Comparison groups	Heliox v AirOX
Number of subjects included in analysis	281
Analysis specification	Post-hoc
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.6

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

1 week

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	5
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Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: It was no reported any non-serious adverse event.

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 319 (1.88%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Intubation			
subjects affected / exposed	6 / 319 (1.88%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 319 (0.00%)		

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/23509160>