Clinical trial results:
Effects of supplemental oxygen on systemic and cerebral hemodynamics in experimental hypovolemia: A randomized, phase IV, crossover study to study the effect of supplemental oxygen vs. room air on cerebral and systemic hemodynamics in healthy volunteers > 18 years during experimental hypovolemia in the lower body negative pressure model of hypovolemia.

Summary

EudraCT number	2021-003238-35
Trial protocol	NO
Global end of trial date	14 June 2022

Results information

Result version number	v1 (current)
This version publication date	13 July 2023
First version publication date	13 July 2023

Trial information

Trial identification

Sponsor protocol code	4_141221

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05150418
WHO universal trial number (UTN)	-
Other trial identifiers	Regional Committees for Medical Research Ethics - : 285164

Notes:

Sponsors

Sponsor organisation name	Oslo University Hospital
Sponsor organisation address	Kirkeveien 166, Oslo, Norway, 0450
Public contact	Department of Anesthesiology, Oslo University Hospital, 47 22119690, lars.oivind.hoiseth@hotmail.com
Scientific contact	Department of Anesthesiology, Oslo University Hospital, 90749409 22119690, lars.oivind.hoiseth@hotmail.com

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	15 April 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 June 2022
Global end of trial reached?	Yes
Global end of trial date	14 June 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Supplemental oxygen is frequently administered in acutely and critically ill patients, specifically, it is often administered in trauma patients to avoid arterial hypoxemia and tissue hypoxia. There is also an increasing focus on potentially deleterious effects of hyperoxia. Further, the hemodynamic response to hyperoxia in hypovolemia is poorly understood.
The present study aims to investigate the effects of supplemental oxygen on systemic and cerebral hemodynamics in simulated hypovolemia in healthy volunteers.

Protection of trial subjects:

The trial was carried out in accordance with the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2021
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	Norway: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Fifteen helathy volunteers were included in this single-centre study performed at Oslo University Hospital, Aker. First visit of first subject was December 2021, and last visit of last subject was June 2022.

Pre-assignment

Screening details:

Sixteen subjects were screened for participation. Fifteen subjects entered and completed all visits.

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Blinding implementation details:

The trial was blinded with a crossover design. Two treatments were administered; medical air and 100% oxygen. Subjects, investigators present during the visits were blinded. Analysis of primary outcome was performed before unblinding.

Arms

Are arms mutually exclusive?	No
Arm title	Medical air

Arm description:

Inhalation of medical air, 21% oxygen, 79% nitrogen.

Arm type	Active comparator
Investigational medicinal product name	Medisinsk luft (Air Liquide (medicin.dkAir Liquide Gas AB))
Investigational medicinal product code	V03A N05
Other name	
Pharmaceutical forms	Medicinal gas, liquefied
Routes of administration	Inhalation use

Dosage and administration details:

Inhalation om mask with rebreather, 15 litres/minute.

Arm title	Oxygen

Arm description:

Inhalation 100% oxygen.

Arm type	Experimental
Investigational medicinal product name	Oxygen, Conoxia
Investigational medicinal product code	V03A N01
Other name	
Pharmaceutical forms	Medicinal gas, compressed
Routes of administration	Inhalation use

Dosage and administration details:

Inhalation om mask with rebreather, 15 litres/minute.

Number of subjects in period 1	Medical air	Oxygen
Started	15	15
Completed	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	7	7	
Male	8	8	

End points

End points reporting groups

Reporting group title	Medical air
Reporting group description:	
Inhalation of medical air, 21% oxygen, 79% nitrogen.	
Reporting group title	Oxygen
Reporting group description:	
Inhalation 100% oxygen.	

Primary: Cardiac output

End point title	Cardiac output
End point description:	
Effect of treatment on cardiac output during lower body negative pressure.	
End point type	Primary
End point timeframe:	
During experimental intervention, approximately 30 min.	

End point values	Medical air	Oxygen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: litres/minute				
arithmetic mean (confidence interval 95%)	-0.22 (-0.26 to -0.19)	0.031 (-0.0152 to 0.077)		

Statistical analyses

Statistical analysis title	Oxygen vs. medical air.
Statistical analysis description:	
Effect of oxygen compared to medical air on change in cardiac output during lower body negative pressure.	
Comparison groups	Medical air v Oxygen
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.188 [1]
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0.031

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.015
upper limit	0.077

Notes:

[1] - There was no statistically significant effect of oxygen compared to air on the changes in cardiac output during LBNP (0.031 L/min/LBNP level, 95% CI: - 0.015 to 0.077, P = 0.188).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs and SAEs were collected from the start of intervention until end of the last visit at the time points specified in the Protocol/ SoA.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	5.0

Reporting groups

Reporting group title	Medical air

Reporting group description:

Inhalation of medical air, 21% oxygen, 79% nitrogen.

Reporting group title	Oxygen

Reporting group description:

Inhalation 100% oxygen.

Serious adverse events	Medical air	Oxygen	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (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 %

Non-serious adverse events	Medical air	Oxygen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 15 (20.00%)	0 / 15 (0.00%)	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
Pharyngitis	Additional description: "Sore throat". No treatment needed (common cold).		
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	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