



Clinical trial results:

Rapid infusion of Ringer's lactate solution at different temperatures and the effects on circulation and perfusion in healthy volunteers – a randomized crossover trial

Summary

EudraCT number	2022-002137-34
Trial protocol	DK
Global end of trial date	02 December 2022

Results information

Result version number	v1 (current)
This version publication date	17 October 2024
First version publication date	17 October 2024

Trial information

Trial identification

Sponsor protocol code	SVS.FAM.01
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05610254
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Emergency Department
Sponsor organisation address	Finsensgade 35, Esbjerg, Denmark, 6700
Public contact	Peter Biesenbach, Hospital of South West Jutland, peter.biesenbach@rsyd.dk
Scientific contact	Peter Biesenbach, Hospital of South West Jutland, +45 53861985, peter.biesenbach@rsyd.dk

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	01 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 December 2022
Global end of trial reached?	Yes
Global end of trial date	02 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This randomized controlled crossover study investigates the effect of Ringer's lactate solution at high and low temperatures on physiological response in healthy adults.

Protection of trial subjects:

During the active part of the trial, discomfort was measured every 5 minutes via a Numeric pain rating scale (NPRS) labelled from zero (no discomfort) to 10 (maximal discomfort imaginable)

Background therapy:

None

Evidence for comparator:

Not applicable

Actual start date of recruitment	05 September 2022
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	Denmark: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	18
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eighteen healthy volunteers were recruited among medical students from the local campus from September to December 2022.

Pre-assignment

Screening details:

The inclusion criteria were defined as adults aged 18 years or older. Exclusion criteria included pregnancy, body mass index >35 kg/m², pre-existing medical problems or regular use of any medication apart from allergy medication, contraceptives or non-steroidal anti-inflammatory drugs.

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?	No
Arm title	Intervention - COLD

Arm description:

Participants received 30 ml/kg of Ringer's lactate (Fresenius Kabi, Denmark). The fluid bolus was infused at cold (15°C, 59°F) temperature over a 30-minute period

Arm type	Active comparator
Investigational medicinal product name	Ringers' lactate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

A 18G peripheral venous catheter was inserted in a vein located in the antecubital fossa and used for the administration of fluids. Participants received 30 ml/kg of Ringer's lactate (Fresenius Kabi, Denmark). The fluid bolus was infused at cold (15°C, 59°F) over a 30-minute period as per the randomization. The infusion bags were insulated within a neoprene wine cooler, and pressure bags were used to ensure a continuous and timely infusion.

Arm title	Intervention - Warm
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Arm description:

Participants received 30 ml/kg of Ringer's lactate (Fresenius Kabi, Denmark). The fluid bolus was infused at body temperature (37°C, 98.6°F) over a 30-minute period.

Arm type	Active comparator
Investigational medicinal product name	Ringers' lactate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

A 18G peripheral venous catheter was inserted in a vein located in the antecubital fossa and used for the administration of fluids. Participants received 30 ml/kg of Ringer's lactate (Fresenius Kabi, Denmark). The fluid bolus was infused at body temperature (37°C, 98.6°F) over a 30-minute period as per the randomization. The infusion bags were insulated within a neoprene wine cooler, and pressure bags were used to ensure a continuous and timely infusion.

Number of subjects in period 1	Intervention - COLD	Intervention - Warm
Started	18	18
Completed	18	18

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
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Reporting group description:

The total number of participants is 18, which were analysed twice due to the cross-over design.

Reporting group values	Overall trial	Total	
Number of subjects	18	18	
Age categorical			
Healthy adult volunteers between 18 and 64.			
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)	18	18	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Three out of the 18 participants were male. All others were female.			
Units: Subjects			
Female	15	15	
Male	3	3	

End points

End points reporting groups

Reporting group title	Intervention - COLD
Reporting group description: Participants received 30 ml/kg of Ringer's lactate (Fresenius Kabi, Denmark). The fluid bolus was infused at cold (15°C, 59°F) temperature over a 30-minute period	
Reporting group title	Intervention - Warm
Reporting group description: Participants received 30 ml/kg of Ringer's lactate (Fresenius Kabi, Denmark). The fluid bolus was infused at body temperature (37°C, 98.6°F) over a 30-minute period.	

Primary: Change in mean arterial pressure after 45 minutes

End point title	Change in mean arterial pressure after 45 minutes
End point description: Blood pressure was measured via a bedside monitor (Intellivue, Phillips, Denmark).	
End point type	Primary
End point timeframe: Measured at 45 minutes after start of intravenous infusion.	

End point values	Intervention - COLD	Intervention - Warm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: mmHg				
number (confidence interval 95%)	6.5 (4.8 to 8.2)	0.6 (-1.6 to 2.8)		

Statistical analyses

Statistical analysis title	Primary outcome analysis
Comparison groups	Intervention - COLD v Intervention - Warm
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	t-test, 2-sided

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

September until December 2022.

Adverse event reporting additional description:

Adverse events were monitored and reported for the total observation period of 2 hours on the day of intervention.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	No dictionary
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Dictionary version	0
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Frequency threshold for reporting non-serious adverse events: 5 %

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: No adverse event of any type were reported. This is perhaps due to three reasons.

1. the short observation period of 2 hours during and after infusion.
2. intravenous isotonic fluids, such as Ringer´s lactate, are the most common type of medicine used globally and extremely safe.
3. the trial participants were all healthy young medical students with no past medical history.

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