



Clinical trial results: Hypertonic saline - the effect of repeating doses Summary

EudraCT number	2013-001733-41
Trial protocol	FI
Global end of trial date	06 June 2014

Results information

Result version number	v1 (current)
This version publication date	06 June 2024
First version publication date	06 June 2024

Trial information

Trial identification

Sponsor protocol code	004,1
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Helsinki University Central Hospital
Sponsor organisation address	Haartmaninkatu 4 C, Helsinki, Finland, 00290
Public contact	Department of ophthalmology, Helsinki University Central Hospital, +358 503804997, pia.inborr@outlook.com
Scientific contact	Department of ophthalmology, Helsinki University Central Hospital, +358 503804997, pia.inborr@outlook.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	23 September 2014
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	06 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Change in eyepressure after intravenous administration of 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland) in two different groups: in Group 1 total dose was 1 mmol/kg and in Group 2 two doses of 0.5 mmol/kg between 10 minutes. We measured before the intravenous hypertonic saline bolus (baseline), 10 and 20 minutes after the single or first bolus, and in Group 2 also 20 minutes after the second bolus.

Protection of trial subjects:

We excluded patients diagnosed with heart and kidney failure, dementia, or another condition that markedly decreased their physical performance; patients with a history of ocular surgery within six months, laser cyclophotocoagulation within one week or either goniotomy or Descemet's membrane or needling of a filtering bleb on the same day as IVHTS; and patients using oral acetazolamide. The study followed the tenets of the Declaration of Helsinki. We required written informed consent from all participants. The study was approved by the institutional review board of the Helsinki University Hospital.

Background therapy:

We cannulated an antecubital vein in either the right or left arm. We rinsed the cannula with 3 ml physiologic saline to confirm its intravenous position. The IVHTS dose corresponds to a 20 ml injection for an 80 kg patient. We infused the bolus at 1 ml/s, and then rinsed the cannula and vein with physiologic saline using 5 ml after the single bolus and 2.5 ml after both repeated boli.

Evidence for comparator: -

Actual start date of recruitment	09 September 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: 33
Worldwide total number of subjects	33
EEA total number of subjects	33

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)	11
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eligible to our study were patients with an IOP of 22–34 mmHg who were 25–80 years old. We required the patients to be fluent in Finnish or Swedish. We required written informed consent from all participants.

Pre-assignment

Screening details:

We measured the IOP with the Goldmann applanation tonometer, and blood pressure and heart rate. We asked the patients to grade the pain at the infusion site on a scale from 0 to 10; zero for no pain, and 10 for the most intense (intolerable) pain. Any other side effect was additionally recorded.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Group 1 received one bolus of 1 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland).

Arm type	Active comparator
Investigational medicinal product name	Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Group 1 received one bolus of 1 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland). We cannulated an antecubital vein in either the right or left arm. We rinsed the cannula with 3 ml physiologic saline to confirm its intravenous position. The IVTHS dose corresponds to a 20 ml injection for an 80 kg patient. We infused the bolus at 1 ml/s, and then rinsed the cannula and vein with physiologic saline using 5 ml after the single bolus and 2.5 ml after both repeated boli.

Arm title	Group 2
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Arm description:

Group 2 received two boli of 0.5 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland) with an interval of 10 minutes.

Arm type	Active comparator
Investigational medicinal product name	Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for suspension for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Group 2 received two boli of 0.5 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland) with an interval of 10 minutes. We cannulated an antecubital vein in either the right or left arm. We rinsed the cannula with 3 ml physiologic saline to confirm its intravenous position. The IVTHS dose corresponds to a 20 ml injection for an 80 kg patient. We infused the bolus at

1 ml/s, and then rinsed the cannula and vein with physiologic saline using 5 ml after the single bolus and 2.5 ml after both repeated boli.

Number of subjects in period 1	Group 1	Group 2
Started	20	13
Completed	20	13

Baseline characteristics

Reporting groups

Reporting group title	Group 1
Reporting group description: Group 1 received one bolus of 1 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland).	
Reporting group title	Group 2
Reporting group description: Group 2 received two boli of 0.5 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland) with an interval of 10 minutes.	

Reporting group values	Group 1	Group 2	Total
Number of subjects	20	13	33
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			
Eligible to our study were patients who were 25–80 years old.			
Units: years			
median	68.5	72	
standard deviation	± 14	± 10	-
Gender categorical			
Units: Subjects			
Female	14	8	22
Male	6	5	11

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: Group 1 received one bolus of 1 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland).	
Reporting group title	Group 2
Reporting group description: Group 2 received two boli of 0.5 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland) with an interval of 10 minutes.	

Primary: Group completion

End point title	Group completion
End point description: In our previous study using the 1.0 mmol/kg bolus, the maximum IOP reduction occurred 10 minutes after the bolus (Inborr et al. 2018). The primary outcome in the present study was the IOP reduction 10 minutes after IVTHS. We compared two different doses, and used a standard deviation (SD) of 2.9 mmHg for power calculation, based on the previous study (Inborr et al. 2018). To show a 3 mmHg difference in IOP reduction with 80% power and 5% significance required at least 12 patients in both groups. We set the group size to 13 patients. We enrolled participants from the Department of Ophthalmology, Helsinki University Hospital, Finland, and continued recruitment until both study groups had at least 13 patients.	
End point type	Primary
End point timeframe: First patient was enrolled to the study 2013-09-26 and last patient 2014-06-06.	

End point values	Group 1	Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	13		
Units: persons	20	13		

Attachments (see zip file)	Change in intraocular pressure (median)/Figure 1 acta.docx
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Statistical analyses

Statistical analysis title	Comparison
Statistical analysis description: The Shapiro-Wilk test was performed to test normal distribution. To compare IOP, BP, HR, and pain grade between the two groups we used the nonparametric Mann-Whitney U test. IOP before and after IVTHS was compared using the Wilcoxon signed-rank test.	
Comparison groups	Group 1 v Group 2

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	≤ 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During the study; 10 and 20 minutes after the single or first bolus, and in Group 2 also 20 minutes after the second bolus. Patients could contact us also after the study if any adverse events occurred later.

Adverse event reporting additional description:

We asked the patients to grade the pain at the infusion site on a scale from 0 to 10; zero for no pain, and 10 for the most intense (intolerable) pain. Any other side effect was additionally recorded.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	VAS
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Dictionary version	VAS
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Reporting groups

Reporting group title	Group 1
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Reporting group description:

Group 1 received one bolus of 1 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland).

Reporting group title	Group 2
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Reporting group description:

Group 2 received two boli of 0.5 mmol/kg 23.4% sodium chloride (Natriumklorid Braun 234 mg/ml, B. Braun Medical, Helsinki, Finland) with an interval of 10 minutes.

Serious adverse events	Group 1	Group 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 13 (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	Group 1	Group 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	12 / 13 (92.31%)	
Vascular disorders			
pain at the site of the infusion			
subjects affected / exposed	18 / 20 (90.00%)	12 / 13 (92.31%)	
occurrences (all)	18	12	
warm sensation in the head			
subjects affected / exposed	13 / 20 (65.00%)	2 / 13 (15.38%)	
occurrences (all)	13	2	

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/35349214>