Clinical trial results:
Reducing high intraocular pressure with hypertonic saline infusion before eyesurgery

Summary

EudraCT number	2012-005025-70
Trial protocol	FI
Global end of trial date	01 January 2021

Results information

Result version number	v1 (current)
This version publication date	24 January 2025
First version publication date	24 January 2025

Trial information

Trial identification

Sponsor protocol code	003,1

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, 00029
Public contact	Department of Ophthalmology, Helsinki University Central Hospital, +358 503804997, ext-pia.inborr@hus.fi
Scientific contact	Department of Ophthalmology, Helsinki University Central Hospital, +358 503804997, ext-pia.inborr@hus.fi

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	17 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 January 2021
Global end of trial reached?	Yes
Global end of trial date	01 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Change in ocular pressure

Protection of trial subjects:

We required the patients to be fluent in Finnish or Swedish. We excluded patients diagnosed with heart and kidney failure, dementia, or another condition that markedly decreased their physical performance. We measured blood pressure and heart rate automatically with an anaesthesia monitor. We took measurements before the bolus (baseline), 5, 10, 20 and 30 minutes after the bolus. 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.

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 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 bolus. The mannitol dose corresponds to a 210 for an 80 kg patient. We infused mannitol during 30 minutes time.

Evidence for comparator: -

Actual start date of recruitment	01 January 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: 11
Worldwide total number of subjects	11
EEA total number of subjects	11

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)	6
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were 25-80 years old. We required the patients to be fluent in Finnish or Swedish. Patients on oral acetazolamide or other medication that could lower blood natrium levels, patients with heart or kidney failure, dementia, any other condition that remarkably decreased the patients' physical performance were ineligible.

Pre-assignment

Screening details:

We recruited study patients among patients who come to HUCH eye hospital for eye surgery. Intra ocular pressure had to be 30 mmHg of more.

Period 1

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

Blinding implementation details:

We used Stata randomiser program to divide patients between two study groups.

Arms

Are arms mutually exclusive?	Yes
Arm title	NaCl group

Arm description:

Patients who received 23.4% NaCl infusion before eye surgery.

Arm type	Experimental
Investigational medicinal product name	Natriumklorid Braun 234 mg/ml
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

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 dosage of IVHTS was 1 mmol/kg sodium chloride in all patients. We infused the bolus at 1 ml/s, and then rinsed the cannula and vein with physiologic saline using 5 ml after the bolus.

Arm title	Mannitol group

Arm description:

Patients who received mannitol infusion before eye surgery.

Arm type	Active comparator
Investigational medicinal product name	Mannitol Braun 150 mg/ml infusion fluid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravascular use

Dosage and administration details:

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. We gave Mannitol Braun 150 mg/ml (15%) or 0,15 g/ml intravenously. Dosage was 0.4 g/kg. Maximum dosage was 270 ml. We gave mannitol infusion during 30 minutes time.

Number of subjects in period 1	NaCl group	Mannitol group
Started	3	8
Completed	3	8

Baseline characteristics

Reporting groups	
Reporting group title	NaCl group
Reporting group description:	
Patients who received 23.4% NaCl infusion before eye surgery.	
Reporting group title	Mannitol group
Reporting group description:	
Patients who received mannitol infusion before eye surgery.	

Reporting group values	NaCl group	Mannitol group	Total
Number of subjects	3	8	11
Age categorical			
Eligible to this study were patients who were 25-80 years old.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	5	6
From 65-84 years	2	3	5
85 years and over	0	0	0
Gender categorical			
Eligible to this study were women and men who were 25-80 years old.			
Units: Subjects			
Female	2	6	8
Male	1	2	3

End points

End points reporting groups

Reporting group title	NaCl group
Reporting group description:	
Patients who received 23.4% NaCl infusion before eye surgery.	
Reporting group title	Mannitol group
Reporting group description:	
Patients who received mannitol infusion before eye surgery.	

Primary: Chance in intra ocular pressure 30 minutes after injection/infusion

End point title	Chance in intra ocular pressure 30 minutes after injection/infusion[1]
End point description:	
We measured intra ocular pressure at baseline and 30 minutes after 23.4% natrium cloride injection or mannitol infusion with iCare gauge. We took three measurements and calculated average. Then we calculated the change in intraocular pressure.	
End point type	Primary
End point timeframe:	
Change in intra ocular pressure 30 minutes after 23.4% natrium cloride injection or mannitol infusion.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Early termination, no final results to be analysed.

End point values	NaCl group	Mannitol group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	8		
Units: mmHg				
number (not applicable)	8	8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

30 minutes after 23.4% natrium cloride injection or mannitol infusion.

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	Systematic

Dictionary used

Dictionary name	VAS
Dictionary version	1

Reporting groups

Reporting group title	NaCl group

Reporting group description:

Patients who received 23.4% NaCl bolus before eye surgery.

Reporting group title	Mannitol group

Reporting group description:

Patients who received mannitol infusion before eye surgery.

Serious adverse events	NaCl group	Mannitol group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (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	NaCl group	Mannitol group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	5 / 8 (62.50%)	
Cardiac disorders			
Ventricular arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Heating of the head			
subjects affected / exposed	3 / 3 (100.00%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
Dizziness			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	
Skin and subcutaneous tissue disorders Pain in the infusion arm subjects affected / exposed occurrences (all)	 3 / 3 (100.00%) 3	 0 / 8 (0.00%) 0	
Musculoskeletal and connective tissue disorders Cold in the infusion arm subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0	 2 / 8 (25.00%) 2	
Metabolism and nutrition disorders The need to pee subjects affected / exposed occurrences (all)	 0 / 3 (0.00%) 0	 4 / 8 (50.00%) 4	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

We planned to study minimum 23 patients per group to show that hypertonic NaCl in as effective as mannitol to reduce intra ocular pressure 30 minutes after injection. We had difficulties to find patients who meet the exclusion criteria.

Notes: