



Clinical trial results:

Ethanol submandibular duct ligation for drooling in children with neurodisabilities

Summary

EudraCT number	2021-004057-23
Trial protocol	NL
Global end of trial date	31 January 2025

Results information

Result version number	v1 (current)
This version publication date	14 May 2025
First version publication date	14 May 2025

Trial information

Trial identification

Sponsor protocol code	2021-12945
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid 10, Nijmegen, Netherlands, 6525 GA
Public contact	Department of Otorhinolaryngology, Radboudumc, 0031 617377830, stijn.bekkers@radboudumc.nl
Scientific contact	dr. Stijn Bekkers, Radboudumc, 0031 617377830, stijn.bekkers@radboudumc.nl

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	31 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2025
Global end of trial reached?	Yes
Global end of trial date	31 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the feasibility of submandibular duct ligation right after intraductal ethanol infusion into the submandibular salivary gland

Protection of trial subjects:

In accordance to section 10, subsection 4, of the WMO, the investigator will suspend the study if there is sufficient ground that continuation of the study will jeopardise subject health or safety. The investigator will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

All participants and/or their caregivers provided informed consent for participation in this study. Participants were able to step out of the study at any given moment.

An insurance for subjects participating in medical research in the Radboudumc, that falls within the scope of the WMO, is available in accordance with the legal requirements of article 7 of the WMO and Medical Research (Human Subjects) Compulsory Insurance Decree of 23 June 2003.

Background therapy:

The ethanol-SDL surgery was performed in a controlled setting under strict monitoring of the Medical Ethics Committee. All interventions were performed between 2021-2024 by the same surgeon, with 25 years of experience with submandibular gland surgery. A radiologist and pediatric surgeon with specific expertise in head and neck sclerotherapy were present during the whole procedure for potential consultation.

Surgery

The intervention was performed under general anesthesia. To prevent excessive post-operative swelling, patients received 1,5 mg / kilogram Di-Adreson-F aquosum per-operatively. Patients received 30mg / kilogram of cefazoline intravenously before the procedure. The floor of the mouth was infiltrated with 1% lidocaine with 1:100.000 epinephrine and incised parallel to the frenulum. The duct was identified, a suture was placed in the surrounding tissue to apply traction, and the duct was dissected for 1 cm to expose the ductal lumen. A 0.025-inch flexible cannula was placed inside the lumen and fixated with a suture. Dehydrated ethanol (EtOH) 96% was diluted with water-soluble contrast (Iomeron 300) in a ratio of 4:1, and 2-4ml of the solution (EtOH – Iomeron 300) was injected into each of the two submandibular ducts under digital subtraction sialography to assess the required injection volume and control for extravasation from the gland capsule. The duct was clipped with two vascular clips after retraction of the canula. A suction tube was present for retrograde leakage if necessary. The sublingual incision was closed with absorbable sutures. A schematic overview of the procedure was illustrated in figure 1.

Post-operative care

Patients were admitted for one-night post-operatively, and all patients received 500/125mg amoxicillin/clavulanic acid for 7 days and 1000mg paracetamol and 25mg diclofenac for 5 days post-operatively.

Evidence for comparator: -

Actual start date of recruitment	26 July 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	Netherlands: 5
Worldwide total number of subjects	5
EEA total number of subjects	5

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)	1
Adolescents (12-17 years)	3
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were selected from the intake consultation at the Saliva Control Clinic of the Radboud University Medical Center based on the in- and exclusion criteria, as stated in the manuscript. All participants and/or their caregivers provided written informed consent.

Pre-assignment

Screening details:

Inclusion criteria

- Moderate to severe drooling
- Aged ≥ 10 at time of surgery
- Contra-indication for SMDR/rejection towards SMDR

Exclusion criteria:

- Progressive neurological disease
- Medical history of salivary gland abnormalities
- prior submandibular gland surgery
- Contraindication for surgery or anesthesia
- Other current drool treatment

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N.A.

Arms

Arm title	Ethanol 2-duct ligation
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Arm description:

Participants received the ethanol 2-duct ligation surgery

Arm type	Experimental
Investigational medicinal product name	Ethanol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Oral use

Dosage and administration details:

Dehydrated ethanol (EtOH) 96% is diluted with water-soluble contrast (Iomeron 300) in ratio 4:1 and an estimated 2-3 mL of the solution (EtOH – Iomeron 300) is injected into the duct under digital subtraction sialography (DSS) in order to control for extravasation from the gland capsule. The maximum amount of Ethanol 96% is 4 mL per gland.

Number of subjects in period 1	Ethanol 2-duct ligation
Started	5
Completed	5

Period 2

Period 2 title	8 weeks post-surgery
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N.A.

Arms

Arm title	Surgery arm
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Arm description:

Ethanol 2-duct ligation

Arm type	Experimental
Investigational medicinal product name	Ethanol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Oral use

Dosage and administration details:

Dehydrated ethanol (EtOH) 96% is diluted with water-soluble contrast (Iomeron 300) in ratio 4:1 and an estimated 2-3 mL of the solution (EtOH – Iomeron 300) is injected into the duct under digital subtraction sialography (DSS) in order to control for extravasation from the gland capsule. The maximum amount of Ethanol 96% is 4 mL per gland.

Number of subjects in period 2	Surgery arm
Started	5
Completed	5

Period 3

Period 3 title	32 weeks post-surgery
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N.A.

Arms

Arm title	Surgery arm
Arm description:	
Ethanol 2-duct ligation	
Arm type	Experimental
Investigational medicinal product name	Ethanol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for solution for infusion
Routes of administration	Oral use

Dosage and administration details:

Dehydrated ethanol (EtOH) 96% is diluted with water-soluble contrast (Iomeron 300) in ratio 4:1 and an estimated 2-3 mL of the solution (EtOH – Iomeron 300) is injected into the duct under digital subtraction sialography (DSS) in order to control for extravasation from the gland capsule. The maximum amount of Ethanol 96% is 4 mL per gland.

Number of subjects in period 3	Surgery arm
Started	5
Completed	5

Baseline characteristics

Reporting groups

Reporting group title	Baseline
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Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	5	5	
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)	1	1	
Adolescents (12-17 years)	3	3	
Adults (18-64 years)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
median	14		
inter-quartile range (Q1-Q3)	11 to 18	-	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	3	3	

End points

End points reporting groups

Reporting group title	Ethanol 2-duct ligation
Reporting group description: Participants received the ethanol 2-duct ligation surgery	
Reporting group title	Surgery arm
Reporting group description: Ethanol 2-duct ligation	
Reporting group title	Surgery arm
Reporting group description: Ethanol 2-duct ligation	

Primary: Feasibility

End point title	Feasibility ^[1]
End point description:	
End point type	Primary
End point timeframe: 32 weeks post-surgery	

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: No statistical analyses were performed on the descriptive statistics, as it was only a registration of the number of completed surgeries, and this study only included 1 arm, with 5 participants.

End point values	Ethanol 2-duct ligation	Surgery arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	5		
Units: Surgery completion	5	5		

Statistical analyses

No statistical analyses for this end point

Primary: Safety

End point title	Safety ^[2]
End point description:	
End point type	Primary
End point timeframe: 32 weeks post-surgery	

Notes:

[2] - 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: No statistical analyses were performed on the descriptive statistics, as it was only a registration of the number of serious adverse events, and this study only included 1 arm, with 5 participants.

End point values	Ethanol 2-duct ligation	Surgery arm	Surgery arm	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	5	
Units: Adverse Events	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

32 weeks post-surgery

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28
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Reporting groups

Reporting group title	Ethanol 2-duct ligation
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Reporting group description:

Participants received the ethanol 2-duct ligation surgery

Serious adverse events	Ethanol 2-duct ligation		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Ethanol 2-duct ligation		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)		
Gastrointestinal disorders			
gastro-enteritis	Additional description: Hospital admission approximately 32-weeks post-surgery with 3 days of gastro-enteritis with fever.		
subjects affected / exposed ^[1]	1 / 1 (100.00%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Allergic skin reaction	Additional description: Mild allergic skin reaction to the antibiotic medication post-surgery		
subjects affected / exposed ^[2]	1 / 1 (100.00%)		
occurrences (all)	1		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The individual participant presented with a gastro-enteritis at 32-weeks post-surgery. This was not related to the exposure to the medical product. No other participants were exposed to gastro-

enteritis.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: This was the only participant who appeared to have an allergic response to the antibiotic treatment. This was not directly related to the exposure to the medical product. No other participants had a similar allergic response to antibiotics.

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