Clinical trial results:
The effect of intravesical Lidocaine solution versus placebo as anesthesia prior to intravesical injection of onabotulinum toxin A. A randomized, double-blind, placebo controlled cross-over study

Summary

EudraCT number	2021-000559-38
Trial protocol	DK
Global end of trial date	10 May 2024

Results information

Result version number	v1 (current)
This version publication date	13 May 2025
First version publication date	13 May 2025

Trial information

Trial identification

Sponsor protocol code	BTXA2021

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05415865
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Herlev and Gentofte Hospital
Sponsor organisation address	Borgmester Ib Juuls Vej 1, 16. etage, Herlev, Denmark, 2730
Public contact	Department of Obstetrics and Gynecology , Herlev and Gentofte University Hospital, Department of Obstetrics and Gynecology, +45 38681406, niels.klarskov@regionh.dk
Scientific contact	Department of Obstetrics and Gynecology , Herlev and Gentofte University Hospital, Department of Obstetrics and Gynecology, +45 38681406, niels.klarskov@regionh.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 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of intravesical alkalinised lidocaine as an anaesthetic treatment on procedural pain duringintradetrusor onabotulinumtoxinA injections for overactive bladder.

Protection of trial subjects:

A follow up call one week was conducted, where patients were asked about adverse effects and experience with the treatment.

Background therapy:

Intradetrusor onabotulinumtoxinA injections

Evidence for comparator:

Alkalinized lidocaine was not previously compared to placebo (saline).

Actual start date of recruitment	15 November 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: 50
Worldwide total number of subjects	50
EEA total number of subjects	50

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)	16
From 65 to 84 years	32
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Women aged ≥18 years referred for treatment with onabotulinumtoxinA injections due to complaints of OAB symptoms. Patients should accept to receive BTX-A injections in an outpatient clinic without the option of sedation.

Pre-assignment

Screening details:

60 women scheduled for BTX-A treatment between September 2022 and May 2023 were screened. Of these, 50 signed informed consent, met eligibility criteria and completed the first treatment period.

Period 1

Period 1 title	First onabotulinumtoxinA inj. in trial
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

All personnel involved in enrolment, randomisation, medication administration, and outcome assessment remained blinded until the outcomes were analysed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Alkalinized lidocaine

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.
In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

Arm type	Active comparator
Investigational medicinal product name	Lidokain SAD
Investigational medicinal product code	
Other name	LIDOCAINE HYDROCHLORIDE
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

Lidocaine hydrochloride20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmoL/mL,10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

Investigational medicinal product name	Natriumbikarbonat SAD
Investigational medicinal product code	
Other name	SODIUM HYDROGEN CARBONATE
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

Lidocaine hydrochloride20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmoL/mL,10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

Arm title	Placebo

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

less

Arm type	Placebo
Investigational medicinal product name	Sodium chloride, NaCl SAD 9 g/l
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

Sodium chloride 9 g/L, 20 mL; sodium chloride9 g/L, 10 mL; and sodium chloride 9 g/L, 10 mL instilled in the bladder with Luer Lock catheter

Number of subjects in period 1	Alkalinized lidocaine	Placebo
Started	25	25
Completed	25	25

Period 2

Period 2 title	Second onabotulinumtoxinA inj in trial
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

All personnel involved in enrolment, randomisation, medication administration, and outcome assessment remained blinded until the outcomes were analysed.

Arms

Are arms mutually exclusive?	Yes
Arm title	Alkalinized lidocaine

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.
In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

Arm type	Active comparator
Investigational medicinal product name	Lidokain SAD
Investigational medicinal product code	
Other name	LIDOCAINE HYDROCHLORIDE
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

Lidocaine hydrochloride20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmoL/mL,10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

Investigational medicinal product name	Natriumbikarbonat SAD
Investigational medicinal product code	
Other name	SODIUM HYDROGEN CARBONATE
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

Lidocaine hydrochloride20 mg/mL, 20 mL was mixed with sodium hydrogen carbonate 1 mmoL/mL,10 mL; and sodium chloride 9 g/L, 10 mL. The buffer was instilled in the bladder with a Luer lock catheter.

Arm title	Placebo

Arm description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period less

Arm type	Placebo
Investigational medicinal product name	Sodium chloride, NaCl SAD 9 g/l
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravesical use

Dosage and administration details:

Sodium chloride 9 g/L, 20 mL; sodium chloride9 g/L, 10 mL; and sodium chloride 9 g/L, 10 mL instilled in the bladder with Luer Lock catheter

Number of subjects in period 2	Alkalinized lidocaine	Placebo
Started	25	25
Completed	21	20
Not completed	4	5
Consent withdrawn by subject	-	1
Changed protocl	-	2
Received Myobloc	-	1
Changed protocol	2	-
Other healthcare issues	1	-
Lost to follow-up	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups

Reporting group title	First onabotulinumtoxinA inj. in trial

Reporting group description: -

Reporting group values	First onabotulinumtoxinA inj. in trial	Total	
Number of subjects	50	50	
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			
Units: years			
median	73		
inter-quartile range (Q1-Q3)	63 to 78	-	
Gender categorical			
Units: Subjects			
Female	50	50	
Male	0	0	

End points

End points reporting groups

Reporting group title	Alkalinized lidocaine

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.
In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

Reporting group title	Placebo

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period less

Reporting group title	Alkalinized lidocaine

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period.
In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period

Reporting group title	Placebo

Reporting group description:

Patients were randomly assigned (1:1) to receive either alkalinized lidocaine or placebo during the first treatment period. In the second treatment period, patients received the alternate treatment, with a maintained double-blind protocol and all procedures consistent with those in the first treatment period less

Primary: Visual analogue scale (VAS) score

End point title	Visual analogue scale (VAS) score

End point description:

End point type	Primary

End point timeframe:

Maximum pain score reported using the 100-mm visual analogue scale (VAS) score immediately after BTX-A injections

End point values	Alkalinized lidocaine	Placebo	Alkalinized lidocaine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	25	21	20
Units: millimetre(s)				
least squares mean (confidence interval 95%)	21.3 (14.7 to 27.8)	41.6 (35 to 48.1)	21.3 (14.7 to 27.8)	41.6 (35 to 48.1)

Statistical analyses

Statistical analysis title	ANCOVA

Statistical analysis description:

The difference in VAS pain scores between alkalinized lidocaine and placebo treatments was calculated using repeated measures analysis of covariance (ANCOVA)

Comparison groups	Alkalinized lidocaine v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Secondary: 5- point satisfaction score

End point title	5- point satisfaction score

End point description:

End point type	Secondary

End point timeframe:

One week after each BTX-A treatment, a follow-up call was scheduled asking the patients about their satisfaction with the BTX-A treatment using a 5-point Likert scale.

End point values	Alkalinized lidocaine	Placebo	Alkalinized lidocaine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	25	21	20
Units: Ordinal				
median (full range (min-max))				
5- point satisfaction scale score	5 (3 to 5)	5 (2 to 5)	5 (3 to 5)	5 (2 to 5)

Statistical analyses

Statistical analysis title	Wilcoxon signed-rank test
Statistical analysis description: Wilcoxon signed-rank test was used to compare 5-point satisfaction score.	
Comparison groups	Alkalinized lidocaine v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Urinary tract infection

End point title	Urinary tract infection
End point description:	
End point type	Secondary
End point timeframe: Urinary tract infection (UTI) one week after each BTX-A treatment	

End point values	Alkalinized lidocaine	Placebo	Alkalinized lidocaine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	25	21	20
Units: Number	5	2	5	2

Statistical analyses

Statistical analysis title	McNemars test
Statistical analysis description: McNemars test was used to compare the UTI rate in intervention and placebo group.	
Comparison groups	Alkalinized lidocaine v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mcnemar
Parameter estimate	Odds ratio (OR)

Confidence interval	
level	95 %
sides	2-sided

Secondary: Hematuria

End point title	Hematuria

End point description:

End point type	Secondary

End point timeframe:

Hematuria during or within one week after each BTX-A treatment

End point values	Alkalinized lidocaine	Placebo	Alkalinized lidocaine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	25	21	20
Units: Frequency	4	2	4	2

Statistical analyses

Statistical analysis title	McNemars test

Statistical analysis description:

McNemars test was used to compare hematuria in the intervention and placebo group.

Comparison groups	Alkalinized lidocaine v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mcnemar
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	95 %
Variability estimate	Standard deviation

Secondary: Clean intermittent catherization (CIC)

End point title	Clean intermittent catherization (CIC)

End point description:

End point type	Secondary

End point timeframe:

Post-void residuals requiring clean intermittent catherization (CIC) within one week after BTX-A treatment

End point values	Alkalinized lidocaine	Placebo	Alkalinized lidocaine	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	25	21	20
Units: Frequency	1	0	0	0

Statistical analyses

Statistical analysis title	McNemars test
Statistical analysis description: McNemars test was used to compare CIC risk in intervention and placebo group.	
Comparison groups	Alkalinized lidocaine v Placebo
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Mcnemar
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were registered on-site during BTX-A treatments or during follow-up calls one week after each BTX-A treatment. Patients were asked about specific adverse events (urinary retention, UTI, hematuria).

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	0

Reporting groups

Reporting group title	Alkalinized lidocaine

Reporting group description:

Intervention

Reporting group title	Placebo

Reporting group description:

Adverse events were registered on-site during BTX-A treatments or during follow-up calls one week after each BTX-A treatment. Patients were asked about specific adverse events (urinary retention, UTI, hematuria).

Serious adverse events	Alkalinized lidocaine	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	0 / 45 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Alkalinized lidocaine	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 48 (45.83%)	23 / 45 (51.11%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 48 (2.08%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	0 / 48 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			

Vaginal bleeding			
subjects affected / exposed	0 / 48 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	7 / 48 (14.58%)	7 / 45 (15.56%)	
occurrences (all)	7	7	
Bladder pain			
subjects affected / exposed	1 / 48 (2.08%)	1 / 45 (2.22%)	
occurrences (all)	1	1	
Pelvic pain			
subjects affected / exposed	1 / 48 (2.08%)	3 / 45 (6.67%)	
occurrences (all)	1	3	
Pollakiuria			
subjects affected / exposed	0 / 48 (0.00%)	2 / 45 (4.44%)	
occurrences (all)	0	2	
Asymptomatic urinary tract infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
Urgency urinary incontinence			
subjects affected / exposed	1 / 48 (2.08%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
Urethral bleeding			
subjects affected / exposed	0 / 48 (0.00%)	1 / 45 (2.22%)	
occurrences (all)	0	1	
hematuria			
subjects affected / exposed	5 / 48 (10.42%)	2 / 45 (4.44%)	
occurrences (all)	5	2	
Urinary retention			
subjects affected / exposed	1 / 48 (2.08%)	0 / 45 (0.00%)	
occurrences (all)	1	0	
UTI			
subjects affected / exposed	5 / 48 (10.42%)	2 / 45 (4.44%)	
occurrences (all)	5	2	
Infections and infestations			

Fever subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 45 (2.22%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 January 2023	We requested a protocol amendment after enrolling the firstthree patients in the trial because the treating nurse observed a milky white appearance in the trial medication after mixing. Our initial protocol followed the same solution administered in a previous RCT by, which comprised 20 mL of 2% lidocaine hydrochloride with 10 mL of 8.4% sodium bicarbonate. As a result, the trial was halted due to the compromised double-blind conditions. We consulted the Capital Region of Denmark's unit for pharmaceutical advice. The unit stated that the mixture of lidocaine hydrochloride 20 mg/mL and sodium hydrogen carbonate 1 mmol/mL was unstable and could precipitate. This could lead to reduced anesthetic effect compared to anticipated results. Additionally, the solution could potentially irritate the bladder mucosa. The hospital pharmacy conducted new analyses and recommended dissolving the mixture in 10 mL of sodium chloride (9 g/L). This prevented the milky white appearance or precipitation of the trial medication. Amendment approval for 10 mL sodium chloride was obtained from the Danish Research Ethics Committees and the Danish Medicines Agency. The trial was resumed in January 2023

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported