Clinical trial results:
ACUTE AND LONG-TERM EFFECTS OF INTRANASAL OXYTOCIN IN ALCOHOL WITHDRAWAL AND DEPENDENCE: A PROSPECTIVE RANDOMIZED PARALLEL GROUP PLACEBO-CONTROLLED TRIAL

Summary

EudraCT number	2015-004463-37
Trial protocol	NO
Global end of trial date	30 November 2017

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	140682

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02903251
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	St. Olavs University Hospital
Sponsor organisation address	St. Olavs hospital HF, Postboks 3250 Torgarden, Trondheim, Norway, 7006
Public contact	PI's representative(Katrine Melby), Lade Behandlingssenter, +47 92886639, katrine.melby@stolav.no
Scientific contact	PI's representative(Katrine Melby), Lade Behandlingssenter, 92886639 92886639, katrine.melby@stolav.no
Sponsor organisation name	St. Olavs University Hospital
Sponsor organisation address	Postboks 3250 Torgarden, Trondheim, Norway, 7006
Public contact	katrine.melby@stolav.no, Department of Clinical Pharmacology, St. Olavs Universtiy Hospital, +47 92886639, katrine.melby@stolav.no
Scientific contact	katrine.melby@stolav.no, Department of Clinical Pharmacology, St. Olavs Universtiy Hospital, +47 92886639, katrine.melby@stolav.no

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric	No

investigation plan (PIP)	
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	30 October 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 November 2017
Global end of trial reached?	Yes
Global end of trial date	30 November 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary aim of the study is to test whether daily intranasal administration of oxytocin is more effective than placebo in decreasing the oxazepam dosages required to control withdrawal symptoms during a 3-day inpatient program of medical detoxification.

Protection of trial subjects:

Treatment as usual, following the procedures for withdrawal symptoms of alcohol detoxification.
Reporting of adverse effects.
Clinical monitor.
Limiting number and duration of clinical tests in the detoxification period.

Background therapy:

Benzodiazepin-treatment as usual, following the CIWA-Ar protocol at the detoxification ward.

Evidence for comparator:

Oxytocin nasal spray alliviated alcohol withdrawal symptoms in a pilot trial.
The main purpose of this study was to try to replicate the study and findings.

Actual start date of recruitment	01 October 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	39
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 40 patients admitted for alcohol detoxification and withdrawal treatment at the Blue Cross Lade Addiction TreatmentCenter (LBS) in Trondheim, Norway.
Eligible subjects were 18–65 years of age and lived in the county of Trøndelag, Norway.
The inclusion period lasted from October 2016 to November 2017.

Pre-assignment

Screening details:

Assessed for eligibility n = 138.
Did not meet inclusion criteria (n = 96)
Daily treatment with benzodiazepines or benzodiazepine-like hypnotics (n = 33)
Negative alcohol breath test and > 15 h since last intake (n = 28)
All other criteria (n= 55)
Invited to participate (n = 42). Declined to participate (n = 2)

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Oxytocin

Arm description:

Subjects were given six insufflations of the nasal spray (containing a total dose of 24 IU oxytocin or placebo) in interchanging nostrils with 15s in between insufflations, twice daily for 3 days.

Arm type	Experimental
Investigational medicinal product name	Syntocinon
Investigational medicinal product code	
Other name	Oxytocin
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

Subjects were given six insufflations of the nasal spray (containing a total dose of 24 IU oxytocin or placebo) in interchanging nostrils with 15s in between insufflations. x 2 daily for 3 days.

Arm title	Placebo

Arm description:

subjects were given six insufflations of the placebo nasal spray (containing placebo) in interchanging nostrils with 15s in between insufflations twice daily for 3 days.

Arm type	Placebo
Investigational medicinal product name	Placebo spray containing the same constituents as Syntocinon, except oxytocin.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Intranasal use

Dosage and administration details:

subjects were given six insufflations of the placebo nasal spray (containing placebo) in interchanging nostrils with 15s in between insufflations twice daily for 3 days.

Number of subjects in period 1	Oxytocin	Placebo
Started	20	20
Completed	20	20

Baseline characteristics

Reporting groups	
Reporting group title	Oxytocin
Reporting group description:	
Subjects were given six insufflations of the nasal spray (containing a total dose of 24 IU oxytocin or placebo) in interchanging nostrils with 15s in between insufflations, twice daily for 3 days.	
Reporting group title	Placebo
Reporting group description:	
subjects were given six insufflations of the placebo nasal spray (containing placebo) in interchanging nostrils with 15s in between insufflations twice daily for 3 days.	

Reporting group values	Oxytocin	Placebo	Total
Number of subjects	20	20	40
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			
arithmetic mean	48.9	46.6	
standard deviation	± 11.3	± 9.7	-
Gender categorical			
Units: Subjects			
Female	7	4	11
Male	13	16	29
Marital status			
Marital status: Single/Cohabiting			
Units: Subjects			
Single	14	14	28
Cohabiting	6	6	12
Employment			
Employment: Yes/No			
Units: Subjects			
Yes	5	4	9
No	15	16	31
Sel-reported daily alcohol intake during the last 14 days			
Units: standard alcohol units			
arithmetic mean	17.0	15.0	
standard deviation	± 8.0	± 6.4	-

Phosphatidylethanol blood concentration at inclusion			
Units: µmol/L			
arithmetic mean	2.26	2.20	
standard deviation	± 1.12	± 1.22	-
Total number of hours in the study			
Units: Hours			
arithmetic mean	53.4	52.4	
standard deviation	± 5.5	± 9.2	-
Total number of nasal spray administration			
Units: Number of nasal sprays			
arithmetic mean	5.80	5.90	
standard deviation	± 0.41	± 0.31	-

End points

End points reporting groups	
Reporting group title	Oxytocin
Reporting group description:	
Subjects were given six insufflations of the nasal spray (containing a total dose of 24 IU oxytocin or placebo) in interchanging nostrils with 15s in between insufflations, twice daily for 3 days.	
Reporting group title	Placebo
Reporting group description:	
subjects were given six insufflations of the placebo nasal spray (containing placebo) in interchanging nostrils with 15s in between insufflations twice daily for 3 days.	

Primary: Total oxazepam dosage in milligrams	
End point title	Total oxazepam dosage in milligrams
End point description:	
End point type	Primary
End point timeframe:	
3 days of detoxification.	

End point values	Oxytocin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Mg				
arithmetic mean (standard deviation)	56.8 (± 72.8)	79.0 (± 122.9)		

Statistical analyses

Statistical analysis title	Total oxazepam dose
Comparison groups	Placebo v Oxytocin
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.49
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-22.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-86.9
upper limit	42.4

Secondary: CIWA-ar

End point title	CIWA-ar

End point description:

End point type	Secondary

End point timeframe:

3 days

End point values	Oxytocin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Score, number				
arithmetic mean (standard deviation)	5.94 (± 3.86)	6.48 (± 3.92)		

Statistical analyses

Statistical analysis title	CIWA-Ar score
Comparison groups	Oxytocin v Placebo
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.665
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.03
upper limit	1.95
Variability estimate	Standard deviation

Secondary: HSCL-10

End point title	HSCL-10

End point description:

End point type	Secondary

End point timeframe:

3 days

End point values	Oxytocin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: HSCL-score				
arithmetic mean (standard deviation)	25.1 (± 5.6)	25.3 (± 7.3)		

Statistical analyses

Statistical analysis title	HSCL-10
Comparison groups	Placebo v Oxytocin
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.945
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.38
upper limit	4.09
Variability estimate	Standard deviation

Secondary: Self-reported sleep

End point title	Self-reported sleep
End point description:	

End point type	Secondary
End point timeframe:	
3 days	

End point values	Oxytocin	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: hours				
arithmetic mean (standard deviation)	5.28 (± 2.95)	5.92 (± 3.17)		

Statistical analyses

Statistical analysis title	Self-reported sleep
Comparison groups	Oxytocin v Placebo
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.535
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.72
upper limit	1.44
Variability estimate	Standard deviation

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
3 days	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.0
Reporting groups	
Reporting group title	Oxytocin
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Oxytocin	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (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: 1 %

Non-serious adverse events	Oxytocin	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
General disorders and administration site conditions			
Discomfort nose	Additional description: Due to amount of nasal spray.		
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	0	0	

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.

Large variability in mg oxazepam.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30784955

http://www.ncbi.nlm.nih.gov/pubmed/32053696

http://www.ncbi.nlm.nih.gov/pubmed/33352584