Clinical trial results:
Efficacy of oral nifedipine, naproxen, or placebo for pain relief during diagnostic hysteroscopy in an office setting: a randomized pilot study

Summary

EudraCT number	2018-001020-19
Trial protocol	BE
Global end of trial date	01 December 2022

Results information

Result version number	v1 (current)
This version publication date	07 June 2024
First version publication date	07 June 2024
Summary attachment (see zip file)	Protocol (2018-001020-19-Protocol.docx) Published Article (van Wessel_Efficacy of oral nifedipine naproxen or placebo for pain relief during diagnostic hysteroscopy in an office setting a randomized co.pdf)

Trial information

Trial identification

Sponsor protocol code	NL65360.18

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Dutch Clinical Trial Registry : NL7750

Notes:

Sponsors

Sponsor organisation name	UZ Ghent
Sponsor organisation address	C. Heymanslaan 10, Gent, Belgium, 9000
Public contact	HIRUZ, Ghent University Hospital, +32 93320500, hiruz.ctu@uzgent.be
Scientific contact	HIRUZ, Ghent University Hospital, 093320000 93320500, hiruz.ctu@uzgent.be

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	29 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2022
Global end of trial reached?	Yes
Global end of trial date	01 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the study is to compare the pain intensity during hysteroscopy after using nifedipine as pain medication versus using naproxen or placebo.

Protection of trial subjects:

- Blood pressure registration before and after treatment allocation
- Medication related side-effects were administered until the day after treatment allocation

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2019
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	Belgium: 59
Country: Number of subjects enrolled	Netherlands: 1
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	60
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This research will examine healthy women scheduled for a hysteroscopy.

Pre-assignment

Screening details:

In order to be eligible to participate in this study, a subject must meet all of the following criteria: at least 18 years of age, no medical history of cardiovascular disease, no hypotension; baseline blood pressure greater than or equal to 120/60 mmHg, otherwise healthy women with an average BMI (BMI<30), scheduled for a diagnostic hysteroscopy i

Period 1

Period 1 title	Period (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Frist group

Arm description:

A multicentre single-blinded pilot study with a naproxen and placebo controlled, randomized study design. We will include 60 women at each side, scheduled for a hysteroscopy. One group will receive two 10 mg capsules short-acting Nifedipine® 60-30 minutes before the hysteroscopy will start. The second group will receive two 250 mg tablets Naproxen® 60-30 minutes before the hysteroscopy will start. The third group will receive two 500 mg placebo tablets 60-30 minutes before the hysteroscopy. Primary outcome is pain intensity, measured with a VAS at the insertion of the instrument, during hysteroscopy, at the end and 30 minutes after the procedure. Secondary outcomes are adverse effects and complications during the hysteroscopy, monitored until 30 minutes after the hysteroscopy and evaluated by phone the following day.

Arm type	Experimental
Investigational medicinal product name	Nifedipine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Other use

Dosage and administration details:

The investigational product is nifedipine, this is a calcium re-entry blocker, which is widely used in cardiovascular treatment. Nifedipine is a dihydropyridine and inhibits the calcium-influx. Nifedipine capsules are short-acting and are used when a rapid effect is needed.8 For the study, Nifedipine® capsules of 10 mg will be used.

Arm title	Second

Arm description:

A multicentre single-blinded pilot study with a naproxen and placebo controlled, randomized study design. We will include 60 women at each side, scheduled for a hysteroscopy. One group will receive two 10 mg capsules short-acting Nifedipine® 60-30 minutes before the hysteroscopy will start. The second group will receive two 250 mg tablets Naproxen® 60-30 minutes before the hysteroscopy will start. The third group will receive two 500 mg placebo tablets 60-30 minutes before the hysteroscopy. Primary outcome is pain intensity, measured with a VAS at the insertion of the instrument, during hysteroscopy, at the end and 30 minutes after the procedure. Secondary outcomes are adverse effects and complications during the hysteroscopy, monitored until 30 minutes after the hysteroscopy and evaluated by phone the following day.

Arm type	Active comparator

Investigational medicinal product name	Naproxen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Other use

Dosage and administration details:

Naproxen is used as a comparator, naproxen is a nonsteroidal anti-inflammatory agent, which is used as pain medication. It is common use in the Netherlands to advice patients to take naproxen before a hysteroscopy. For the study, Naproxen® tablets of 250 mg will be used.

Arm title	Third

Arm description:

A multicentre single-blinded pilot study with a naproxen and placebo controlled, randomized study design. We will include 60 women at each side, scheduled for a hysteroscopy. One group will receive two 10 mg capsules short-acting Nifedipine® 60-30 minutes before the hysteroscopy will start. The second group will receive two 250 mg tablets Naproxen® 60-30 minutes before the hysteroscopy will start. The third group will receive two 500 mg placebo tablets 60-30 minutes before the hysteroscopy. Primary outcome is pain intensity, measured with a VAS at the insertion of the instrument, during hysteroscopy, at the end and 30 minutes after the procedure. Secondary outcomes are adverse effects and complications during the hysteroscopy, monitored until 30 minutes after the hysteroscopy and evaluated by phone the following day.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Other use

Dosage and administration details:

The placebos will contain 500 mg lactose each

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: See attachments

Number of subjects in period 1	Frist group	Second	Third
Started	21	19	20
Completed	21	19	20

Baseline characteristics

Reporting groups

Reporting group title	Period

Reporting group description: -

Reporting group values	Period	Total	
Number of subjects	60	60	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	60	60	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	60	60	
Male	0	0	

End points

End points reporting groups

Reporting group title	Frist group

Reporting group description:

A multicentre single-blinded pilot study with a naproxen and placebo controlled, randomized study design. We will include 60 women at each side, scheduled for a hysteroscopy. One group will receive two 10 mg capsules short-acting Nifedipine® 60-30 minutes before the hysteroscopy will start. The second group will receive two 250 mg tablets Naproxen® 60-30 minutes before the hysteroscopy will start. The third group will receive two 500 mg placebo tablets 60-30 minutes before the hysteroscopy. Primary outcome is pain intensity, measured with a VAS at the insertion of the instrument, during hysteroscopy, at the end and 30 minutes after the procedure. Secondary outcomes are adverse effects and complications during the hysteroscopy, monitored until 30 minutes after the hysteroscopy and evaluated by phone the following day.

Reporting group title	Second

Reporting group description:

A multicentre single-blinded pilot study with a naproxen and placebo controlled, randomized study design. We will include 60 women at each side, scheduled for a hysteroscopy. One group will receive two 10 mg capsules short-acting Nifedipine® 60-30 minutes before the hysteroscopy will start. The second group will receive two 250 mg tablets Naproxen® 60-30 minutes before the hysteroscopy will start. The third group will receive two 500 mg placebo tablets 60-30 minutes before the hysteroscopy. Primary outcome is pain intensity, measured with a VAS at the insertion of the instrument, during hysteroscopy, at the end and 30 minutes after the procedure. Secondary outcomes are adverse effects and complications during the hysteroscopy, monitored until 30 minutes after the hysteroscopy and evaluated by phone the following day.

Reporting group title	Third

Reporting group description:

A multicentre single-blinded pilot study with a naproxen and placebo controlled, randomized study design. We will include 60 women at each side, scheduled for a hysteroscopy. One group will receive two 10 mg capsules short-acting Nifedipine® 60-30 minutes before the hysteroscopy will start. The second group will receive two 250 mg tablets Naproxen® 60-30 minutes before the hysteroscopy will start. The third group will receive two 500 mg placebo tablets 60-30 minutes before the hysteroscopy. Primary outcome is pain intensity, measured with a VAS at the insertion of the instrument, during hysteroscopy, at the end and 30 minutes after the procedure. Secondary outcomes are adverse effects and complications during the hysteroscopy, monitored until 30 minutes after the hysteroscopy and evaluated by phone the following day.

Primary: Main

End point title	Main[1]

End point description:

The main study parameter will be the intensity of pain. This pain will be measured using a VAS.

End point type	Primary

End point timeframe:

During the study

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: See attachments

End point values	Frist group	Second	Third	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	19	20	
Units: VAS				
number (not applicable)	21	19	20	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
During the study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	0

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: See attachments

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 July 2019	Inclusion criteria - blood pressure 110/60 mmHg
28 November 2019	Inclusion criteria - BMI 35
01 November 2022	We never started to include in the Netherlands because of logistical and administrative reasons. Therefore, this was a moncentric pilot study, including 60 women (in stead of a multicentric study including 120 patients). This could only be registered through entering 59 inclusion in Belgium and 1 inclusion in the Netherlands. The actual inclusion rate was 60 in Belgium and none in the Netherlands.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported