Clinical trial results:
Double-blind randomized clinical trial to compare presurgery anxiolysis in children treated with hydroxyzine versus non-pharmacological intervention (distractoria technique clown).

Summary

EudraCT number	2016-002890-37
Trial protocol	ES
Global end of trial date	21 February 2021

Results information

Result version number	v1 (current)
This version publication date	25 May 2022
First version publication date	25 May 2022

Trial information

Trial identification

Sponsor protocol code	1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03324828
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Esther Aleo Lujan
Sponsor organisation address	profesor martin lagos s/n, Madrid, Spain, 28040
Public contact	Servicio de Pediatría Hospital Clinico San Carlos, Esther Aleo Lujan, +34 913303000, fibucicec.hcsc@salud.madrid.org
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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 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 February 2021
Global end of trial reached?	Yes
Global end of trial date	21 February 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether the association of pharmacological measures (hydroxyzine) and not pharmacological (distraction by clowns) decreases preoperative anxiety (POA) for children who will be undergoing outpatient surgery.

Protection of trial subjects:

The study was approved by the Clinical Research Ethics Committee of the hospital. The confidentiality of subject data was always maintained in
accordance with current legislation. Written informed consent was obtained before any intervention from all subjects, legal surrogates, parents, or legal guardians for minor subjects.
This study was carried out following international ethical recommendations for conducting human research and clinical trials contained in the latest revision of the Declaration of Helsinki as well as those established in the Good Clinical Practice Guidelines and current legislation. All subjects were supervised by qualified medical personnel during their participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 October 2018
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	Spain: 165
Worldwide total number of subjects	165
EEA total number of subjects	165

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)	128
Adolescents (12-17 years)	37

Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

We studied 165 patients with ages between 2 and 16 years (mean 7.4, SD 4.2). 127 were boys, and 41 were girls. The declaration of the COVID-19 global pandemic forced the premature ending of the study, and thus, the objective sample size was only reached in groups 1 (hydroxyzine) and 2 (placebo).

Period 1

Period 1 title	Time-Point 0 (M0) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Pharmacological intervention (oral hydroxyzine 2 mg/kg masked with 5 ml of juice, administered at least 30 min prior to surgery) plus standard management consisting of parental accompaniment during the preoperative period, postanesthesia recovery area, and up to hospital discharge

Arm type	Active comparator
Investigational medicinal product name	Hidroxicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

mg/kg masked with 5 ml of juice, administered at least 30 min prior to surgery

Arm title	Group 2

Arm description:

Standard management

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 3

Arm description:

Standard management + Dr. Sonrisas + oral hydroxyzine

Arm type	Experimental
Investigational medicinal product name	Hidroxicine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

2 mg/kg masked with 5 ml of juice, administered at least 30 min prior to surgery

Arm title	Group 4

Arm description:

Standard management + Dr. Sonrisas

Arm type	Placebo
Investigational medicinal product name	Placevo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

5 ml of juice, administered at least 30 min prior to surgery

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	59	52	25
Completed	53	48	24
Not completed	6	4	1
Screening failure	3	3	-
Consent withdrawn by subject	1	-	-
Lost to follow-up	1	1	-
discontinuation	1	-	1

Number of subjects in period 1	Group 4
Started	29
Completed	27
Not completed	2
Screening failure	2
Consent withdrawn by subject	-
Lost to follow-up	-
discontinuation	-

Baseline characteristics

Reporting groups	
Reporting group title	Group 1
Reporting group description:	
Pharmacological intervention (oral hydroxyzine 2 mg/kg masked with 5 ml of juice, administered at least 30 min prior to surgery) plus standard management consisting of parental accompaniment during the preoperative period, postanesthesia recovery area, and up to hospital discharge	
Reporting group title	Group 2
Reporting group description:	
Standard management	
Reporting group title	Group 3
Reporting group description:	
Standard management + Dr. Sonrisas + oral hydroxyzine	
Reporting group title	Group 4
Reporting group description:	
Standard management + Dr. Sonrisas	

Reporting group values	Group 1	Group 2	Group 3
Number of subjects	59	52	25
Age categorical			
Age (years) Mean ± SD			
Units: Subjects			
Children (2-11 years)	46	41	19
Adolescents (12-17 years)	13	11	6
Age continuous			
Age (years) Mean ± SD			
Units: years			
arithmetic mean	7.7	8.0	7.7
standard deviation	± 4.1	± 4.3	± 4.1
Gender categorical			
Units: Subjects			
Female	53	40	19
Male	6	12	6

Reporting group values	Group 4	Total	
Number of subjects	29	165	
Age categorical			
Age (years) Mean ± SD			
Units: Subjects			
Children (2-11 years)	22	128	
Adolescents (12-17 years)	7	37	
Age continuous			
Age (years) Mean ± SD			
Units: years			
arithmetic mean	6.4		
standard deviation	± 3.3	-	

Gender categorical Units: Subjects			
Female	21	133	
Male	8	32	

End points

End points reporting groups	
Reporting group title	Group 1
Reporting group description:	
Pharmacological intervention (oral hydroxyzine 2 mg/kg masked with 5 ml of juice, administered at least 30 min prior to surgery) plus standard management consisting of parental accompaniment during the preoperative period, postanesthesia recovery area, and up to hospital discharge	
Reporting group title	Group 2
Reporting group description:	
Standard management	
Reporting group title	Group 3
Reporting group description:	
Standard management + Dr. Sonrisas + oral hydroxyzine	
Reporting group title	Group 4
Reporting group description:	
Standard management + Dr. Sonrisas	

Primary: m-YPAS at the time of anaesthetic induction	
End point title	m-YPAS at the time of anaesthetic induction
End point description:	
End point type	Primary
End point timeframe:	
M3: at the time of anaesthetic induction	

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	48	24	27
Units: m-YPAS scale				
geometric mean (standard deviation)	39.2 (± 27.9)	37 (± 26.1)	34.7 (± 25.5)	32.4 (± 20.5)

Statistical analyses

Statistical analysis title	ANOVA
Comparison groups	Group 1 v Group 2 v Group 3 v Group 4
Number of subjects included in analysis	152
Analysis specification	Post-hoc
Analysis type	equivalence
P-value	≤ 0.05
Method	ANOVA

Secondary: ICC values

End point title	ICC values

End point description:

End point type	Secondary

End point timeframe:

M3: at the time of anaesthetic induction

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	48	24	27
Units: ICC values				
geometric mean (standard deviation)	1.8 (± 3.4)	1.5 (± 3)	1.2 (± 2.4)	1.5 (± 3.0)

Statistical analyses

No statistical analyses for this end point

Adverse events

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

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: There are no non-serious adverse events recorded for these results.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 August 2017	Elimination STAI/SCAP anxiety scale. Exclusion criteria actualization.
01 November 2017	Selection Criteria actualization.
12 December 2017	Criteria selection actualization
10 August 2018	Data proteccion actualization
10 April 2019	Inclusion an analysis of ACTH and cortisol level

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported