Clinical trial results:
A comparison of analgesic and respiratory effects from tapentadol versus oxycodone after laparoscopic hysterectomy.

Summary

EudraCT number	2017-001285-23
Trial protocol	NO
Global end of trial date	28 February 2019

Results information

Result version number	v1 (current)
This version publication date	16 October 2021
First version publication date	16 October 2021
Summary attachment (see zip file)	Tapentadol versus oxycodone analgesia and side effects. Comelon. EJA 2021 (Tapentadol_versus_oxycodone_analgesia_and_side. Comelon. EJA 2021.pdf)

Trial information

Trial identification

Sponsor protocol code	170317-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03314792
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Oslo University Hospital
Sponsor organisation address	Kirkeveien 166, Oslo, Norway, 0424
Public contact	Dept. of Anesthesiology, Ullevaal, Oslo University Hospital, 0047 2219690, marlin.comelon@ous-hf.no
Scientific contact	Dept. of Anesthesiology, Ullevaal, Oslo University Hospital, 0047 2219690, marlin.comelon@ous-hf.no

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 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2019
Global end of trial reached?	Yes
Global end of trial date	28 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary goal of our study is to examine the analgesic effects in patients receiving either tapentadol or oxycodone during the first postoperative day after hysterectomy.

Protection of trial subjects:

All patients recived standard peri- and postoperative pain treatment according to hospital protocol in addition to the study medicine they were allocated to. All patients also recived information and thorough follow-up on what to expect and how to handle postoperative pain.

Background therapy:

Perioperatively: paracetamol iv, etoricoxib (NSAID) po, dexamethasone iv, bupivacaine infiltration. Postoperativt pro re nata Fentanyl iv.

Evidence for comparator:

Tapentadol is a new mixed ligand opioid which acts as a μ-opioid receptor (MOR) agonist and also inhibits noradrenaline reuptake in the central nervous system. This dual mechanism of action is believed to result in synergistic analgesic effects. Since opioid side effects are strongly related to MOR stimulation, tapentadol is expected to have less side effects than the pure opioid agonists.
Tapentadol has been shown effective for acute and chronic nociceptive, neuropathic or cancer related pain, but there is lack of broad-based evidence for tapentadol in the postsurgical setting. To our knowledge, the published studies on analgesic effects from tapentadol are mainly industry funded studies on orthopaedic and dental patients, and few are related to procedures with major components of visceral pain, such as laparoscopy. A review of tapentadol studies in the postoperative setting indicated less nausea, vomiting, constipation and pruritus compared with oxycodone, but no difference in somnolence, headache or dizziness. Studies on respiratory depression from tapentadol in any setting are sparse.
Oxycodone is a well-known opioid for postoperative pain treatment in all surgical settings. It is known to have several side effects such as nausea, vomiting, sedation, constipation and respiratory sedation.

Actual start date of recruitment	01 December 2017
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: 86
Worldwide total number of subjects	86
EEA total number of subjects	86

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)	86
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Women assigned for elective hysterectomy for benigne reasons at Oslo University Hospital, Norway between December 2017 and February 2019.

Pre-assignment

Screening details:

Patients w/weight <55 kg, >85 kg or BMI >31 were excluded. Exclusion criteria: chronic pain syndromes, severe heart, lung, liver or kidney failure, severe psychiatric disorders, malignancy previous five yr, chronic medication opioids, steroids, benzodiazepines, gabapentanoids, tramadol, clonidine or serotonin-noradrenaline or allergies to study med

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, Assessor

Blinding implementation details:

Study medication was distributed in opaque, identical looking dosing boxes prepacked by a physician not participating in the treatment or evaluation of the patients. A dummy dosing box was demonstrated to the patients at the time of inclusion in order to prepare them for self-administration of rescue medicine. The researchers involved in inclusion, treatment and evaluation of the patients were blinded to which study medication the patients received.

Arms

Are arms mutually exclusive?	Yes
Arm title	Tapentadol (group T)

Arm description:

According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.

Arm type	Experimental
Investigational medicinal product name	Tapentadol
Investigational medicinal product code	
Other name	Palexia
Pharmaceutical forms	Tablet
Routes of administration	Enteral use

Dosage and administration details:

According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received extended release (ER) tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. Immediate release (IR) tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.

Arm title	Oxycodone (group O)

Arm description:

According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.

Arm type	Active comparator

Investigational medicinal product name	Oxycodone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Enteral use

Dosage and administration details:

According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.

Number of subjects in period 1	Tapentadol (group T)	Oxycodone (group O)
Started	43	43
Completed	37	36
Not completed	6	7
Received analgesics outside protocol	-	3
Change of surgical procedure	1	-
Received epidural	2	1
Change of anesthesia procedure	1	-
Did not receive allocated intervention	1	-
Received opioids outside protocol	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Tapentadol (group T)
Reporting group description:	
According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.	
Reporting group title	Oxycodone (group O)
Reporting group description:	
According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.	

Reporting group values	Tapentadol (group T)	Oxycodone (group O)	Total
Number of subjects	43	43	86
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			
18-64 years			
Units: years			
arithmetic mean	43.1	44.6	
standard deviation	± 5.9	± 7.4	-
Gender categorical Units: Subjects			
Female	43	43	86
Male	0	0	0

End points

End points reporting groups

Reporting group title	Tapentadol (group T)
Reporting group description:	
According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.	
Reporting group title	Oxycodone (group O)
Reporting group description:	
According to a computer-generated code, using block randomisation by blocks of ten, patients were allocated to receive either tapentadol (group T) or oxycodone (group O) during the study period. Group T received ER tapentadol 50 mg p.o. and group O received ER oxycodone 10 mg p.o. as part of premedication. After 12 h all patients received an additional dose of ER study medication. IR tapentadol 50 mg or oxycodone 10 mg were available as rescue medication.	

Primary: Pain at rest 1 h postoperatively

End point title	Pain at rest 1 h postoperatively
End point description:	
The primary outcome, pain at rest 1 h postoperatively, was evaluated with the NRS	
End point type	Primary
End point timeframe:	
The primary outcome, pain at rest 1 h postoperatively, was evaluated with the NRS	

End point values	Tapentadol (group T)	Oxycodone (group O)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	36		
Units: pain score				
arithmetic mean (confidence interval 95%)	4.4 (3.8 to 5.0)	4.6 (3.8 to 5.3)		

Statistical analyses

Statistical analysis title	T- test on pain at rest 1 h postoperatively
Comparison groups	Tapentadol (group T) v Oxycodone (group O)
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05
Method	t-test, 2-sided

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 0-72 h postoperatively	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

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: No relevant non serious adverse events were reported during the study

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