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Parecoxib-midazolam compared with fentanyl-midazolam as pain relief during transvaginal ultrasound controlled egg retrieval

Submission date
30/05/2022

Recruitment status
No longer recruiting

Registration date
06/06/2022

Overall study status
Completed

Last Edited
06/06/2022

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
In vitro fertilization (IVF) accounts for 1.6% and 4.5% of all live births in the United States and Europe, respectively. IVF is a four-stage procedure involving ovarian stimulation protocols to induce the development of multiple follicles, oocyte (egg) retrieval, fertilization, and finally embryo transfer. Ultrasound-guided transvaginal follicle aspiration has become the gold standard technique for oocyte retrieval, and it may be the most painful stage of IVF.
Pain relief options for the retrieval procedure include conscious sedation which uses a combination of drugs to produce a state of relaxation and pain relief. The addition of a paracervical block further reduces the pain level during retrieval under conscious sedation. In their recommendations for good practice in ultrasound ovum pick up, the European Society of Human Reproduction and Embryology (ESHRE) suggests fentanyl-midazolam for normal conscious sedation without an anaesthetist and notes that the addition of para-cervical local anaesthetic infiltration appears to be better than sedation alone, but a meta-analysis did not support one method or technique over another in providing effective conscious sedation and analgesia for pain relief during and after oocyte recovery.
Midazolam is the benzodiazepine of choice in endoscopic procedures owing to its faster onset of action and shorter duration of action than diazepam. Fentanyl is preferred to pethidine because the former is associated with more rapid onset and clearance, with less nausea. When giving fentanyl-midazolam as conscious sedation, fentanyl must be given first as the synergy increases the potency of midazolam. However, combining midazolam with opioids increases the risk of hypoxemia (low blood oxygen) and apnoea (breathing difficulties), so avoiding this combination in conscious sedation for medical procedures is of value. Parecoxib sodium is an alternative treatment for the prevention of moderate to severe postoperative pain. Its onset of action is rapid, from 7 minutes. The aim of this study is to find out whether parecoxib-midazolam is as effective as fentanyl-midazolam in providing sedation and pain relief for ovum pick up.

Who can participate?
Women aged 18 to 45 years old who undergoing oocyte retrieval as an IVF procedure

What does the study involve?
Participants are randomly allocated to be treated with either fentanyl-midazolam or parecoxib-midazolam as conscious sedation and pain relief before ultrasound controlled transvaginal ovum pick up. In addition, lignocaine will be given to all participants.

What are the possible benefits and risks of participating?
The conventional fentanyl-midazolam provides effective conscious sedation for ultrasound controlled transvaginal ovum pick up but the drug combination increases the side effects of respiratory depression and hypoxaemia. The alternative of parecoxib-midazolam is plausibly safer with regard to respiratory depression and hypoxaemia and may also be as effective as conscious sedation but the data is preliminary and limited.

Where is the study run from?
University Malaya Medical Center (Malaysia)

When is the study starting and how long is it expected to run for?
December 2021 to June 2023

Who is funding the study?
University Malaya Medical Center (Malaysia)

Who is the main contact?
1. Dr Nurul Ain binti Roslan, nurulain.r@ummc.edu.my
2. Prof. PC Tan, tanpengchiong@yahoo.com
3. Assoc. Prof. Nuguelis binti Razali, nuguelis@ummc.edu.my

Study website
Not applicable

Contact information

Type(s)
Principal Investigator

Contact name
Dr Nurul Ain Roslan

Contact details
University of Malaya Medical Centre
Jalan Professor Ungku Aziz
Petaling jaya
Kuala Lumpur
Malaysia
59100
+60 (0)3 7949 3209/2251
nurulain.r@ummc.edu.my

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
MECID number 20211216-10841

Study information

Scientific Title
Parecoxib-midazolam compared with fentanyl-midazolam as conscious sedation during transvaginal ultrasound controlled oocyte retrieval: a double-blind randomized trial

Study objectives
Parecoxib-midazolam is non inferior to fentanyl-midazolam as conscious sedation in transvaginal oocyte retrieval during in vitro fertilisation treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/5/2022, Medical Research Ethics Committee of University Malaya Medical Centre (Level 2, Kompleks Pendidikan Sains Kejururawatan, University of Malaya Medical Centre Jalan Professor Ungku Aziz
59100 Kuala Lumpur, Malaysia; +60 (0)3 7949 3209/2251; ummc-mrec@ummc.edu.my), ref: 20211216-10841

Study design
Interventional single-center double-blinded randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See trial outputs table

Health condition(s) or problem(s) studied
Women undergoing ultrasound controlled transvaginal oocyte retrieval for in vitro fertilisation

Interventions
1. Intravenous parecoxib 40 mg followed by IV midazolam 5 mg bolus 15 minutes before the procedure
2. Intravenous fentanyl 50 mcg followed by IV midazolam 5mg bolus 15 min prior to the procedure

All participants will receive paracervical lignocaine (10 ml of 1% lignocaine) infiltration prior to commencement of the ovum pick up.
The trial medications will be freshly-prepared in a private area by an investigator not involved in recruitment, periprocedural care and data collection. The trial medications will be placed in identical syringes as equal volumes of colourless fluids and the syringes will be labelled for sequential intravenous administration. Syringes prepared are placed in a sealed numbered envelope by the investigator for random allocation. The investigator will dispose of identifiable wastes securely to sustain blinding. Randomisation is by opening of a sealed numbered opaque envelope with assignment of the lowest numbered envelope remaining to the latest recruit in strict sequential order.

The medications will be administered in sequence by a medical officer who is blinded. The blinded provider performing the ovum pick up will rate the adequacy of the conscious sedation and request rescue analgesia as needed. Trial outcomes will be collected by a blinded assessor.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Midazolam, fentanyl, parecoxib

Primary outcome measure
Successful sedation assessed using the Procedural Sedation Assessment Survey (PROSAS) at 30 minutes after awakening in the recovery area. “In accordance with patients’ priorities, procedural sedation was judged as successful when there was no adverse event, no issues with sedation leading to an incomplete procedure, when patient-reported procedural discomfort was scored 2 or less, and the patient was comfortable with the level of sedation obtained with a sedation preference score of between -2 and 2”

Secondary outcome measures
1. Pain measured using the numerical rating scale 0-10 at awakening, 15, 30, 45, 60 minutes and just before discharge
2. Nausea measured by asking Yes or No at awakening, 15, 30, 45, 60 minutes and just before discharge
3. Vomiting measured by asking Yes or No at awakening, 15, 30, 45, 60 minutes and just before discharge
4. Surgeon satisfaction with the sedation-pain relief during ovum pick up measured using the numerical rating scale after completing the oocyte retrieval procedure
5. Hypotension/hypertension (systolic blood pressure [SBP] <90 or >160 mmHg) measured using automated blood pressure during procedures and upon awakening, 15, 30, 45, 60 minutes and just before discharge
6. Tachycardia/bradycardia (heart rate > 120/min or < 50/min) measured using automated pulse

oximetry during procedures and upon awakening, 15, 30, 45, 60 minutes and just before discharge
7. Oxygen desaturation (any episode of desaturation <90% on pulse oximetry) measured using automated pulse oximetry during procedures and upon awakening, 15, 30, 45, 60 minutes and just before discharge
8. Number of oocytes retrieved and charted using the standardised form provided in the Fertility Unit during the procedure, and the result will be obtained on completion of embryologist report

Overall study start date
16/12/2021

Completion date
30/06/2023

Eligibility

Key inclusion criteria
1. Women undergoing ovum pick up aged 18 to 45 years old
2. Suitable for conscious sedation

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Female

Target number of participants
134

Key exclusion criteria
1. Previous history of hypersensitivity or contraindication to midazolam/fentanyl/parecoxib
2. Women not suitable for conscious sedation OPU e.g., medical comorbidity such as hypertension on treatment, inflammatory bowel disease, ischemic heart disease and heart failure on anticoagulants, history of bronchospasm, history of cerebrovascular disease and upper GI perforation, severe hepatic impairment
3. Extreme anxiety
4. Anticipated complicated ovum pick up: extensive endometriosis, pelvic adhesions, difficult to access ovaries
5. Prior issues with conscious sedation

Date of first enrolment

20/06/2022

Date of final enrolment
30/06/2023

Locations

Countries of recruitment
Malaysia

Study participating centre
University Malaya Medical Centre
Jalan Prof. DiRaja Ungku Aziz
Kuala Lumpur
Malaysia
59100

Sponsor information

Organisation
University Malaya Medical Centre

Sponsor details
Department of Obstetrics and Gynaecology
Jalan Professor Ungku Aziz
Petaling Jaya
Malaysia
59100
+60 (0)3 79494422
ummc@ummc.edu.my

Sponsor type
Hospital/treatment centre

Website
https://www.ummc.edu.my

ROR
https://ror.org/00vkrxq08

Funder(s)

Funder type

Hospital/treatment centre

Funder Name
University Malaya Medical Center

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/12/2023

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1	18/02/2022	01/06/2022	No	Yes
Protocol file	version 2		01/06/2022	No	No