

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	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 06/06/2022	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 06/06/2022	Condition category Pregnancy and Childbirth	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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?

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Contact information

Type(s)

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number

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

Study type(s)

Treatment

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(s)

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"

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Upper age limit

45 years

Sex

Female

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

ROR

<https://ror.org/00vkrxq08>

Funder(s)

Funder type

Hospital/treatment centre

Funder Name

University Malaya Medical Center

Results and Publications

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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2		01/06/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes