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Does the sedative drug ketamine play a role in pain relief following wisdom teeth extractions?

Submission date
20/04/2017

Recruitment status
No longer recruiting

Registration date
24/04/2017

Overall study status
Completed

Last Edited
12/09/2017

Condition category
Oral Health

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

Plain English summary of protocol

Background and study aims
Surgery to remove the wisdom teeth is a routine dental surgery but it is still an invasive procedure that often involves cutting of gum tissue and removal of surrounding bone in order to safely retrieve the tooth. Although the use of numbing injections (local anaesthesia) can provide temporary pain relief, the hole left once the tooth is removed can be very uncomfortable once this wears off. Ketamine is a medication used for starting and maintaining anesthesia. Many studies have shown that the drug ketamine when used in small amounts have shown benefits of extended pain relief in patients undergoing larger surgeries such as heart surgery, hip/knee replacement surgery, and spinal surgery. The aim of this study is to find out whether combining ketamine with other sedation medications, can provide patients with extended pain relief once following wisdom teeth surgery.

Who can participate?
Participants aged 16 to 25 years old who have at least three wisdom teeth and are otherwise generally healthy.

What does the study involve?
Participants are randomly allocated to one of two groups. All participants are injected with numbing medications in order to provide pain relief in the mouth during surgery. Those in the first group also receive ketamine through a drip. Those in the second group receive a dummy drug (placebo) in the form of a salt water solution (saline) through a drip. Wisdom teeth removal surgery is then performed according to standard practice for all participants. During recovery and then every six hours for the first 28 hours after surgery, participants are asked to fill in a questionnaire rating their level of pain and use of pain killers.

What are the possible benefits and risks of participating?
Participants who receive the ketamine may benefit from less pain during and after surgery. In addition, this could mean that they do not need to take as many pain killers after their surgery, minimising the side effects caused by these medications. There is a small risk that low doses of ketamine can cause pre-existing mental health issues to temporarily worsen.

Where is the study run from?
Victoria General Hospital, Oral and Maxillofacial Surgery Clinic (Canada)

When is study starting and how long is it expected to run for?
June 2017 to June 2020

How long will the trial be recruiting participants for?
1. Canadian Association of Oral and Maxillofacial Surgeons (Canada)
2. Dalhousie University Dental School (Canada)

Who is the main contact?
Dr Johnson Cheung
johnson.cheung01@dal.ca

Contact information

Type(s)
Public

Contact name
Dr Johnson Cheung

ORCID ID
http://orcid.org/0000-0003-0430-8742

Contact details
Victoria General Hospital
1276 South Park Street
Halifax
Canada
B3H 2Y9

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1022300

Study information

Scientific Title
The role of ketamine in post-operative analgesia following third molar surgery

Study objectives

Does the use of ketamine during intravenous procedural sedation anaesthesia provide patients with extended pain relief following wisdom teeth surgery?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Nova Scotia Health Authority Research Ethics Board, 10/04/2017, ref: 1022300

Study design
Single-centre double-blinded randomized placebo-controlled clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Wisdom teeth extractions

Interventions
Each patient would spend approximately 2 hours at the Oral and Maxillofacial surgery outpatient clinic at the Victoria General Hospital from pre-operative assessment, undergoing surgery, and to discharge from the recovery room. Note that patients are expected to fast (nothing by mouth) for 8 hours prior to arriving for surgery.

After registration of the participant's information by the clinic receptionist (uninvolved in the study), the participant will visit the pre-operative assessment nurse (also not related to the study). A standard pre-operative history and physical would be performed and pre-operative vitals would also be obtained at this time. This will include blood pressure, heart rate, oxygen saturation at room air, respiratory rate, and BMI. This process would take approximately 20-30 minutes. The pre-operative assessment nurse will verify the participant's confirmation in the study but will not know if the patient will receive placebo or treatment of ketamine in the study.

Pre-operatively, the surgeon will randomly assign the patient to receive either ketamine or placebo by a simple coin toss (i.e. heads = ketamine, tails = placebo). For all participants, the medications used to induce PSA for the procedure will be midazolam and fentanyl. These medications will be given at standardized dosages as described below:
Midazolam: Medication (in the form of a 1 mg/mL solution) to be administered via IV at 0.1 mg /kg per dose every 2 minutes to a maximum of 10 mg per surgery. The dosing increment will be

titrated to achieve appropriate PSA effect.
Fentanyl: Medication (in the form of a 100 mcg/ml solution) to be administered via IV at a rate of 0.5-2 mcg/kg, and will increase in small increments at 2 minute intervals to a maximum of 100 mcg per surgery. The dosing increment will be titrated to achieve appropriate PSA effect.

Placebo: Participants are administered 0.9% saline
Ketamine: Participants are administered ketamine at a standardized sub-anaesthetic dosage of 0.1-0.5 mg/kg or placebo (0.9% saline) via IV access following midazolam and fentanyl, and prior to the administration by injection of local anaesthetic (at 5 ml of 2% lidocaine with 1:100000 epinephrine, per wisdom tooth).

Vital signs would be recorded at five minute intervals during the sedation. Routine third molar surgery is then performed, and the total surgical time will be recorded. Surgery time includes time of initial incision to placement of final suture if applicable. At the end of the surgery, the surgeons will fill out their post-surgical survey documenting difficulty of surgery and overall satisfaction of the case.

Patients will rest in the post-operative recovery area for approximately 30 minutes during which they will be routinely assessed for meeting appropriate discharge criteria. The patient will be under the care of a recovery room nurse at this time and he/she will be aware if the patient was in the treatment or control arm of the study since they will review the medication records. However, this nurse is not part of the study. The patient would be discharged home with a medication package containing ibuprofen 600 mg to be taken every 6 hours for pain, Tylenol #3 to be taken every 4-6 hours for breakthrough pain relief, and 0.12% chlorhexidine anti-septic oral rinse to be used 12 hours apart for two weeks after surgery.

Patients complete a post-operative pain survey (in the form of visual analogue scales) in the post-operative recovery area, and the patient is to complete this questionnaire at home at exactly 6-hour post-operative intervals up to 48 hours. These time intervals will be indicated on their questionnaire. Instructions for this questionnaire would be provided by the investigators of this study. Briefly, the visual analogue scale (of 0-10, with 0 being no pain and 10 being worst pain) is user friendly for the patient and a convenient format to answer. The patient is to also document in the survey if they took pain medication such as Tylenol, Ibuprofen, or Tylenol #3 as well as the amount/dosage taken. Patients are asked to mail back the survey using a self-addressed envelope provided with the survey. Phone calls to the participants will be made at 24 hours post-op to the patient to check on their post-operative status, and to remind them of completing and mailing the survey. The pre-operative or recovery room nurses will make these phone calls should the 24-hour post-operative period fall on a weekday. Otherwise, an investigator for this study will conduct these phone calls on the weekend and also repeat the reminder call at the 48-hour mark.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ketamine

Primary outcome measure

Degree of post-operative pain experienced is assessed by use of a take-home questionnaire containing multiple scales to describe the intensity of post-operative pain experienced (from 0-10, with 0 being no pain and 10 being most intense pain) at 6 hour intervals for up to 48 hours following wisdom teeth surgery

Secondary outcome measures
Use of pain medication (including type and dosage) is assessed by use of a take-home questionnaire at 6 hour intervals for up to 48 hours following wisdom teeth surgery

Overall study start date
07/01/2016

Completion date
12/01/2020

Eligibility

Key inclusion criteria
1. Male and female
2. Aged 16 to 25 years old
3. Health status is ASA I or ASA II
4. Presence of at least 3 wisdom teeth
5. Wisdom teeth present are associated with disease such as cavities or periodontal condition or
6. Wisdom teeth are impacted and will not predictably erupt functionally into the dentition

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
128

Key exclusion criteria
1. Patients younger than 16 and older than 25 years old
2. Patients with obvious pathology including cysts or tumors associated with wisdom tooth
3. Patients that are ASA class III or higher
4. Pregnant or lactating patients
5. Patients with fewer than 3 wisdom teeth for removal

Date of first enrolment
06/01/2017

Date of final enrolment
06/01/2020

Locations

Countries of recruitment
Canada

Study participating centre
Victoria General Hospital
Centennial Building
Oral and Maxillofacial Surgery Clinic
1276 South Park Street
Halifax
Canada
B3H 2Y9

Sponsor information

Organisation
Nova Scotia Health Authority Research Ethics Board

Sponsor details
Centre for Clinical Research Building
118-5790 University Avenue
Halifax
Canada
B3H 1V7

Sponsor type
Research council

ROR
https://ror.org/035gna214

Funder(s)

Funder type
Other

Funder Name
Canadian Association of Oral and Maxillofacial Surgeons

Funder Name
Dr. John Laba Memorial Research Fund 2016

Results and Publications

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

Intention to publish date
12/01/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Dr Johnson Cheung (johnson.cheung@dal.ca).

Added 12/09/2017:
Type of data - Postoperative pain VAS scores and analgesic/drug consumption dosages
When data will be available - End of trial in approximately 2 years time and available for 1 year
Access criteria - To be determined once data collection is complete at the end of the trial
Who to share data with - Other researchers in the same field studying the post-operative analgesic effects of ketamine
Type of analysis or mechanism - Yet to be determined with statisticians
Consent from patients are obtained for data sharing/publications and all data are anonymous as all identifiers from patients are removed during data analysis

IPD sharing plan summary
Available on request