ISRCTN12454921 https://doi.org/10.1186/ISRCTN12454921

Effect on ventilatory pattern with an opioid under fake postsurgical conditions in men and women

Submission date
16/01/2024

Recruitment status
No longer recruiting

Registration date
21/05/2024

Overall study status
Completed

Last Edited
21/05/2024

Condition category
Other

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

Plain English summary of protocol

Background and study aims
While it is well known that an opioid overdose produces immediate respiratory depression, the effect of surgical doses of opioids on the postoperative ventilatory pattern. One large study, the PRODIGY study, claimed that about half of all postoperative patients on opioids for pain relief will experience at least one apnea event (no breathing for at least 30 s). However, we remain uninformed whether this is truly opioid related as ventilatory pattern under control conditions was not tested and there may be effects from other drugs as well. Here we will mimic surgical administration of the opioid fentanyl and will measure the ventilatory pattern during and following sham surgery.

The objective is to explore the ventilatory pattern of volunteers during and following administration of fentanyl, mimicking the perioperative dosing of fentanyl

Who can participate?
12 healthy volunteers (6 men/6 women), aged 18-45 years, with a body mass index of 19-30 kg /m².

What does the study involve?
We're going to simulate the administration of fentanyl during a fake surgery that lasts 150 minutes. We'll be giving doses of fentanyl every 30 minutes and monitoring how much air a person breathes in and out for each breath, starting from when we give the first dose until 90 minutes after the fake surgery ends. Only fentanyl will be used, with no other drugs.

Here's the breakdown of the fentanyl doses:
1. At the beginning of the simulation, we'll give 100 micrograms of fentanyl through an IV.
2. Then, at 30 and 60 minutes into the fake surgery, we'll administer 75 micrograms of fentanyl each time.
3. At 90 and 120 minutes into the fake surgery, we'll give a reduced dose of 50 micrograms of fentanyl.

This method allows us to observe how the increasing amounts of fentanyl affect the way the person breathes. The doses gradually increase from 150 to 250 micrograms at 60 minutes and then to 350 micrograms at 120 minutes into the fake surgery.

After that, we'll continue monitoring the person's breathing until 90 minutes after the fake surgery concludes. The entire process, including the surgery simulation and the follow-up, will take 240 minutes (4 hours). It's important to note that all the mentioned doses are calculated based on a total body weight of 70 kilograms.

What are the possible benefits and risks of participating?
These volunteers in this experimental trial will not gain any medical benefit from the study. The benefit lies within the gained knowledge in our ability to understand and consequently treat, reverse and prevent opioid-induced respiratory depression in perioperative patients.
The burden of the study is related to the measurements and interventions. However, the burden and risk are contained in the highly controlled setting. The investigators have ample experience, most are anesthesiologists, and have performed multiple similar protocols without any inflicted harm or long-term effects to the participants. The subjects will receive an appropriate yet modest reimbursement for their participation.

Where is the study run from?
Leiden University Medical Center (Netherlands)

When is the study starting and how long is it expected to run for?
October 2023 to January 2025

Who is funding the study?
Leiden University Medical Center (Netherlands)

Who is the main contact?
Prof. Albert Dahan, a.dahan@lumc.nl

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Prof Albert Dahan

ORCID ID
http://orcid.org/0000-0003-3161-3945

Contact details
Albinusdreef 2
Leiden
Netherlands
2333 ZA
-
a.dahan@lumc.nl

Additional identifiers

EudraCT/CTIS number
2023-508915-22-00

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
P23.097

Study information

Scientific Title
Fentanyl effect on ventilatory pattern under sham postsurgical conditions – an exploratory study in healthy men and women

Acronym
FAME

Study objectives
While it is well known that an opioid overdose produces immediate respiratory depression, the effect of surgical doses of opioids on the postoperative ventilatory pattern. One large study, the PRODIGY study, claimed that about half of all postoperative patients on opioids for pain relief will experience at least one apnea event (no breathing for at least 30 s). However, we remain uninformed whether this is truly opioid related as ventilatory pattern under control conditions was not tested and there may be effects from other drugs as well. Here we will mimic surgical administration of the opioid fentanyl and will measure the ventilatory pattern during and following sham surgery.

The objective is to explore the ventilatory pattern of volunteers during and following administration of fentanyl, mimicking the perioperative dosing of fentanyl.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 15/01/2024, METC-LDD (Albinusdreef 2, Leiden, 2333ZA, Netherlands; +31 0071-5263241; metc-ldd@lumc.nl), ref: P23.097

Study design
Open-label exploratory observational design

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Safety

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Fentanyl effect on ventilatory pattern under sham postsurgical conditions

Interventions
We will mimic fentanyl dosing for a 150 min sham surgical procedure. We will dose fentanyl at 30 min interval and measure minute ventilation on a breath-to-breath basis from the start of administration until 90 min after sham surgery. We will administer just fentanyl without any other drugs. Upon induction we will give 100 µg fentanyl intravenously, followed by 75 µg at t = 30 and 60 min of surgery and 50 µg at 90 and 120 min of surgery. This approach allows the detecting of escalating doses of fentanyl on the ventilatory pattern. The dose increases from 150 to 250 µg at t = 60 min to 350 at t = 120 min of surgery. We will next continue measuring ventilation until t = 90 min after surgery. Total duration is 150 min of surgery + 90 min follow-up = 240 min (4 h) of breath-to-breath data. All doses are per 70 kg total body weight.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic

Phase
Phase III/IV

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

Primary outcome measure
Arterial PCO2 in the recovery phase (last 90 min of the study) measured using arterial blood gas at specific time points in the recovery phase

Secondary outcome measures
The occurrence of a respiratory event as defined by:
1. Respiratory rate ≤5 breaths/min for ≥ 3 min;
2. Oxygen saturation ≤ 85% for ≥ 3 min;
3. End-tidal PCO2 ≤ 2 kPa or ≥ 8 kPa for ≥ 3 min;
4. Apnea for at least 30 s;
5. Any other respiratory event;
all measured using a continuous flowsensor, gas analyzer, and custom made software to identify the respiratory rate

6. The comparison of arterial vs venous vs end-tidal PCO2 measured using the custom made software, gas analyzer and flowsensor in combination with the arterial blood gas with the blood gas analyzer

Overall study start date
01/10/2023

Completion date
01/01/2025

Eligibility

Key inclusion criteria
1. Aged 18-45 years
2. Body mass index 19-30 kg/m²

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
45 Years

Sex
Both

Target number of participants
12

Key exclusion criteria
1. Currently meet the criteria for diagnosis of moderate or severe substance use disorder according to the DSM-5 criteria on any substances other than caffeine, or nicotine-
2. Any active medical condition, organ disease or concurrent medication or treatment that may either compromise subject safety or interfere with study endpoints;
3. Pregnancy or lactation;
4. A positive drug urine dipstick on the screening or study days.
5. History or presence of allergic response to study medication;

Date of first enrolment
01/02/2024

Date of final enrolment
01/01/2025

Locations

Countries of recruitment
Netherlands

Study participating centre
Leiden University Medical Center
Albinusdreef 2
Leiden
Netherlands
2333ZA

Sponsor information

Organisation
Leiden University Medical Center

Sponsor details
Albinusdreef 2
Leiden
Netherlands
2333ZA
-
a.dahan@lumc.nl

Sponsor type
Hospital/treatment centre

Website
https://www.lumc.nl/?setlanguage=English&setcountry=en

ROR
https://ror.org/05xvt9f17

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Leids Universitair Medisch Centrum

Alternative Name(s)

Leiden University Medical Center, LUMC

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Netherlands

Results and Publications

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

Intention to publish date
01/01/2025

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

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